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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2021
or

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

Commission file number 000-29889

RIGEL PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	**94-3248524** (IRS Employer Identification No.)
1180 Veterans Blvd. South San Francisco, California (Address of principal executive offices)	**94080** (Zip Code)

(650) 624-1100
(Registrant's telephone number, including area code)

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

Title of each class:	**Trading Symbol(s)**	**Name of each exchange on which registered:**
Common Stock, par value $.001 per share	RIGL	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 (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

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

The approximate aggregate market value of the Common Stock held by non-affiliates of the registrant, based upon the closing price of the registrant's common stock as reported on the Nasdaq Global Select on June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, was $740.0 million. Shares of the registrant's outstanding common stock held by each executive officer, director and affiliates of the registrant's outstanding common stock have been excluded. The determination of affiliate status for the purposes of this calculation is not necessarily a conclusive determination for other purposes.

As of February 24, 2022, there were 171,683,545 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K incorporate information by reference from the definitive proxy statement for the registrant's 2022 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains statements indicating expectations about future performance and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), and the Private Securities Litigation Reform Act of 1995, that involve risks and uncertainties. We usually use words such as "may," "will," "should," "could," "expect," "plan," "anticipate," "might," "believe," "estimate," "predict," "intend" or the negative of these terms or similar expressions to identify these forward- looking statements. These statements appear throughout this Annual Report on Form 10-K and are statements regarding our current expectations, beliefs or intent, primarily with respect to our operations and related industry developments. Examples of these statements include, but are not limited to, statements regarding the following: our expectations regarding the impact of the global COVID-19 pandemic; our business and scientific strategies; risks and uncertainties associated with the commercialization and marketing of TAVALISSE in the United Stated (US) and in Europe; risks that the US Food and Drug Administration (FDA), European Medicines Agency (EMA) or other regulatory authorities may make adverse decisions regarding fostamatinib; the progress of our and our collaborators' product development programs, including clinical testing, and the timing of results thereof; our corporate collaborations and revenues that may be received from our collaborations and the timing of those potential payments; our expectations with respect to regulatory submissions and approvals; our drug discovery technologies; our research and development expenses; protection of our intellectual property; sufficiency of our cash and capital resources and the need for additional capital; and our operations and legal risks. You should not place undue reliance on these forward-looking statements. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including as a result of the risks and uncertainties discussed in "Part I, Item 1A, Risk Factors" of this Annual Report on Form 10-K. Any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events, except as required by applicable law. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

RISK FACTOR SUMMARY

Investing in our securities involves a high degree of risk. Below is a summary of the material factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, as well as other risks that we face, can be found below under the heading "Part 1, Item 1A, Risk Factors" and should be carefully considered, together with other information in this Form 10-K and our other filings with the SEC, before making an investment decision regarding our common stock.

- Our prospects are highly dependent on our first commercial product, TAVALISSE (fostamatinib disodium hexahydrate). To the extent that the commercial success of TAVALISSE or fostamatinib in the US and respective territories outside of the US is diminished or is not commercially successful, our business, financial condition and results of operations may be adversely affected, and the price of our common stock may decline.

- Our business is currently adversely affected and could be materially and adversely affected in the future by the evolving effects of the COVID-19 pandemic as a result of the current and potential future impacts on our commercialization efforts, supply chain, regulatory, clinical development and corporate development activities and other business operations, in addition to the impact of a global economic slowdown.

- We may not be able to obtain Emergency Use Authorization (EUA) for fostamatinib for the treatment of hospitalized patients with COVID-19, and, even if we do, absent supplemental New Drug Application (NDA) approval for that indication, such EUA would be revoked when the COVID-19 emergency terminates.

- We might not be able to successfully develop or commercialize our product candidates if problems arise in the clinical testing and approval process. There is a high risk that drug discovery and development efforts might not generate successful product candidates.
- Even if we, or any of our collaborative partners, are able to continue to commercialize TAVALISSE or any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or labeling restrictions, all of which may vary from country to country and any of which could harm our business.
- If we are unable to successfully market and distribute TAVALISSE and retain experienced sales force, our business will be substantially harmed.
- We are subject to stringent and evolving privacy and information security laws, regulations, rules, policies and contractual obligations, and changes in such laws, regulations, rules, policies, contractual obligations and our actual or perceived failure to comply with such requirements could subject us to significant investigations, fines, penalties, and claims, any of which may have a material adverse effect on our business, financial condition, results of operations or prospects.
- If manufacturers obtain approval for generic versions of TAVALISSE, or of products with which we compete, our business may be harmed.
- Unforeseen safety issues could emerge with TAVALISSE that could require us to change the prescribing information to add warnings, limit use of the product, and/or result in litigation. Any of these events could have a negative impact on our business.
- We rely and may continue to rely on two distribution facilities for the sale of TAVALISSE and potential sale of any of our product candidates.
- We lack the capability to manufacture compounds for clinical development and we intend to rely on third parties for commercial supply, manufacturing and distribution if any of our product candidates which receive regulatory approval and we may be unable to obtain required material or product in a timely manner, at an acceptable cost or at a quality level required to receive regulatory approval.
- Any product for which we have obtained regulatory approval, or for which we obtain approval in the future, is subject to, or will be subject to, extensive ongoing regulatory requirements by the FDA, EMA and other comparable regulatory authorities, and if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, we may be subject to penalties, we will be unable to generate revenue from the sale of such products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.
- If our corporate collaborations or license agreements are unsuccessful, or if we fail to form new corporate collaborations or license agreements, our research and development efforts could be delayed.
- Our success is dependent on intellectual property rights held by us and third parties, and our interest in such rights is complex and uncertain.
- If a dispute arises regarding the infringement or misappropriation of the proprietary rights of others, such dispute could be costly and result in delays in our research and development activities and partnering.
- If our competitors develop technologies that are more effective than ours, our commercial opportunity will be reduced or eliminated.
- If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

PART I

Item 1. Business

Overview

We are a biotechnology company dedicated to discovering, developing and providing novel small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer and rare immune diseases. Our pioneering research focuses on signaling pathways that are critical to disease mechanisms. Our first product approved by the FDA is TAVALISSE® (fostamatinib disodium hexahydrate) tablets, the only approved oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. The product is also commercially available in Europe, the United Kingdom (UK) (TAVLESSE) and Canada (TAVALISSE) for the treatment of chronic ITP in adult patients.

Fostamatinib is currently being studied in a Phase 3 trial for the treatment of warm autoimmune hemolytic anemia (wAIHA); a Phase 3 clinical trial for the treatment of hospitalized high-risk patients with COVID-19; a National Institute of Health (NIH)/National Heart, Lung, and Blood Institute (NHLBI) sponsored Phase 3 trial (ACTIV-4 Host Tissue Trial) for the treatment of COVID-19 in hospitalized patients; and a Phase 2 trial for the treatment of COVID-19 being conducted by Imperial College London.

Our other clinical programs include our interleukin receptor-associated kinase (IRAK) inhibitor program and a receptor-interacting serine/threonine-protein kinase (RIPK1) inhibitor program in clinical development with partner Eli Lilly and Company (Lilly). In addition, we have product candidates in clinical development with partners BerGenBio ASA (BerGenBio) and Daiichi Sankyo (Daiichi).

Business Update

TAVALISSE in ITP

In 2021, our net product sales of TAVALISSE were $63.0 million, a 2% increase compared to 2020. The increase in our net product sales was primarily driven by the increase in quantities sold as well as the increase in price per bottle of TAVALISSE. The increase in our net product sales resulting from the increase in quantities sold and price per bottle were partially offset by the increase in revenue reserves mainly due to higher government program rebates.

Due to the evolving effects of the COVID-19 pandemic, we continue to deploy resources to enable our field-based employees to continue to engage virtually with health care providers. These virtual engagements have enabled our field team to support existing prescribers, as well as develop new prescribers to identify appropriate patients for TAVALISSE. We also conducted market research with chronic ITP prescribers in 2020 to understand the impact of COVID on chronic ITP management. More than half of respondents reported that COVID had an impact on their management of chronic ITP, and about a third of respondents anticipate a surge of patients post-COVID. This is because clinicians have found it challenging to both start a therapy, and switch to new therapies. Starting in 2021, we began to see an increase in in-person engagements with health care providers, while also maintaining our level of virtual engagements. In the third quarter of 2021, we expanded our sales force by increasing our territories. In the fourth quarter of 2021, we saw an increasing trend of in-person engagements until the Omicron variant surge in December 2021 which again limited our access.

A post-hoc analysis from our Phase 3 clinical program in adult patients with chronic ITP, highlighting the potential benefit of using TAVALISSE in earlier lines of therapy, was published in the British Journal of Haematology in July 2020. Inclusion in one of the leading peer-reviewed journals in the field of hematology underscores the significance of the 78% (25/32) response rate defined as at least one platelet count of at least 50,000/μL when TAVALISSE was used as a second-line therapy in our Phase 3 clinical program. Adverse events were manageable and consistent with those previously reported with fostamatinib. Our sales force is sharing this data with physicians.

Fostamatinib in wAIHA

We are on track to report topline data from our FORWARD study, Phase 3 pivotal trial of fostamatinib on oral SYK inhibitor in patients with wAIHA, which we initiated in March 2019. In November 2021, we completed the enrollment of our FORWARD study. We expect to report topline data from the 24-week study in mid-2022 and proceed with regulatory filings if the data is positive. If approved, fostamatinib has the potential to be the first-to-market therapy for patients with wAIHA in 2023.

Fostamatinib in Hospitalized COVID-19 patients

In April 2021, we reported positive topline results from a multi-center, Phase 2 clinical trial sponsored by the NIH/NHLBI, evaluating the safety of fostamatinib, our oral SYK inhibitor, for the treatment of hospitalized patients with COVID-19. The trial met its primary endpoint of comparable safety than standard of care (SOC) and showed broad and consistent improvement in numerous efficacy endpoints, including mortality, ordinal scale assessment, and number of days in the ICU. In late-May 2021, the trial data were submitted as part of a request for an EUA from the FDA for the fostamatinib as a treatment for hospitalized patients with COVID-19. In August 2021, the FDA informed us that the clinical data submitted from the NIH/NHLBI-sponsored Phase 2 trial of fostamatinib to treat hospitalized patients suffering from COVID-19 are insufficient to support an EUA. In September 2021, the data from the NIH/NHLBI-sponsored Phase 2 trial was published in Clinical Infectious Diseases, an official publication of the Infectious Disease Society of America.

In November 2020, we launched a Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients without respiratory failure that have certain high-risk prognostic factors. We continue to focus on enrolling patients in our Phase 3 clinical trial and anticipate providing further safety and efficacy data from this larger trial of fostamatinib in COVID-19 patients. If this trial meets its endpoints, we plan to resubmit an application for EUA with this additional data.

In June 2021, we announced that fostamatinib has been selected for NIH ACTIV-4 (Accelerating COVID-19 Therapeutic Inventions and Vaccines) trial in hospitalized patients with COVID-19. The ACTIV-4 Host study, initiated and funded by NHLBI, is a randomized, placebo-controlled trial of therapies, including fostamatinib, targeting the host response to COVID-19 in hospitalized patients. The ACTIV-4 Host Tissue study will evaluate fostamatinib in a population targeted to include approximately 300 hospitalized patients with COVID-19.

Global Strategic Partnership with Lilly

In February 2021, we entered into a global exclusive license agreement and strategic collaboration with Lilly (the Lilly Agreement), to develop and commercialize R552, a RIPK1 inhibitor, for the treatment of non-central nervous system (non-CNS) diseases. In addition, the collaboration is aimed at developing additional RIPK1 inhibitors for the treatment of central nervous system (CNS) diseases. Pursuant to the terms of the license agreement, we granted to Lilly the exclusive rights to develop and commercialize R552 and related RIPK1 inhibitors in all indications worldwide. The parties' collaboration is governed through a joint governance committee and appropriate subcommittees. The agreement became effective in March 2021 upon clearance under the Hart-Scott-Rodino (HSR) Antitrust Improvements Act of 1976.

We are responsible for 20% of development costs for R552 in the US, Europe, and Japan, up to a specified cap. Lilly is responsible for funding the remainder of all development activities for R552 and other non-CNS disease development candidates. We have the right to opt-out of co-funding the R552 development activities in the US, Europe and Japan at two different specified times. If we exercise our first opt-out right (no later than September 30, 2023), we are required to fund our share of the R552 development activities in the US, Europe, and Japan up to a maximum funding commitment of $65.0 million through April 1, 2024. We are responsible for performing and funding initial discovery and identification of CNS disease development candidates. Following candidate selection, Lilly will be responsible for performing and funding all future development and commercialization of the CNS disease development candidates.

Under the terms of the Lilly Agreement, we were entitled to receive an upfront cash payment of $125.0 million, which we received in April 2021, with the potential for an additional $330.0 million in milestone payments upon the achievement of specified development and regulatory milestones by non-CNS disease products and $255.0 million in milestone payments upon the achievement of specified development and regulatory milestones by CNS disease products. We are also eligible to receive up to $100.0 million in sales milestone payments on a product-by-product basis for non-CNS disease products and up to $150.0 million in sales milestone payments on a product-by-product basis for CNS disease products. In addition, depending on the extent of our co-funding of R552 development activities, we would be entitled to receive tiered royalty payments on net sales of non-CNS disease products at percentages ranging from the mid-single digits to high-teens, subject to certain standard reductions and offsets. We would be entitled to receive tiered royalty payments on net sales of CNS disease products up to low-double digits, subject to certain standard reductions and offsets.

R552, a potent and selective RIPK1 inhibitor, will advance into Phase 2 development in psoriasis in the first half of 2022. RIPK1 is implicated in a broad range of key inflammatory cellular processes and plays a key role in Tumor Necrosis Factor (TNF) signaling, especially in the induction of pro-inflammatory necroptosis. The program also includes RIPK1 compounds that cross the blood-brain barrier (CNS-penetrants) to address neurodegenerative diseases such as Alzheimer's disease and Amyotrophic Lateral Sclerosis (ALS). We are completing early discovery work on a potential candidate that Lilly may advance into clinical development.

Update on Current and Potential Future Impact of COVID-19 on our Business

We are continuing to monitor the impact of the evolving effects of the COVID-19 pandemic and have undertaken, and plan to continue to undertake, safety measures to keep our staff, patients, investigators and stockholders safe and to help the communities where we live and work to reduce the number of people exposed to the virus. Although we have recently initiated the first phase of our return-to-work initiatives, the majority of our employees continue to work remotely. Through our existing Crisis Management Team (CMT), we implemented and continue to monitor our business continuity plans to prevent or minimize business disruption and ensure the safety and well-being of our personnel. Our CMT meets regularly to assess the effectiveness of our business continuity plans and make adjustments accordingly as COVID-19 continues to evolve. We initiated plans to re-open our South San Francisco, CA headquarters office. We have put together guidelines in this re-opening plan and continue to evaluate the workplace for compliance with this plan and may modify or update at any time to ensure the safety of our employees, contractors and visitors. We endeavor to provide the safest and most effective work environment under the circumstances, but we cannot guarantee that employees who come to the office will not be exposed to COVID-19 while at the office. It will be the responsibility of all employees to participate and cooperate in safety and cleaning protocols. We expect all employees, contractors, and visitors to our facility to comply with this plan. A proof of vaccination is required for all employees, contractors, and visitors to enter the facility. Employees may submit a request for exemption from this policy to the Human Resources due to a qualifying medical or religious reason.

The ultimate impact of the COVID-19 pandemic on our business and financial condition is highly uncertain and subject to change, and as such, we cannot ascertain the full extent of the impacts on our sales of our products, our ability to continue to secure new collaborations and support existing collaboration efforts with our partners and our clinical and regulatory activities. Since the COVID-19 pandemic was declared, we have observed reduced patient-doctor interactions and our representatives are having fewer visits with health care providers, which negatively affected our ability to grow our product sales and may continue to negatively affect our product sales in the future. Resources have been deployed to enable our field team to have virtual engagements to support existing prescribers as well as partner with new prescribers to identify appropriate patients for TAVALISSE. Other commercial related activities, such as our marketing programs, speaker bureaus, and market access initiatives that were in live forums have been conducted virtually, delayed or cancelled as a result of the COVID-19 pandemic. Starting in 2021, we began to see an increase in in-person engagements with health care providers, particularly as we completed our sales force expansion in the third quarter of 2021, which increased the territories we cover. That growth of in-person interactions continued until December 2021when the Omicron variant surge which again limited our access. We have plans in place to continue implementing both virtual and live initiatives to ensure we are able to meet the needs of health care providers as the pandemic continues to evolve.

With respect to our supply chain, we currently do not anticipate significant disruption in the supply chain for our commercial product. However, we do not know the full extent of the impact on our supply chain if the COVID-19 pandemic continues and persists for an extended period of time.

See also "Part I, Item 1A, Risk Factors" of this Annual Report on Form 10-K for additional information on risks and uncertainties related to the ongoing COVID-19 pandemic.

Strategy

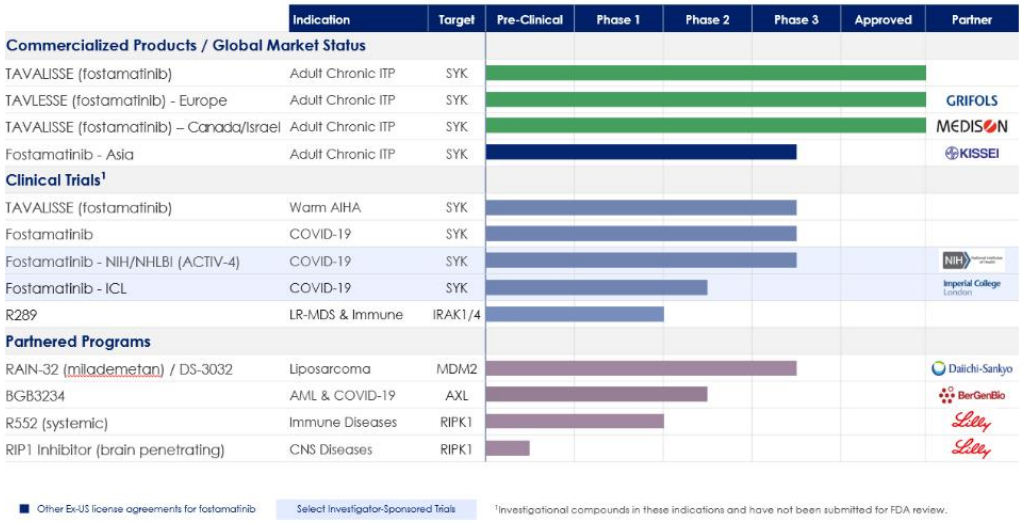
Our goal is to establish ourselves as a successful commercial stage biopharmaceutical company with significant development capabilities. We aim to expand our commercial business in the US on our own and globally through partnerships. We continue our research and development of novel small molecule drugs that significantly improve the lives of patients with hematological disorders, cancer and immune diseases. We continue to maintain a strong commercial team in the US to enable us to execute successfully on our commercialization strategy for TAVALISSE in chronic ITP. We entered into partnerships for the expansion of fostamatinib into Europe, Asia, Turkey, Canada, and Israel, and will be concentrating on the further development of the utility of fostamatinib in other indications on our own or through our partners. We also aim to expand our development pipeline on our own and/or with partnerships with pharmaceuticals and biotechnology companies to further develop and market additional product candidates.

In particular, there are four key elements that we believe are value drivers, which we plan to continue to execute on:

- growing sales of TAVALISSE in the estimated over $2.0 billion Global ITP market;
- completing the Phase 3 pivotal trial of fostamatinib in wAIHA, potentially becoming the first FDA-approved product in this indication and capitalizing on a potential $1.0 billion US market;
- completing our clinical trial programs to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients; and
- expanding our development pipeline on our own and/or with collaboration partner(s).

Our Product Portfolio

The following table summarizes our portfolio:



Commercial Product

TAVALISSE in ITP

Disease background. Chronic ITP affects an estimated 81,300 adult patients in the US. In patients with ITP, the immune system attacks and destroys the body's own blood platelets, which play an active role in blood clotting and healing. ITP patients can suffer extraordinary bruising, bleeding and fatigue as a result of low platelet counts. Current therapies for ITP include steroids, blood platelet production boosters that imitate thrombopoietin (TPOs) and splenectomy.

Orally-available fostamatinib program. Taken in tablet form, fostamatinib blocks the activation of SYK inside immune cells. ITP is typically characterized by the body producing antibodies that attach to healthy platelets in the blood stream. Immune cells recognize these antibodies and affix to them, which activates the SYK enzyme inside the immune cell, and triggers the destruction of the antibody and the attached platelet. When SYK is inhibited by fostamatinib, it interrupts this immune cell function and allows the platelets to escape destruction. The results of our Phase 2 clinical trial, in which fostamatinib was orally administered to 16 adults with chronic ITP, published in *Blood*, showed that fostamatinib significantly increased the platelet counts of certain ITP patients, including those who had failed other currently available agents.

Our Fostamatinib for Immune Thrombocytopenia (FIT) Phase 3 clinical program had a total of 150 ITP patients which were randomized into two identical multi-center, double-blind, placebo-controlled clinical trials. The patients were diagnosed with persistent or chronic ITP, and had blood platelet counts consistently below 30,000 per microliter of blood. Two-thirds of the subjects received fostamatinib orally at 100 mg twice daily bid and the other third received placebo on the same schedule. Subjects were expected to remain on treatment for up to 24 weeks. At week four of treatment, subjects who failed to meet certain platelet counts and met certain tolerability thresholds could have their dosage of fostamatinib (or corresponding placebo) increased to 150 mg bid. The primary efficacy endpoint of this program was a stable platelet response by week 24 with platelet counts at or above 50,000 per microliter of blood for at least four of the final six qualifying blood draws. In August 2015, the FDA granted our request for Orphan Drug designation for fostamatinib for the treatment of ITP.

In August 2016, we announced the results of the first FIT study, reporting that fostamatinib met the study's primary efficacy endpoint. The study showed that 18% of patients receiving fostamatinib achieved a stable platelet response compared to none receiving a placebo control (p=0.0261). In October 2016, we announced the results of the second FIT study, reporting that the response rate (16% in the treatment group, versus 4% in the placebo group) was consistent with the first study, although the difference was not statistically significant. In the ITP double-blind studies, the most commonly-reported adverse reactions occurring in at least 5% of patients treated with TAVALISSE were diarrhea, hypertension, nausea, dizziness, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), respiratory infection, rash, abdominal pain, fatigue, chest pain, and neutropenia. Serious adverse drug reactions occurring in at least 1% of patients treated with TAVALISSE in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis.

TAVALISSE was approved by the FDA in April 2018 for the treatment of ITP in adult patients who have had an insufficient response to a previous treatment, and successfully launched in the US in May 2018. In January 2020, the EC granted our Marketing Authorization Application (MAA) in Europe for fostamatinib for the treatment of chronic ITP in adult patients who are refractory to other treatments. In February 2020, Kissei Pharmaceutical Co., Ltd. (Kissei) was granted orphan drug designation from the Japanese Ministry of Health, Labor and Welfare for R788 (fostamatinib) in chronic idiopathic thrombocytopenic purpura.

Commercial activities, including sales and marketing

A significant portion of our business operations is related to our commercial activities for TAVALISSE. Specifically, our marketing and sales efforts are focused on hematologists and hematologist-oncologists in the US, who manage chronic adult ITP patients. In addition, our collaborative partner Grifols S.A. (Grifols) has launched TAVLESSE in the UK, Germany, France, Italy, Spain, the Czech Republic and Norway and continues a phased rollout across the rest of Europe which is expected to include Denmark, Finland and Sweden.

We have a fully integrated commercial team consisting of sales, marketing, market access, and commercial operations functions. Our sales team promotes TAVALISSE in the US using customary pharmaceutical company practices, and we concentrate our efforts on hematologists and hematologists-oncologists. TAVALISSE is sold initially through third-party wholesale distribution and specialty pharmacy channels and group purchasing organizations before being ultimately prescribed to patients. To facilitate our commercial activities in the US, we also enter into arrangements with various third parties, including advertising agencies, market research firms and other sales-support-related services as needed. We believe that our commercial team and distribution practices are adequate to ensure that our marketing efforts reach relevant customers and deliver our products to patients in a timely and compliant fashion. Also, to help ensure that all eligible patients in the US have appropriate access to TAVALISSE, we have established a reimbursement and patient support program called Rigel One Care (ROC). Through ROC, we provide co-pay assistance to qualified, commercially insured patients to help minimize out-of-pocket costs and also provide free TAVALISSE to uninsured or under-insured patients who meet certain established clinical and financial eligibility criteria. In addition, ROC is designed to provide reimbursement support, such as information related to prior authorizations, benefits investigations and appeals.

Competitive landscape for TAVALISSE

Our industry is intensely competitive and subject to rapid and significant technological change. TAVALISSE is competing with other existing therapies. In addition, a number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. For example, there are existing therapies and drug candidates in development for the treatment of ITP that may be alternative therapies to TAVALISSE.

Currently, corticosteroids remain the most common first line therapy for ITP, occasionally in conjunction with intravenous immunoglobulin (IVIg) or anti-Rh(D) to help further augment platelet count recovery, particularly in emergency situations. However, it has been estimated that frontline agents lead to durable remissions in only a small percentage of newly-diagnosed adults with ITP. Moreover, concerns with steroid-related side effects often restrict therapy to approximately four weeks. As such, many patients progress to persistent or chronic ITP, requiring other forms of therapeutic intervention. In long-term treatment of chronic ITP, patients are often cycled through several therapies over time in order to maintain a sufficient response to the disease.

Other approaches to treat ITP are varied in their mechanism of action, and there is no consensus about the sequence of their use. Options include splenectomy, thrombopoietin receptor agonists (TPO-RAs) and various immunosuppressants (such as rituximab). The response rate criteria of the above-mentioned options vary, precluding a comparison of response rates for individual therapies.

Even with the above treatment options, a significant number of patients remain severely thrombocytopenic for long durations and are subject to risk of spontaneous or trauma-induced hemorrhage. The addition of fostamatinib to the currently available treatment options could be beneficial because it has a different mechanism of action than any of the therapies that are currently available. Fostamatinib is a potent and relatively selective SYK inhibitor, and its inhibition of Fc receptors and B-cell receptors of signaling pathways make it a potentially broad immunomodulatory agent.

Other products in the US that are approved by the FDA to increase platelet production through binding and TPO receptors on megakaryocyte precursors include PROMACTA® (Novartis International AG (Novartis)), Nplate® (Amgen, Inc.) and DOPTELET® (Swedish Orphan Biovitrum AB).

Fostamatinib in Global Markets

We have entered into various license agreements to commercialize fostamatinib globally. The following describes the arrangements we have in place with Grifols, Kissei and Medison Pharma Trading AG (Medison Canada) and Medison Pharma Ltd. (Medison Israel, and together with Medison Canada, Medison). We retain the global rights to fostamatinib outside of the Grifols, Kissei and Medison territories.

Fostamatinib in Europe/Turkey

In January 2019, we entered into an exclusive commercialization license agreement with Grifols to commercialize fostamatinib for the treatment, palliation, or prevention of human diseases, including chronic or persistent ITP and Autoimmune hemolytic anemia (AIHA) in Europe and Turkey. Pursuant to the terms of the license agreement, Grifols has exclusive rights to commercialize, and non-exclusive rights to develop, fostamatinib in Europe and Turkey. Grifols also received an exclusive option to expand the territory under its exclusive and non-exclusive licenses to include the Middle East, North Africa and Russia (including Commonwealth of Independent States). In November 2020, Grifols exercised its option to include these territories under the agreement.

We are responsible for performing and funding certain development activities for fostamatinib for ITP and AIHA and Grifols is responsible for all other development activities for fostamatinib in such territories. We remain responsible for the manufacturing and supply of fostamatinib for all development and commercialization activities under the agreement. Under the terms of the agreement, we received an upfront cash payment of $30.0 million and will be eligible to receive regulatory and commercial milestones of up to $297.5 million. In January 2020, the European Commission granted a MA for fostamatinib for the treatment of chronic ITP in adult patients who are refractory to other treatments. With this approval, we received a $20.0 million non-refundable milestone payment, comprised of a $17.5 million payment due upon MAA approval by the EMA of fostamatinib for the first indication and a $2.5 million creditable advance royalty payment due upon EMA approval of fostamatinib in the first indication. We will also receive tiered royalty payments ranging from the mid-teens to 30% of net sales of fostamatinib in Europe and Turkey.

Fostamatinib in Japan/Asia

In October 2018, we entered into an exclusive license and supply agreement with Kissei to develop and commercialize fostamatinib in all current and potential indications in Japan, China, Taiwan and the Republic of Korea. Kissei is a Japan-based pharmaceutical company addressing patients' unmet medical needs through its research, development and commercialization efforts, as well as through collaborations with partners.

Under the terms of the agreement, we received an upfront cash payment of $33.0 million, with the potential for an additional $147.0 million in development and commercial milestone payments, and will receive product transfer price payments in the mid to upper twenty percent range based on tiered net sales for the exclusive supply of fostamatinib. Kissei receives exclusive rights to fostamatinib in ITP and all future indications in Japan, China, Taiwan, and the Republic of Korea.

In September 2019, Kissei initiated a Phase 3 trial in Japan of fostamatinib in adult patients with chronic ITP. The efficacy and safety of orally administered fostamatinib will be assessed by comparing it with placebo in a randomized, double-blind study. Japan has the third highest prevalence of chronic ITP in the world behind the US and Europe. In February 2020, Kissei was granted orphan drug designation from the Japanese Ministry of Health, Labor and Welfare for R788 (fostamatinib) in chronic ITP. In December 2021, Kissei reported positive topline results for a Phase 3 clinical trial of fostamatinib in adult Japanese patients with chronic ITP, meeting its primary endpoint. The Phase 3 clinical study showed that patients receiving fostamatinib achieved a stable platelet response significantly higher than patients receiving a placebo control. A stable platelet response was defined as achieving greater than or equal to 50,000 platelets per μL of blood on at least four of the last six scheduled visits between weeks 14 and 24 of treatment. Kissei is preparing a new drug application for submission to Japan's Pharmaceuticals and Medical Devices Agency (PMDA).

Fostamatinib in Canada/Israel

In October 2019, we entered into exclusive commercial and license agreements with Medison to commercialize fostamatinib in all potential indications in Canada and Israel. Under the terms of the agreements, we received an upfront payment of $5.0 million with the potential for approximately $35.0 million in regulatory and commercial milestones. In addition, we will receive royalty payments beginning at 30% of net sales. Under our agreement with Medison for the Canada territory, we have the option to buy back all rights to the product upon regulatory approval in Canada for the indication of AIHA. The buyback provision, if exercised, would require both parties to mutually agree on commercially reasonable terms for us to purchase back the rights, taking into account Medison's investment and the value of the rights, among others. Pursuant to this exclusive commercialization license agreement, in August 2020, we entered into a commercial supply agreement with Medison.

In November 2020, Health Canada approved the New Drug Submission for TAVALISSE for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to other treatments. In August 2021, Medison Israel received the licenses for registrational approval from the Ministry of Health, which triggered the first milestone that is the regulatory approval of the product in Israel for the first indication, for a non-refundable payment of $0.1 million.

Clinical Stage Programs

Fostamatinib in wAIHA

Disease background. Autoimmune hemolytic anemia is a rare, serious blood disorder where the immune system produces antibodies that result in the destruction of the body's own red blood cells. Symptoms can include fatigue, shortness of breath, rapid heartbeat, jaundice or enlarged spleen. While no medical treatments are currently approved for AIHA, physicians generally treat acute and chronic cases of the disorder with corticosteroids, other immuno-suppressants, or splenectomy. Research has shown that inhibiting SYK with fostamatinib may reduce the destruction of red blood cells. AIHA affects an estimated 45,000 Americans, and approximately 36,000 of those patients have wAIHA, where no approved treatment options currently exist.

Orally-available fostamatinib program. We completed our Phase 2 clinical trial, also known as the SOAR study in patients with wAIHA. This trial was an open-label, multi-center, two-stage study that evaluated the efficacy and safety of fostamatinib in patients with wAIHA who had previously received treatment for the disorder but have relapsed. The primary efficacy endpoint of this study was to achieve increased hemoglobin levels by week 12 of greater than 10 g/dL, and greater than or equal to 2 g/dL higher than baseline. In November 2019, we announced updated data that in a Phase 2 open-label study of fostamatinib in patients with wAIHA, data showed that 44% (11/25) of evaluable patients met the primary efficacy endpoint of a Hgb level >10 g/dL with an increase of ≥2 g/dL from baseline by week 24. Including one late responder at week 30, the overall response rate was 48% (12/25). Adverse events were manageable and consistent with those previously reported with fostamatinib.

In March 2019, we initiated our wAIHA pivotal Phase 3 clinical study of fostamatinib, known as the FORWARD study. The clinical trial protocol calls for a placebo-controlled study of approximately 90 patients with primary or secondary wAIHA who have failed at least one prior treatment. The primary endpoint will be a durable Hgb response, defined as Hgb > 10 g/dL and > 2 g/dL increase from baseline and durability measure, with the response not being attributed to rescue therapy. In November 2020, we reached an agreement with the FDA on the durable response measure for the primary efficacy endpoint of the study as well as the inclusion of additional secondary endpoints. In November 2021, we completed the enrollment of this study. Following the six-month treatment period after the last patient enrollment, we expect to report topline data from the 24-week study in mid-2022 and proceed with regulatory filings if the data is positive. If approved, fostamatinib has the potential to be the first to market therapy for patients with wAIHA.

In January 2021, we announced that the FDA had granted Fast Track designation to fostamatinib for the treatment of wAIHA. The FDA previously granted fostamatinib Orphan Drug designation for the treatment of wAIHA in January 2018.

Fostamatinib in Hospitalized COVID-19 Patients

Disease background. COVID-19 is the infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). SARS-CoV-2 primarily infects the upper and lower respiratory tract and can lead to acute respiratory distress syndrome (ARDS). Additionally, some patients develop other organ dysfunction including myocardial injury, acute kidney injury, shock resulting in endothelial dysfunction and subsequently micro and macrovascular thrombosis. Much of the underlying pathology of SARS-CoV-2 is thought to be secondary to a hyperinflammatory immune response associated with increased risk of thrombosis. SYK is involved in the intracellular signaling pathways of many different immune cells. Therefore, SYK inhibition may improve outcomes in patients with COVID-19 via inhibition of key Fc gamma receptor (FcγR) and c-type lectin receptor (CLR) mediated drivers of pathology such as inflammatory cytokine release by monocytes and macrophages, production of NETs by neutrophils, and platelet aggregation. Furthermore, SYK inhibition in neutrophils and platelets may lead to decreased thromboinflammation, alleviating organ dysfunction in critically ill patients with COVID-19.

Rigel-led Phase 3 Trial. In November 2020, we launched a Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients without respiratory failure that have certain high-risk prognostic factors. In January 2021, we were awarded $16.5 million from the US Department of Defense's Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND) to support this Phase 3 clinical trial. This multi-center, double-blind, placebo-controlled, adaptive design study will randomly assign either fostamatinib plus SOC or matched placebo plus SOC (1:1) to 308 targeted evaluable patients. Treatment will be administered orally twice daily for 14 days with follow up to day 60. In December, we expanded the inclusion criteria to include patients with more severe disease (NIAID Ordinal Scale 6) to more accurately reflect the clinically predominant patient population hospitalized with COVID-19 and help speed enrollment. In collaboration with the FDA and Department of Defense, we also updated the primary endpoint for the study from progression to severe disease within 29 days, to the number of days on oxygen through day 29. This endpoint allows for closer comparison of the results with earlier results from the NIH/NHLBI Phase 2 trial with fostamatinib and various other NIH-sponsored trials, such as ACTIV-4, which uses a similar outcome measure as a primary endpoint. As of February 28, 2022, we enrolled approximately 265 of the targeted 308 patients.

NIH/NHLBI-sponsored Phase 2 Trial. In September 2020, we announced a Phase 2 clinical trial sponsored by the NIH/NHLBI in order to evaluate the safety of fostamatinib for the treatment of hospitalized COVID-19 patients. This multi-center, double-blind, placebo-controlled study randomly assigned fostamatinib or matched placebo (1:1) to 59 evaluable patients. Treatment was administered orally twice daily for 14 days, and a follow-up period to day 60. The primary endpoint of this study was cumulative incidence of SAE through day 29. The trial also included multiple secondary endpoints designed to assess the early efficacy and clinically relevant endpoints of disease course. The study completed the enrollment in March 2021, and in April 2021, we announced that this Phase 2 clinical trial met its primary endpoint of safety. In September 2021, the data from the NIH/NHLBI-Sponsored Phase 2 trial was published in Clinical Infectious Diseases, an official publication of the Infectious Disease Society of America.

Key findings within the fostamatinib Phase 2 trial include:

- The study met the primary endpoint showing fostamatinib did not increase the incidence of serious adverse events (SAEs) compared with placebo.
- The overall incidence of SAEs by Day 29 was approximately 50% less in the fostamatinib group (10.5%) compared with the placebo group (22.0%) (p=0.2). The most frequent SAE reported by Day 29 was hypoxia, occurring in 1 patient receiving fostamatinib and 3 patients receiving placebo.
- At Day 29, in the overall population there were zero deaths in the fostamatinib group of 30 patients compared to three deaths in the placebo group of 29 patients (p=0.07). In more severe patients, those with an ordinal scale assessment of 6 or 7, the difference was zero of nineteen patients compared to three of seventeen patients (p=0.049), respectively.
- There were four intubated patients in the trial on mechanical ventilation (ordinal scale 7) with two patients randomized to each treatment group. Both patients in the fostamatinib group improved within 7 days and came off the ventilator, while both patients in the placebo group deceased.
- The median number of days in the ICU was reduced by 4 days, from 7 days in the placebo group to 3 days in the fostamatinib group (p=0.07).
- The median number of days on oxygen was 8 in the fostamatinib group compared to 20 in the placebo group (p=0.2). The difference was even greater in more severe patients with the fostamatinib group at 10 days compared to placebo at 28 days (p=0.027).
- At Day 15, 65.5% of patients were free of supplemental oxygen in the fostamatinib group compared to 39.9% in the placebo group (p=0.08). In more severe patients, the difference was 57.9% compared to 20% (p=0.016).
- Fostamatinib was superior to placebo in accelerating improvement in clinical status by day 15 (mean change -3.6 compared to -2.6, p=0.035) and by day 29 (mean change -4.2 compared to -3.3, p=0.12) using ordinal scale assessments.
- The median time to recovery was 8 days in both groups. The greatest benefits were observed in more severe patients where the median time to recovery was reduced from 13 days in the placebo group to 10 days in the fostamatinib group.
- Despite general SOC use of both steroids and remdesivir in all 59 patients, there was a greater reduction in NETosis and other inflammatory biomarkers (CRP, Ferritin, D-Dimer, Fibrinogen) at most timepoints in the fostamatinib group as compared to the placebo group.

In May 2021, the NIH/NHLBI Phase 2 clinical data were submitted as part of a request for EUA from the FDA for fostamatinib as a treatment for hospitalized patients with COVID-19. In August 2021, the FDA informed us that the clinical data submitted from the NIH/NHLBI-sponsored Phase 2 trial of fostamatinib to treat hospitalized patients suffering from COVID-19 was insufficient for EUA. We continue to focus on enrolling patients in our Rigel-led Phase 3 clinical trial. We anticipate providing further safety and efficacy data from this larger trial of fostamatinib in COVID-19 patients. If this trial meets its endpoints, we plan to resubmit our EUA application with this additional data.

ACTIV-4 Host Tissue Phase 3 Trial. Following the completed NIH/NHLBI-sponsored Phase 2 study as discussed above, in June 2021, we announced that fostamatinib has been selected for an NIH ACTIV-4 (Accelerating COVID-19 Therapeutic Inventions and Vaccines) trial in hospitalized patients with COVID-19. The ACTIV-4 Host study, initiated and funded by NHLBI, is a randomized, placebo-controlled trial of therapies, including fostamatinib, targeting the host response to COVID-19 in hospitalized patients. The master protocol for this study is designed to be flexible in the number of study arms, the use of a single placebo group, and the stopping and adding of new therapies. Each active arm will include approximately 300 patients. Eligible participants will include patients hospitalized for COVID-19 with laboratory-confirmed SARS-CoV-2 infection on oxygen therapy. The primary outcome is oxygen-free days through day 28. Secondary outcomes include hospital mortality, use of mechanical ventilation, and severity of disease as measured by World Health Organization scale scores.

Imperial College of London Phase 2 Trial. In July 2020, we announced a Phase 2 clinical trial sponsored by Imperial College London to evaluate the efficacy of fostamatinib for the treatment of COVID-19 pneumonia. This is a two-stage, open label, controlled clinical trial with patients randomized (1:1:1) to fostamatinib plus SOC, ruxolitinib plus SOC, or standard of care alone. Treatment will be administered twice daily for 14 days and patients will receive a follow-up assessment at day 14 and day 28 after the first dose. The primary endpoint of this study is progression from mild to severe COVID-19 pneumonia within 14 days in hospitalized patients. In November 2020, we announced that the Imperial College London-sponsored clinical trial began enrolling patients, and we are currently enrolling patients under this study.

Other Publications. Researchers at MIT and Harvard led a screen to identify FDA-approved compounds that reduce MUC1 protein abundance. MUC1 is a biomarker used to predict the development of ALI and ARDS and correlates with poor clinical outcomes. In June 2020, the results were presented, and of the 3,713 compounds that were screened, fostamatinib was the only compound identified which both decreased expression of MUC1 and is FDA approved. Fostamatinib demonstrated preferential depletion of MUC1 from epithelial cells without affecting cell viability. The research was focused on drug repurposing for the much lower risk of toxicity and the ability of FDA-approved treatments to be delivered on a shortened timescale, which is critical for patients afflicted with lung disease resulting from COVID-19.

In addition, the in vitro studies led by the Amsterdam University Medical Center at the University of Amsterdam, showed that R406, the active metabolite of fostamatinib, blocked macrophage hyperinflammatory responses to a combination of immune complexes formed by anti-Spike IgG in serum from severe COVID-19 patients. Anti-Spike IgG levels are known to correlate with the severity of COVID-19. These results, presented in July 2020, suggest that by inhibiting anti-Spike IgG-mediated hyperinflammation, R406 could potentially play a role in the prevention of cytokine storms as well as pulmonary edema and thrombosis associated with severe COVID-19.

In December 2020, the Journal of Infectious Diseases published research from NIH which demonstrated that R406, the active metabolite of fostamatinib, was able to inhibit NETosis ex vivo in donor plasma from patients with COVID-19. NETosis is a unique type of cell death resulting in the release of NETs. NETs contribute to thromboinflammation and have been associated with mortality in COVID-19. These data provide insights for how fostamatinib may mitigate neutrophil-associated mechanisms contributing to COVID-19 immunopathogenesis.

R289, an Oral IRAK1/4 Inhibitor for Autoimmune, Inflammatory and Hematology-Oncology Diseases

Orally Available IRAK 1/4 Inhibitor Program. During the second quarter of 2018, we selected R835, the active metabolite of R289, a proprietary molecule from our IRAK 1/4 preclinical development program, for human clinical trials. This investigational candidate is an orally administered, potent and selective inhibitor of IRAK1 and IRAK4 that blocks inflammatory cytokine production in response to toll-like receptor (TLR) and the interleukin-1 (IL-1R) family receptor signaling. TLRs and IL-1Rs play a critical role in the innate immune response and dysregulation of these pathways can lead to a variety of inflammatory conditions including psoriasis, rheumatoid arthritis, inflammatory bowel disease and gout (among others). R835 prevents cytokine release in response to TLR and IL-1R activation in vitro. R835 is active in multiple rodent models of inflammatory disease including psoriasis, arthritis, lupus, multiple sclerosis and gout. Preclinical studies show that R835 inhibits both the IRAK1 and IRAK4 signaling pathways, which play a key role in inflammation and immune responses to tissue damage. Dual inhibition of IRAK1 and IRAK4 allows for more complete suppression of pro-inflammatory cytokine release.

In October 2019, we announced results from a Phase 1 clinical trial of R835 in healthy subjects to assess safety, tolerability, protein kinase (PK) and pharmacodynamics. The Phase 1 study was a randomized, placebo-controlled, double-blind trial in 91 healthy subjects, ages 18 to 55. The Phase 1 trial showed positive tolerability and PK data as well as established proof-of-mechanism by demonstrating the inhibition of inflammatory cytokine production in response to a lipopolysaccharide (LPS) challenge.

We continue to advance the development of our IRAK1/4 program, completing the evaluation of a new pro-drug formulation of R835, R289, in single-ascending and multiple ascending dose studies with positive results in 2021. In January 2022, we received clearance from the FDA on our clinical trial design to explore R289 in low-risk myelodysplastic syndromes (LR MDS). The open-label, Phase 1b study will determine the tolerability and preliminary efficacy of R289 in patients with LR MDS who are relapsed, refractory/resistant, intolerant or have inadequate response to prior therapies such as erythropoietin (EPO), thrombopoietin (TPO), luspatercept, or hypomethylating agents (HMAs) for MDS. In June 2021, we entered into a research collaboration with MD Anderson Cancer Center to evaluate novel IRAK 1/4 inhibitors in a series of preclinical studies of MDS and chronic myelomonocytic leukemia (CMML). The translational research generated from these studies will add to the body of data generated to-date on R835 and further elucidate the therapeutic potential of targeting deregulated innate immune signaling in MDS and CMML. In other immune diseases, we are exploring opportunities including palmoplantar pustulosis (PPP), hidradenitis suppurativa (HS), and others.

Partnered Clinical Programs

BGB324 – BerGenBio

We have an exclusive, worldwide research, development and commercialization agreement with BerGenBio for our investigational AXL receptor tyrosine kinase (AXL) inhibitor, BGB324/R428 (now referred to as bemcentinib).

The product is being investigated in two Phase 2 clinical trials for the treatment of hospitalized patients with COVID-19. Clinical trials are also ongoing across oncology indications with high unmet medical need including acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), and non-small cell lung cancer (NSCLC).

DS-3032 - Daiichi

DS-3032 is an investigational oral selective inhibitor of the murine double minute 2 (MDM2) protein investigated by Daiichi in three Phase 1 clinical trials for solid and hematological malignancies including AML, acute lymphocytic leukemia, chronic myeloid leukemia in blast phase, lymphoma and MDS. Preliminary safety and efficacy data from a Phase 1 study of DS-3032 suggests that DS-3032 may be a promising treatment for hematological malignancies including relapsed/refractory AML and high-risk MDS.

In September 2020, worldwide rights to DS-3032 were out-licensed from Daiichi to Rain Therapeutics Inc. (Rain). In July 2021, Rain announced that it initiated the Phase 3 study which will evaluate the efficacy and safety of milademetan (RAIN-32), a MDM2 inhibitor, for the treatment of de-differentiated liposarcoma, a rare cancer originating from fat cells located in the soft tissues of the body. In late 2021, Rain commenced its second clinical trial for RAIN-32 in patients with MDM2-applified advance solid tumors.

AZ-D0449 – AZ

In June 2012, we entered into an agreement with AZ for exclusive, worldwide rights to develop and commercialize our proprietary JAK inhibitor. In preclinical studies, this molecule was shown to be a potent inhibitor of IL-13 and IL-4 signaling. Inhibiting the IL-13 and IL-14 pathways could reduce the severity of inflammation and improve lung function by mechanisms associated with several hallmarks of asthma such as bronchoconstriction, mucus overproduction and airway remodeling. In December 2021, AZ provided a notice of termination of the agreement effective April 19, 2022.

Research/Preclinical Programs

We are conducting proprietary research in the broad disease areas of inflammation/immunology, immuno-oncology and cancers. Within these disease areas, our researchers are investigating mechanisms of action as well as screening compounds against potential novel targets and optimizing those leads that appear to have the greatest potential.

Pharmacology and Preclinical Development

Our pharmacology and preclinical development group facilitates lead optimization by characterizing lead compounds with respect to PK, potency, efficacy and selectivity. The generation of proof-of-principle data in animals and the establishment of standard pharmacological models with which to assess lead compounds represent integral components of lead optimization. As programs move through the lead optimization stage, our pharmacology and preclinical development groups support our chemists and biologists by performing the necessary studies, including toxicology, for IND application submissions.

Clinical Development

We have assembled a team of experts in drug development to design and implement clinical trials and to analyze the data derived from these trials. The clinical development group possesses expertise in project management and regulatory affairs. We work with external clinical research organizations with expertise in managing clinical trials, drug formulation, and the manufacture of clinical trial supplies to support our drug development efforts.

Commercialization and Sponsored Research and License Agreements

For a discussion of our Commercialization and Sponsored Research and License, see "Note 4 - Sponsored Research and License Agreements and Government Contract" to our "Notes to Financial Statements" contained in "Part II, Item 8, Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

Intellectual Property

We are able to protect our technology from unauthorized use by third parties only to the extent that it is covered by valid and enforceable patents or is effectively maintained as a trade secret. Accordingly, patents and other proprietary rights are an essential element of our business. As of December 31, 2021, we had 51 pending patent applications and 358 issued and active patents in the US, as well as corresponding pending foreign patent applications and issued foreign patents. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek US and international patent protection for a variety of technologies, including new screening methodologies and other research tools, target molecules that are associated with disease states identified in our screens, and lead compounds that can affect disease pathways. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel drugs. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various license agreements that give us rights to use technologies in our research and development.

We currently hold a number of issued patents in the US, as well as corresponding applications that allow us to pursue patents in other countries, some of which have been allowed and/or granted and others of which we expect to be granted. Specifically, in most cases where we hold a US issued patent, the subject matter is covered at least by an application filed under the Patent Cooperation Treaty (PCT), which is then used or has been used to pursue protection in certain countries that are members of the treaty. Our patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. Some of these patents may be eligible for patent term extensions, depending on their subject matter and length of time required to conduct clinical trials. Our material patents relate to fostamatinib, an oral SYK inhibitor, that is the active pharmaceutical ingredient in TAVALISSE, and R406, the active metabolite of fostamatinib. These patents will expire at various dates from 2023 to 2034.

Fostamatinib. Fostamatinib is covered as a composition of matter in a US issued patent that has an expected expiration date of September 2031, after taking into account a patent term adjustment and extension rules. Fostamatinib is also covered under broader composition of matter claims in a US issued patent that has an expiration date in March 2026, after taking into account a patent term adjustment. Additional patents covering fostamatinib composition of matter, methods for use, formulations, methods for making and intermediates expire at various dates from 2023 to 2041. Corresponding applications have been filed in foreign jurisdictions under the PCT, and are at various stages of prosecution. Of note, a patent covering fostamatinib as a composition of matter and in compositions for use treating various diseases has been granted by the European Patent Office.

R406. R406 is covered as a composition of matter in a US issued patent and, with a patent term adjustment, has an expiration date in February 2025. R406 is also covered under two broader composition of matter patents issued in the US expiring in February 2023 and July 2024. Methods of using R406 to treat various indications and compositions of matter covering certain intermediates used to make R406 are also covered under patents described above. Corresponding applications have been filed in foreign jurisdictions under the PCT and are at various stages of prosecution.

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Many of the drugs that we are attempting to discover will be competing with existing therapies. In addition, a number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting.

There are existing therapies and drug candidates in development for the treatment of ITP that may be alternative therapies to TAVALISSE. Currently, corticosteroids remain the most common first line therapy for ITP, occasionally in conjunction with intravenous immuglobulin (IVIg) or anti-Rh(D) as added agents to help further augment platelet count recovery, particularly in emergency situations. However, it has been estimated that frontline agents lead to durable remissions in only a small percentage of newly-diagnosed adults with ITP. Moreover, concerns with steroid-related side effects often restrict therapy to approximately four weeks. As such, many patients progress to persistent or chronic ITP, requiring other forms of therapeutic intervention.

The FDA can approve an Abbreviated New Drug Application (ANDA) for a generic version of a branded drug without the ANDA applicant undertaking the clinical testing necessary to obtain approval to market a new drug. In September 2019, the FDA published product-specific bioequivalence guidance on fostamatinib disodium to let potential ANDA applicants understand the data the FDA would expect to see for approval of a generic version of TAVALISSE. The earliest an ANDA may be filed by a generic company is April 17, 2022. The ANDA process can result in generic competition if the patents at issue are not upheld or if the generic competitor is found not to infringe our patents. In September 2019, the FDA published product-specific bioequivalence guidance on fostamatinib disodium to let potential ANDA applicants understand the data FDA would expect to see for approval of a generic version of TAVALISSE.

Other approaches to treat ITP are varied in their mechanism of action, and there is no consensus about the sequence of their use. Options include splenectomy, thrombopoietin receptor agonists (TPO-RAs) and various immunosuppressants (such as rituximab). The response rate criteria of the above-mentioned options vary, precluding a comparison of response rates for individual therapies. According to the most recent ITP guideline from the ASH, there was a lack of evidence to support strong recommendations for various management approaches. In general, strategies that avoided medication side effects were favored. A large focus was placed on shared decision-making especially with regard to second-line therapy.

Even with the above treatment options, a significant number of patients remain severely thrombocytopenic for long durations and are subject to risk of spontaneous or trauma-induced hemorrhage. The addition of fostamatinib to the treatment options could be beneficial since it has a different mechanism of action than the TPO agonists. Fostamatinib is a potent and relatively selective SYK inhibitor, and its inhibition of Fc receptors and B-cell receptors signaling pathways make it a potentially broad immunomodulatory agent.

Other products in the US that are approved by the FDA to increase platelet production through binding and TPO receptors on megakaryocyte precursors include PROMACTA® (Novartis), Nplate® (Amgen, Inc.) and DOPTELET® (Dova Pharmaceuticals).

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as from academic and research institutions and government agencies, both in the US and abroad. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions as our research programs. Our major competitors include fully integrated pharmaceutical companies that have extensive drug discovery efforts and are developing novel small molecule pharmaceuticals. We also face significant competition from organizations that are pursuing the same or similar technologies, including the discovery of targets that are useful in compound screening, as the technologies used by us in our drug discovery efforts.

Competition may also arise from:

- new or better methods of target identification or validation;
- generic version of TAVALISSE or of products with which we compete;
- other drug development technologies and methods of preventing or reducing the incidence of disease;
- new small molecules; or
- other classes of therapeutic agents.

Our competitors or their collaborative partners may utilize discovery technologies and techniques or partner with collaborators in order to develop products more rapidly or successfully than we or our collaborators are able to do. Many of our competitors, particularly large pharmaceutical companies, have substantially greater financial, technical and human resources and larger research and development staffs than we do. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies and may establish exclusive collaborative or licensing relationships with our competitors.

We believe that our ability to compete is dependent, in part, upon our ability to create, maintain and license scientifically advanced technology and upon our and our collaborators' ability to develop and commercialize pharmaceutical products based on this technology, as well as our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary technology or processes and secure sufficient capital resources for the expected substantial time period between technological conception and commercial sales of products based upon our technology. The failure by any of our collaborators or us, including our commercial team, in any of those areas may prevent the successful commercialization of our potential drug targets.

Many of our competitors, either alone or together with their collaborative partners, have significantly greater experience than we do in:

- identifying and validating targets;
- screening compounds against targets; and
- undertaking preclinical testing and clinical trials.

Accordingly, our competitors may succeed in obtaining patent protection, identifying or validating new targets or discovering new drug compounds before we do.

Our competitors might develop technologies and drugs that are more effective or less costly than any that are being developed by us or that would render our technology and product candidates obsolete and noncompetitive. In addition, our competitors may succeed in obtaining the approval of the FDA or other regulatory agencies for product candidates more rapidly. Companies that complete clinical trials, obtain required regulatory agency approvals and commence commercial sale of their drugs before us may achieve a significant competitive advantage, including certain patent and FDA marketing exclusivity rights that would delay or prevent our ability to market certain products. Any drugs resulting from our research and development efforts, or from our joint efforts with our existing or future collaborative partners, might not be able to compete successfully with competitors' existing or future products or obtain regulatory approval in the US or elsewhere.

We face and will continue to face intense competition from other companies for commercial and collaborative arrangements with pharmaceutical and biotechnology companies, for establishing relationships with academic and research institutions and for licenses to additional technologies. These competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective than ours.

Our ability to compete successfully will depend, in part, on our ability to:

- identify and validate targets;
- discover candidate drug compounds that interact with the targets we identify;
- attract and retain scientific and product development personnel;
- obtain patent or other proprietary protection for our new drug compounds and technologies; and
- enter commercialization agreements for our new drug compounds.

Government Regulation

Government authorities in the US, at the federal, state and local level, and in other countries and jurisdictions, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sampling, tracking and tracing, sales, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the US and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, such as those governing personal information and information security, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the US

In the US, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and implementing regulations. The failure to comply with requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties.

A drug product candidate must be approved by the FDA through the new drug application (NDA). An applicant seeking approval to market and distribute a new drug product in the US must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice (GLP) regulations;
- submission to the FDA of an Investigational New Drug application (IND), which must take effect before human clinical trials may begin;

- approval by an independent institutional review board (IRB) for each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (GCP) to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, if requested by the FDA;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices (cGMP), requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and potentially post-market requirement, or PMR, and commitment, or PMC, studies.

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation as well as in vitro and animal studies to assess product chemistry, formulation, and toxicity, as well as the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

An IND is an exemption from the FDCA that allows an unapproved new drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. In support of the IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin or resume. An IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. An IRB can suspend or terminate approval of a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Human clinical trials are typically conducted in sequential phases, which may overlap or be combined:

- ***Phase 1***. The drug is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- ***Phase 2***. The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- ***Phase 3***. These clinical trials are commonly referred to as "pivotal" studies, which denote a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, identify adverse effects, establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.
- ***Phase 4***. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

In most cases the FDA requires at least two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances, such as where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with current good manufacturing practices (cGMP) requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

The FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

Review and Approval of Drugs in the EU and the UK

Similar rules governing clinical trials to those in place in the US apply in the European Union (EU) and the UK, with a clinical trial application (CTA) required to be submitted for each clinical trial to each EU Member State's national competent authority (NCA) and an independent Ethics Committee. Following the UK's exit from the EU, commonly referred to as Brexit, and the end of the transition period that was in place until the end of 2020, clinical trials that take place in the UK will be seen by the EMA as trials that have taken place in a "third country" and will only be considered during the course of a marketing authorization application if they are carried out on a basis that is in line with the regulations governing clinical trials in the EU. As of January 31, 2022, clinical trials in the EU must be conducted in accordance with the requirements of the EU Clinical Trials Regulation (EU) No 536/2014 (CTR) that has amended the system of approval for clinical trials in the EU. Under the CTR, sponsors must apply for authorizations through the Clinical Trials Information System (CTIS), the new clinical trials portal and database that allows a coordinated and streamlined application and authorization process for clinical trials and ethical approvals throughout the EU. The UK will not apply the CTR and therefore its regulatory framework on clinical trials is not aligned with the EU CTR. This may result in trials that take place in the UK potentially carrying less weight when applying for a marketing authorization in the EU.

Review of an NDA by the FDA

If clinical trials are successful, the next step in the drug development process is the preparation and submission to the FDA of an NDA. The NDA is the vehicle through which drug applicants formally propose that the FDA approve a new drug for marketing and sale in the US for one or more indications. The NDA must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. The submission of most NDAs is subject to an application user fee and the sponsor of an approved NDA is also subject to annual program user fees. These fees are typically increased annually.

Following submission of an NDA, the FDA conducts a preliminary review of an NDA to determine whether the application is sufficiently complete to permit substantive review. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to goals to review and act within ten months from filing for standard review NDAs and within six months for NDAs that have been designated for "priority review".

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease or condition to be treated by the drug, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA intends to review such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Expedited approval pathways

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as Fast Track designation, Breakthrough Therapy designation and Priority Review designation. In addition, accelerated approval offers the potential for approval based on a surrogate or intermediate clinical endpoint. In May 2014, the FDA published a final Guidance for Industry titled "Expedited Programs for Serious Conditions Drugs and Biologics," which provides guidance on the FDA programs that are intended to facilitate and expedite development and review of new drug candidates as well as threshold criteria generally applicable to concluding that a drug candidate is a candidate for these expedited development and review programs.

The FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and nonclinical or clinical data demonstrate the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's review clock for a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

A product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing available therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross disciplinary project lead for the review team; rolling review; and, taking other steps to design the clinical trials in an efficient manner.

FDA intends to review applications for standard review drug products within ten months of the 60-day filing date; and, applications for priority review drugs within six months. Priority review can be applied to drugs that the FDA determines treat a serious condition, and if approved, would offer a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation.

Accelerated approval pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides a meaningful therapeutic advantage to patients over available treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such drug for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality (IMM) and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug. The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. In addition, all promotional materials for drugs approved under accelerated regulations are subject to prior review by the FDA.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA, EMA and MHRA approvals are subject to pervasive and continuing regulation by the FDA, EMA and MHRA and other national competent authorities in the EU including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, tracking and tracing, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

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

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCSA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to track and trace drug products, ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Many jurisdictions, including the EU and the UK, require each marketing authorization holder, national competent authority and the EMA to operate a pharmacovigilance system to ensure that the safety of all medicines is monitored throughout their use. The overall EU pharmacovigilance system operates through cooperation between the EU Member States, EMA and the European Commission.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the US, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the US for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA for the drug and rare disease or condition. Orphan drug designation does not shorten the goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the application fee. After the FDA grants Orphan Drug Designation, the name of the drug and its potential orphan-designated use are disclosed publicly by the FDA.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

In the EU and UK, under Regulation (EC)141/2000 and the UK Human Medicines Regulation 2012 (as amended), respectively, medicinal products may be granted an orphan drug designation if they are used to treat or prevent life-threatening or chronically debilitating conditions that affect no more than five in 10,000 people in the EU/ UK and for which there is no satisfactory method of diagnosis, prevention or treatment when the application is made, or when the medicinal product is of significant benefit to those affected by the condition. In addition, orphan drug designation can be granted to drugs used to treat or prevent life-threatening or chronically debilitating conditions which, for economic reasons, would be unlikely to be developed without incentives.

The application for orphan designation must be submitted to and approved by the EMA in respect of the EU or to the MHRA for Great Britain before an application is made for marketing authorization for the product. Medicinal products which benefit from orphan status, which they successfully maintain post-grant of the marketing authorization, can benefit from up to ten years of market exclusivity in respect of the approved indication. This prevents regulatory authorities in the EU or Great Britain, as the case may be, from granting marketing authorizations for similar medicinal products for the same therapeutic indication, unless another applicant can show that the similar medicinal product in question is safer, more effective or clinically superior to the orphan-designated product or if the marketing authorization holder consents to the second orphan medicinal product application, or where the marketing authorization holder cannot supply the needs of the market.

The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify the maintenance of market exclusivity. Conversely, the 10-year exclusivity period can be further extended by 2 years, when pediatric studies are conducted in accordance with an agreed pediatric investigation plan (PIP) and in completion of all the legal requirements.

Pediatric studies and exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act of 2012 (the FDASIA), sponsors must also submit pediatric study plans prior to the assessment data.

Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Abbreviated New Drug Applications for generic drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme allowing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application (ANDA) to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug (RLD).

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form and the strength of the drug. An applicant may submit an ANDA suitability petition to request the FDA's prior permission to submit an abbreviated application for a drug that differs from the RLD in route of administration, dosage form, or strength, or for a drug that has one different active ingredient in a fixed combination drug product (i.e., a drug product with multiple active ingredients). At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator

drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists may consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

505(b)(2) New Drug Applications

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant, and for which the applicant has not obtained a right of reference. If the 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional bridging studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new drug candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch-Waxman patent certification and the 30-month stay

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Orange Book.

When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent, known as a Section VIII statement. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory process. The allowable patent term extension is typically calculated as one-half the time between the effective date of an IND application and the submission date of a NDA, plus the time between NDA submission date and the NDA approval date up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue

approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of product approval. Only one patent applicable to an approved drug is eligible for extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent in question. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements.

Exclusivity under the Hatch-Waxman Amendments

In addition, under the Hatch-Waxman Amendments, the FDA may not approve an ANDA or 505(b)(2) NDA referencing a particular drug until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity (NCE). For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505(b)(2) NDA may not be submitted to the FDA until the expiration of five years from the date the NDA is approved, unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it does, however, block the FDA from approving ANDAs or 505(b)(2) NDAs during the period of exclusivity. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

FDA Emergency Use Authorization

Section 564 of the FDCA allows the FDA to authorize the shipment of drugs, biological products (including vaccines), or medical devices that either lack required approval, licensure, or clearance (unapproved products), or are approved but are to be used for unapproved ways to diagnose, treat, or prevent serious diseases or conditions in the event of an emergency declaration by the HHS Secretary.

On February 4, 2020, HHS Secretary Alex M. Azar II declared a public health emergency for COVID-19, under 21 U.S.C. § 360bbb-3(b)(1), justifying the authorization of emergency use of IVDs for detection and/or diagnosis of COVID-19. This determination was published in the Federal Register on February 7, 2020.

While this emergency declaration is effective, the FDA may authorize the use of an unapproved product or an unapproved use of an approved product if it concludes that:

- an agent referred to in the emergency declaration could cause a serious or life-threatening disease or condition;
- it is reasonable to believe that the authorized product may be effective in diagnosing, treating, or preventing that disease or condition or a serious or life-threatening disease or condition caused by an approved product or a product marketed under an EUA;
- the known and potential benefits of the authorized product, when used for that disease or condition, outweigh known and potential risks, taking into consideration the material threat of agents identified in the emergency declaration;

- there is no adequate, approved, and available alternative to the authorized product for diagnosing, preventing, or treating the relevant disease or condition;
- any other criteria prescribed by the FDA is satisfied.

To date, FDA has submitted all EUAs it has received for vaccine candidates to treat COVID-19 for advisory committee review prior to issuing an EUA.

Medical products that are granted an EUA are only permitted to commercialize their products under the terms and conditions provided in the authorization. The FDCA authorizes FDA to impose such conditions on an EUA as may be necessary to protect the public health. Consequently, postmarketing requirements will vary across EUAs. In addition, FDA has, on occasion, waived requirements for drugs marketed under an EUA.

Generally, EUAs for unapproved products or unapproved uses of approved products require that manufacturers distribute factsheets for healthcare providers, addressing significant known and potential benefits and risk, and the extent to which benefits and risks are unknown, and the fact that FDA has authorized emergency use; and, distribution of factsheets for recipients of the product, addressing significant known and potential benefits and risk, and the extent to which benefits and risks are unknown, the option to accept or refuse the product, the consequences of refusing, available alternatives, and the fact that FDA has authorized emergency use.

Generally, EUAs for unapproved products and, per FDA's discretion, EUAs for unapproved uses of approved products, include requirements for adverse event monitoring and reporting, and other recordkeeping and reporting requirements. Note, however, that approved products are already subject to equivalent requirements.

In addition, FDA may include various requirements in an EUA as a matter of discretion as deemed necessary to protect the public health, including restrictions on which entities may distribute the product, and how to perform distribution (including requiring that distribution be limited to government entities), restrictions on who may administer the product, requirements for collection and analysis of safety and effectiveness data, waivers of cGMP, and restrictions applicable to prescription drugs or restricted devices (including advertising and promotion restrictions).

The FDA may revoke an EUA where it is determined that the underlying health emergency no longer exists or warrants such authorization, if the conditions for the issuance of the EUA are no longer met, or if other circumstances make revocation appropriate to protect the public health or safety.

Pharmaceutical Coverage, Pricing and Reimbursement

In the US and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Third-party payors include federal and state government health programs such as Medicare and Medicaid, commercial health insurers, managed care organizations, and other organizations. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. For example, there have been several recent US Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. In the US, some of these proposals at the federal level have included directing Medicare to negotiate directly with manufacturers for the costliest drugs; various Medicare Part D and Medicaid reforms; price reporting transparency; importation rulemaking; an international pricing index proposal to require additional discounts to Medicare, as well as a proposal requiring manufacturers to pay a rebate to the federal government if the price of a Medicare Part B or Part D drug increases more than the rate of inflation. For example, included in the Consolidated Appropriations Act of 2021 were several drug price reporting and transparency measures, such as a new requirement for certain Medicare plans to develop tools to display Medicare Part D prescription drug benefit information in real time and for group and health insurance issuers to report information on pharmacy benefit and drug costs to the Secretaries of the Departments of Health and Human Services, Labor and the Treasury. Additionally, on March 11, 2021, Congress enacted the American Rescue Plan Act of 2021, which included among its provisions a sunset of the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act (the Affordable Care Act)'s cap on

pharmaceutical manufacturers' rebate liability under the Medicaid Drug Rebate Program (MDRP). Under the Affordable Care Act, manufacturers' rebate liability was capped at 100% of the average manufacturer price for a covered outpatient drug. Effective January 1, 2024, manufacturers' MDRP rebate liability will no longer be capped, potentially resulting in a manufacturer paying more in MDRP rebates than it receives on the sale of certain covered outpatient drugs. 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, to encourage importation from other countries and bulk purchasing. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for the product. It is likely that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for a pharmaceutical manufacturer's products or additional pricing pressure.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have an adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that adequate reimbursement will be approved at a rate that covers our costs, including research, development, manufacture, sale and distribution. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments and third-party payors have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for medical products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the EU, pricing and reimbursement methods can differ in each Member State. Some Member States and the UK may require that health technology assessments (HTA) be completed to obtain reimbursement or pricing approval. The outcome of HTA assessments is decided on a national basis and some Member States may decide not to reimburse the use of medicines or may reduce the rate of reimbursement. In December 2021, the EU adopted a new Regulation on Health Technology Assessment which allows Member States to carry out joint clinical assessments and operate joint clinical consultations. It is expected that the new Regulation will come into effect in 2025.

Healthcare and Privacy Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and other healthcare providers, patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable

healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which is a criminal law that prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The intent standard under the federal Anti-Kickback Statute was amended by the Affordable Care Act to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. A conviction for violation of the federal Anti-Kickback Statute can result in criminal fines and/or imprisonment and requires mandatory exclusion from participation in federal health care programs. Exclusion may also be imposed if the government determines that an entity has committed acts that are prohibited by the federal Anti-Kickback Statute. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as speakers or consultants, may be subject to scrutiny if they do not fit squarely within an exception or safe harbor. Moreover, the Anti-Kickback Statute safe harbors have been the subject of recent regulatory reforms. In late 2020, the U.S. Department of Health and Human Services, Office of Inspector General issued two final rules finalizing significant safe harbor modifications related to (1) value-based and coordinated care arrangements and (2) certain point-of-sale discounts and the existing discount safe harbor (the "Rebate Rule"). Implementation of the Rebate Rule is uncertain due, at least in part, to ongoing litigation and a Congress-passed moratorium on implementation before January 1, 2026. We cannot predict the future of the Rebate Rule, the full impact of the Rebate Rule, if implemented, or subsequent regulatory actions on our operations. As a general matter, however, any changes to the safe harbors may impact our future contractual and other arrangements with pharmacy benefit managers, group purchasing organizations, third-party payors, wholesalers and distributors, healthcare providers and prescribers, and other entities, as well as our future pricing strategies. Moreover, 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 civil False Claims Act;

- the federal civil and criminal false claims laws and civil monetary penalty laws, including the civil False Claims Act, which prohibits, among other things, (i) knowingly presenting, or causing to be presented, claims for payment of government funds that are false or fraudulent; (ii) knowingly making, or using or causing to be made or used, a false record or statement material to a false or fraudulent claim; (iii) knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government; or (iv) knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. Private individuals, commonly known as "whistleblowers," can bring FCA *qui tam* actions, on behalf of the government and may share in amounts paid by the entity to the government in recovery or settlement. Pharmaceutical companies have been investigated and/or subject to government enforcement actions asserting liability under the FCA in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product. 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 FCA. Moreover, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. FCA liability is potentially significant in the healthcare industry because the statute provides for treble

damages and significant mandatory penalties per false or fraudulent claim or statement for violations. Such per-claim penalties are currently set at $11,803 to $23,607 per false claim or statement for penalties assessed after December 13, 2021, with respect to violations occurring after November 2, 2015. Criminal penalties, including imprisonment and criminal fines, are also possible for making or presenting a false, fictitious or fraudulent claim to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program, including any 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 or representations, or making false statements relating to healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, including protected health information (PHI). 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 federal courts to enforce HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, implemented as the Open Payments Program, which requires certain manufacturers of drugs, devices, biologics and medical supplies, among others, to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the US Department of Health and Human Services (HHS), information related to payments and other transfers of value made by that entity to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also are required to report such information regarding its payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year; 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 that are reimbursed by non-governmental third-party payors, including private insurers.

Some state, local and foreign laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, restrict payments that may be made to healthcare providers and other potential referral sources, and/or require drug manufacturers to report information related to payments and transfers of value made to physicians and other health care providers or entities or marketing expenditures. In addition, there are state and local laws that require registration of sales representatives; state laws that require drug manufacturers to report information related to drug pricing; data privacy and security laws and regulations in foreign jurisdictions that may be more stringent than those in the US (such as the EU's General Data Protection Regulation (EU GDPR), which became effective in May 2018); federal and state laws governing the privacy and security of personal information (including health information) many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; and state laws related to insurance fraud in the case of claims involving private insurers.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, individual imprisonment, 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, possible exclusion from participation in federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Healthcare Reform

The US and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the US Congress enacted the Affordable Care Act, which included changes to the coverage and payment for drug products under government health care programs. There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts to repeal or replace certain aspects of the Affordable Care Act. For example, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been enacted. The Tax Cuts and Jobs Act of 2017 includes a provision that repealed the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Further, the Consolidated Appropriations Act of 2020 fully repealed the Affordable Care Act's mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and also eliminated the health insurer tax. The Bipartisan Budget Act of 2018 (BBA) amended the Affordable Care Act to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In December 2018, CMS published a new final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a US District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and because it was repealed as part of the Tax Cuts and Job Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. Additionally, on December 18, 2019, the US Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. On June 17, 2021, the US Supreme Court dismissed the most recent judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the law. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. 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 Affordable Care Act. It is unclear how future actions before the Supreme Court, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act.

Other legislative changes have been proposed and adopted in the US since the Affordable Care Act 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. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect into 2031, unless additional Congressional action is taken. However, COVID-19 relief

support legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Sequestration will start again on April 1, 2022. From April 1 to June 30, 2022, payment for Medicare fee-for-service claims will be adjusted downwards by 1%; beginning July 1, 2022, the payment will be adjusted downwards by 2%. In January 2013, former President Obama signed into law the American Taxpayer Relief Act of 2012 (ATRA), which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

In addition, there has been heightened governmental scrutiny in the US of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection under the federal Anti-Kickback Statute for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through Pharmacy Benefit Managers (PBMs), unless the price reduction is required by law. The implementation of the rule has been delayed by ongoing litigation and a Congress-passed moratorium on implementation before January 1, 2026. The rule also creates a new safe harbor manufacturer for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between PBMs and manufacturers, the implementation of which have also been delayed until January 1, 2026. On November 20, 2020, the Centers for Medicare & Medicaid Services (CMS) also issued an interim final rule implementing former 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, effective January 1, 2021. On December 28, 2020, the US District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. CMS issued a final rule, effective February 28, 2022, rescinding the Most Favored Nation Model interim rule. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which among other changes, eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacture price, for single source and innovator multiple source drugs, beginning January 1, 2024. The American Rescue Plan Act also temporarily increased premium tax credit assistance for individuals eligible for subsidies under the ACA for 2021 and 2022 and removed the 400% federal poverty level limit that otherwise applies for purposes of eligibility to receive premium tax credits. The Biden administration has begun taking executive actions to address drug pricing and other healthcare policy changes, including reversing certain measures taken by the Trump administration. For example, on July 9, 2021, President Biden signed an Executive Order to promote competition in the US economy that included several initiatives addressing prescription drugs. Among other provisions, the Executive Order directed the Secretary of HHS to issue a report to the White House within 45 days that includes a plan to, among other things, reduce prices for prescription drugs, including prices paid by the federal government for such drugs. In response to the Executive Order, on September 9, 2021, HHS issued a Comprehensive Plan for Addressing High Drug Prices that identified potential legislative policies and administrative tools that Congress and the agency can pursue in order to make drug prices more affordable and equitable, improve and promote competition throughout the prescription drug industry, and foster scientific innovation. 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.

Outside the US, ensuring adequate coverage and payment for our products will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products. Recent budgetary pressures in many EU countries are also

causing governments to consider or implement various cost-containment measures, such as price freezes, increased price cuts and rebates. If budget pressures continue, governments may implement additional cost-containment measures. Cost-control initiatives could decrease the price we might establish for products that we may develop or sell, which would result in lower product revenues or royalties payable to us. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Manufacturing and Raw Materials

We currently do not have the manufacturing capabilities or experience necessary to produce TAVALISSE/TAVLESSE or any product candidates for clinical trials, including fostamatinib in COVID-19, wAIHA, our IRAK 1/4 inhibitor program and our RIPK1 inhibitor program. We do not own or operate manufacturing or distribution facilities or resources for clinical or commercial production and distribution of our product for commercial use or for preclinical and clinical trials. We assign internal personnel to manage and oversee third parties working on our behalf under contract. These third parties manufacture raw materials, the active pharmaceutical ingredient (API) and finished drug product for commercial distribution and for use in clinical studies. We currently rely on and will continue to rely on these third-party contract manufacturers to produce sufficient quantities of our products.

Human Capital Resources

As of December 31, 2021, we have 165 full-time employees. Of these employees, 51 were engaged in research and development activities, 81 were engaged in commercial activities, and 33 were engaged in general and administrative activities. We also engage temporary employees and consultants. In November 2021, we announced our plan to exit early-stage research and focus resources on our mid to late-stage development programs and commercial efforts which resulted in elimination of positions primarily in research organization.

None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. We aim to provide a stimulating and rewarding work environment, with recognition for accomplishments and the opportunity to advance our employees' careers while sharing in the excitement of our growth and success. We know that our success depends on the experience, intellect, and talent of our highly motivated team, and we truly value the people who make our organization great. We provide a collaborative work environment that is both personally fulfilling and enables our employees to work together to achieve the purpose and goals of the organization. Our human capital efforts focus on maintaining a sufficient number of skilled employees in each respective department. Recruiting and retaining experienced and qualified sales and marketing personnel to successfully commercialize our product and scientific personnel to continue to perform research and development work in the future will be critical to our business success. Our ability to recruit, develop and retain highly skilled talent is a significant determinant of our success. To facilitate talent attraction, retention, and development, we strive to be an inclusive, diverse, and safe workplace with opportunities for our employees to grow and develop in their careers, supported by competitive compensation, opportunities for equity ownership, development opportunities that enable continued learning and growth and employment packages that promote well-being across all aspects of our employees' lives, including health care, retirement planning and paid time off.

The health, safety, and wellness of our employees is a priority in which we have always invested and intend to continue to do. We provide our employees with access to a variety of innovative, flexible, and convenient health and wellness programs. Additionally, we offer programs to help support employees physical and mental health by providing tools and resources to help them improve or maintain their health status, encourage engagement in healthy behaviors, and offer choices where possible so they are customized to meet their needs. In light of the COVID-19 pandemic, we have undertaken and plan to continue to undertake, safety measures to keep our employees' health, safety, and wellness a priority. We implemented significant changes that we determined were in the best interest of our employees, as well as the communities in which we operate, in compliance with government regulations. We endeavor to provide the safest and most effective work environment under the circumstances, but we cannot guarantee that employees who come to the office will not be exposed to COVID-19 while at the office. It will be the responsibility of all employees to participate and cooperate in safety and cleaning protocols. We expect all employees, contractors, and visitors to our facility to comply

with our COVID-19 guidelines plan. A proof of vaccination is required for all employees, contractors, and visitors to enter the facility. Employees may submit a request for exemption from this policy to Human Resources due to a qualifying medical or religious reason. Regular COVID-19 testing is required if an employee receives an exemption.

We provide compensation and benefits programs to help meet the needs of our employees. In addition to base compensation, these programs include annual bonuses, Stock Award Plans, Employee Stock Purchase Plans, 401(k), healthcare and insurance benefits, paid time off, health and fitness benefits and various additional employee programs. We have robust annual performance review processes for reviewing employees' performance and pay.

Scientific and Medical Advisors

We utilize scientists, key opinion leaders and physicians to advise us on scientific and medical matters as part of our ongoing commercialization activities and research and product development efforts, including experts in clinical trial design, preclinical development work, chemistry, biology, immunology, oncology and immuno-oncology. Certain of our consultants receive non-employee options to purchase our common stock and certain of our scientific and medical advisors receive honorarium for time spent assisting us.

Corporate Information

Our principal executive office is located at 1180 Veterans Boulevard, South San Francisco, California 94080. Our telephone number is (650) 624-1100.

Available Information

We electronically file with the Securities and Exchange Commission (SEC) our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy and information statements and amendments to such reports and statements filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make copies of these reports available free of charge on or through our website at *www.rigel.com*, as soon as reasonably practicable after we electronically file these reports with, or furnish them to, the SEC. The information found on our website is not part of or incorporated by reference into this Annual Report on Form 10-K.

The SEC also maintains an internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at *www.sec.gov*.

Item 1A. Risk Factors

In evaluating our business, you should carefully consider the following risks, as well as the other information contained in this Annual Report on Form 10-K. These risk factors could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. If any of the following risks actually occurs, our business, financial condition and operating results could be harmed. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business.

Risks Related to Our Business and Our Industry

If the market opportunities for TAVALISSE and product candidates are smaller than we believe they are, our revenues may be adversely affected, and our business may suffer.

Certain of the diseases that TAVALISSE and our other product candidates being developed to address are in underserved and underdiagnosed populations. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who will seek treatment utilizing our products or product candidates, may not be accurate. If our estimates of the prevalence or number of patients potentially on therapy prove to be inaccurate, the market opportunities for fostamatinib and our other product candidates may be smaller than what we believe they are, our prospects for generating expected revenue may be adversely affected and our business may suffer. For example, complications due to COVID-19 may be prevented or well-addressed by others entering the market with vaccines or therapeutics to prevent or treat COVID-19, thereby affecting projections of the market for our product candidate negatively, and adversely affecting our business.

We may need to continue to increase the size of our organization and we may encounter difficulties with managing our growth, which could adversely affect our business and results of operations.

Although we have recently substantially increased the size of our organization, we may need to add additional qualified personnel and resources to support our commercial sales force. Our current infrastructure may be inadequate to support our development and commercialization efforts and expected growth. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees, and may take time away from running other aspects of our business, including commercialization of TAVALISSE and development of our other product candidates.

Our future financial performance and our ability to sustain successful commercialization of TAVALISSE and our ability to commercialize other product candidates that may receive regulatory approval will depend, in part, on our ability to manage any future growth effectively. In particular, as we continue to commercialize TAVALISSE, we will need to support the training and ongoing activities of our sales force and will likely need to continue to expand the size of our employee base for managerial, operational, financial and other resources. To that end, we must be able to successfully:

- manage our development efforts effectively;
- integrate additional management, administrative and manufacturing personnel;
- further develop our marketing and sales organization; and
- maintain sufficient administrative, accounting and management information systems and controls.

We may not be able to accomplish these tasks or successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals. Our failure to accomplish any of these goals, including as a result of business or other interruptions resulting from the ongoing COVID-19 pandemic, could adversely affect our business and operations.

Our business is currently adversely affected and could be materially and adversely affected in the future by the evolving effects of the COVID-19 pandemic as a result of the current and potential future impacts on our sales force and commercialization efforts, supply chain, regulatory, clinical development and corporate development activities and other business operations, in addition to the impact of a global economic slowdown.

The COVID-19 pandemic has resulted in extended travel and other restrictions in order to reduce the spread of the disease. During 2020 and 2021, several states and counties across the country including California and the San Francisco Bay Area issued orders and restrictions, including directing individuals to shelter in place, prohibiting certain non-essential gatherings, directing businesses and governmental agencies to cease non-essential operations at physical locations and advising against non-essential travel. In response to these public health directives and orders, we previously implemented work-from-home policies for certain employees and closed our office in South San Francisco requiring most of our personnel, including our administrative employees, to work remotely, and restricted on-site access to only those personnel performing essential activities. Although we have recently initiated the first phase of our return-to-work initiatives, the majority of our employees continue to work remotely. Our continued reliance on personnel working from home may negatively impact productivity, disrupt, delay, or otherwise adversely impact our business. In addition, with most of our employees continuing to work remotely, our exposure to cybersecurity risk has increased. This also creates data accessibility concerns and make us more susceptible to communication disruptions. Although most states and counties have since eased restrictions as the number of COVID-19 cases declined, the resurgence of COVID-19 cases and emergence of new variants of the virus, including the highly infectious Delta and Omicron variants of the virus, could force states and counties to reinstate more severe restrictions to reduce the spread of the disease. The evolving effects of the COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as significant reductions in business related activities have occurred, supply chains have been disrupted, and manufacturing and clinical development activities have been curtailed or suspended.

Since the COVID-19 pandemic was declared, we have continued to observe reduced patient-doctor interactions and our representatives have had fewer visits with health care providers, which negatively affected our product sales and may continue to negatively affect our product sales in the future. Physicians with practices severely impacted by the COVID-19 pandemic, and who currently prescribe TAVALISSE, may eventually decide to close their independent practices and join a larger medical organization with a practice that does not prescribe TAVALISSE. Additionally, commercial related activities, such as our marketing programs, speaker bureaus, and market access initiatives have been conducted virtually, delayed or cancelled as a result of the COVID-19 pandemic. Resources have been deployed to enable our field-based employees to continue to engage virtually with health care providers. Although these virtual engagements have enabled our field team to support existing prescribers, as well as partner with new prescribers to identify appropriate patients for TAVALISSE, we cannot rule out the future impact on our business if the pandemic continues for an extended period of time.

With respect to clinical development, we have taken, and continue to take, measures to implement remote and virtual approaches, including remote patient monitoring where possible per recent FDA guidance and working with our investigators for appropriate care of these patients in a safe manner consistent with agency guidelines. We have a number of ongoing clinical trials, including our global Phase 3 clinical studies in wAIHA and COVID. A number of our clinical trial investigators have paused, postponed or delayed new patient enrollment and restricted site visits of existing patients enrolled. Although some sites have resumed patient screening, the progress is slow, and we continue to experience delays in new patient enrollment. We are continuing to make decisions country-by-country to minimize risk to the patients and clinical trial sites. We also rely heavily on our clinical trial investigators to inform us of the best course of action with respect to resuming enrollment/screening, considering the ability of sites to ensure patient safety or data integrity. Patients already enrolled in our studies continue to receive study drug, and we remain focused on supporting our sites in providing care for these patients and providing continued investigational drug supply. We continue to experience slower than anticipated enrollment in some of our clinical trials, and at this time we cannot currently fully forecast the scope of impact that the COVID-19 pandemic may have overall on clinical study results, including the timing thereof, or our ability to continue to treat patients enrolled in our trials, enroll and assess new patients, supply study drug and obtain complete data points in accordance with study protocol.

With respect to our supply chain, we currently do not anticipate significant disruption in the supply chain for our commercial product, TAVALISSE. However, we do not know the full extent of the impact on our supply chain if the COVID-19 pandemic continues and persists for an extended period of time. We currently rely on third parties to, among other things, manufacture and ship our commercial product, raw materials and product supply for our clinical trials, perform quality testing and supply other goods and services to help manage our commercial activities, our clinical trials and our operations in the ordinary course of business. We have engaged actively with various elements of our supply chain and distribution channel, including our customers, contract manufacturers, and logistics and transportation provider, to meet demand for TAVALISSE and to remain informed of any challenges within our supply chain. We continue to monitor demand, and intend to adapt our plans as needed to continue to drive our business and meet our obligations during the evolving COVID-19 pandemic. However, if the COVID-19 pandemic continues and persists for an extended period of time, we may face continued disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of TAVALISSE. Such supply disruptions would adversely impact our ability to generate sales of and revenues from TAVALISSE and our business, financial condition, results of operations and growth prospects could be adversely affected.

The COVID-19 pandemic has similarly affected our collaboration and licensing partners for the commercialization of fostamatinib globally, as well as our ability to advance our various clinical stage programs. We do not yet know the full impact of such disruptions on our partners' ability to advance commercialization of fostamatinib in the market and the timing of enrollment and completion of various clinical trials being conducted by our collaboration partners.

Health regulatory agencies globally may experience prolonged disruptions in their operations as a result of the COVID-19 pandemic. For example, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products inspections of domestic manufacturing facilities through April 2020. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. On July 10, 2020, the FDA announced that it is working toward the goal of restarting on-site inspections it deems to be "mission critical." On August 19, 2020, the FDA published guidance clarifying how it intends to conduct inspections during the COVID-19 pandemic, including how it plans to determine which inspections are "mission critical." The Agency published an updated form of this guidance on May 17, 2021. Additionally, on April 14, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites. According to the guidance, the FDA intends to request such remote interactive evaluations in situations where an in-person inspection would not be prioritized, deemed mission-critical, or where direct inspection is otherwise limited by travel restrictions, but where the FDA determines that remote evaluation would still be appropriate. It is unclear how the FDA's policies and guidance will impact any inspections of our facilities, including our clinical trial sites. Regulatory authorities outside the US may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. It is unknown how long these disruptions could continue. Any de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the completion of our clinical trials.

In addition, the evolving effects of the COVID-19 pandemic have already resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we could experience an inability to access additional capital or we may not be able to meet the requirements under our credit agreement with MidCap Financial Trust (MidCap) in order for us to access the funds remaining under such credit agreement. We could also experience an impact on liquidity, which could in the future negatively affect our capacity for certain corporate development transactions or our ability to make other important, opportunistic investments. In addition, a recession or market correction resulting from the impact of the evolving effects of COVID-19 could materially affect our business and the value of our common stock. While we expect the evolving effects of the COVID-19 pandemic to adversely affect our business operations and financial results, the extent of the impact on our ability to generate sales of and revenues from our approved products, our ability to continue to secure new collaborations and support existing collaboration efforts with our partners, our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration and severity of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the US and other countries, and the effectiveness of actions taken globally to

contain and treat the disease. For example, if remote work policies for certain portions of our business, or that of our business partners, are continuously extended and become more restrictive, we may need to reassess our priorities and our corporate objectives. Given the global economic slowdown, the risks and uncertainties associated with the pandemic could adversely affect our business, financial condition, results of operations and growth prospects in the future periods.

To the extent the evolving effects of the COVID-19 pandemic continues to adversely affect our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described elsewhere in this "Risk Factors" section.

There is a high risk that drug discovery and development efforts might not generate successful product candidates.

At the present time, a significant portion of our operations are focused on various stages of drug identification and development. We currently have various product candidates in the clinical testing stage. In our industry, it is statistically unlikely that the limited number of compounds that we have identified as potential product candidates will actually lead to successful product development efforts. We have invested a significant portion of our efforts and financial resources into the development of fostamatinib. Our ability to generate product revenue, which will not occur until after regulatory approval, if ever, will depend on the successful development, regulatory approval and eventual commercialization of one of our product candidates.

Our compounds in clinical trials and our future leads for potential drug compounds are subject to the risks and failures inherent in the development of pharmaceutical products. These risks include, but are not limited to, the inherent difficulty in selecting the right drug and drug target and avoiding unwanted side effects, as well as unanticipated problems relating to product development, testing, enrollment, obtaining regulatory approvals, maintaining regulatory compliance, manufacturing, competition and costs and expenses that may exceed current estimates. In future clinical trials, we or our partners may discover additional side effects and/or a higher frequency of side effects than those observed in previously completed clinical trials. The results of preliminary and mid-stage clinical trials do not necessarily predict clinical or commercial success, and larger later-stage clinical trials may fail to confirm the results observed in the previous clinical trials. Similarly, a clinical trial may show that a product candidate is safe and effective for certain patient populations in a particular indication, but other clinical trials may fail to confirm those results in a subset of that population or in a different patient population, which may limit the potential market for that product candidate. With respect to our own compounds in development, we have established anticipated timelines with respect to the initiation of clinical trials based on existing knowledge of the compounds. However, we cannot provide assurance that we will meet any of these timelines for clinical development. Additionally, the initial results of a completed earlier clinical trial of a product candidate do not necessarily predict final results and the results may not be repeated in later clinical trials.

Because of the uncertainty of whether the accumulated preclinical evidence (PK, pharmacodynamic, safety and/or other factors) or early clinical results will be observed in later clinical trials, we can make no assurances regarding the likely results from our future clinical trials or the impact of those results on our business. For example, if our Phase 3 clinical trial in wAIHA or Phase 3 clinical trial to further evaluate fostamatinib in hospitalized patients with COVID-19, or any of our clinical trials fail to meet the primary efficacy endpoints, the commercial prospects of our business may be harmed, our ability to generate product revenues may be delayed or eliminated or we may be forced to undertake other strategic alternatives that are in our shareholders' best interests, including cost reduction measures. If we are unable to obtain adequate financing or engage in a strategic transaction on commercially reasonable terms or at all, we may be required to implement further cost reduction strategies which could significantly impact activities related to our commercial efforts and/or research and development of our future product candidates, and could significantly harm our business, financial condition and results of operations. In addition, these cost reduction strategies could cause us to further curtail our operations or take other actions that would adversely impact our shareholders.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and other federal and state healthcare laws, and the failure to comply with such laws could result in substantial penalties. Our employees, independent contractors, consultants, principal investigators, CROs, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payers and customers, may expose us to broadly applicable federal, state and foreign fraud and abuse and other healthcare laws and regulations including anti-kickback and false claims laws, data privacy and security laws, and transparency reporting laws. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any product for which we have obtained regulatory approval, or for which we obtain regulatory approval in the future. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws and regulations intended to prevent fraud, misconduct, bribery kickbacks, self-dealing and other abusive or inappropriate practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including promoting off-label uses of our products, commission compensation, certain customer incentive programs, certain patient support offerings, and other business arrangements generally. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of patient recruitment for clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. See "Part I, Item 1, Business – Government Regulation – Healthcare and Privacy Law and Regulation and Healthcare Reform" of this Annual Report on Form 10-K for more information on the healthcare laws and regulations that may affect our ability to operate.

We are also exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, principal investigators, CROs, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with the laws of the FDA and other similar foreign regulatory bodies; provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies; comply with manufacturing standards we have established; comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the US and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

We are also subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. Efforts to ensure that our business arrangements will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, 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, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We are subject to stringent and evolving privacy and information security laws, regulations, rules, policies, and contractual obligations, and changes in such laws, regulations, rules, policies, contractual obligations and our actual or perceived failure to comply with such requirements could subject us to significant investigations, fines, penalties and claims, any of which may have a material adverse effect on our business, financial condition, results of operations or prospects.

We are subject to, or affected by, various federal, state and foreign laws, rules, directives, and regulations, as well as regulatory guidance, policies and contractual obligations relating to privacy and information security, governing the acquisition, collection, access, use, disclosure, processing, modification, retention, storage, transfer, destruction, protection, and security (collectively, "processing") of personal information and other sensitive information about individuals. The global privacy and information security landscape is evolving rapidly, and implementation standards and enforcement practices are likely to continue to develop for the foreseeable future and may result in conflicting or inconsistent compliance obligations. Legislators and regulators are increasingly adopting or amending privacy and information security laws, rules, directives, and regulations that may create uncertainty in our business, affect our or our collaborators', service providers' and contractors' ability to operate in certain jurisdictions or to process personal information, transfer data internationally, necessitate the acceptance of more onerous obligations in our contracts, result in enforcement actions, litigation or other liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us or our collaborators, service providers and contractors to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing the processing of personal information could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions, litigation, and other consequences for noncompliance with privacy and information security laws and regulations are rising. Compliance with applicable privacy and information security laws and regulations, as well as regulatory guidance, policies and contractual obligations, is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms to ensure compliance with the new privacy and information security requirements. If we fail to comply with any such obligations, we may face significant investigations, fines, penalties and claims that could materially and adversely affect our business, financial condition, results of operations, ability to process personal information and income from certain business initiatives.

In the US, these obligations include various federal, state, and local statutes, rules, and regulations relating to privacy and data security. The Federal Trade Commission (FTC) has authority under Section 5 of the FTC Act to regulate unfair or deceptive or practices, and has used this authority to initiate enforcement actions against companies that implement inadequate controls around privacy and information security in violation of their externally facing policies. The US federal government has also enacted statutes to address privacy and information security issues impacting particular industries or activities, including the following laws and regulations: the Electronic Communications Privacy Act, the Computer Fraud and Abuse Act, the Health Insurance Portability and Accountability Act, the Health Information Technology for Economic and Clinical Health Act, the Telephone Consumer Protection Act, the CAN-SPAM Act, and other laws and regulations. In addition, state legislatures have enacted statutes to address privacy and information security issues, including the California Consumer Privacy Act of 2018(the CCPA), and similar state laws such as Virginia's Consumer Data Protection Act and the Colorado Privacy Act. For example, the CCPA establishes a privacy framework applicable to for-profit entities that are doing business in California, including an expansive definition of personal information and data privacy rights for California residents, and authorizes potentially severe statutory damages and creates a private right of action for certain data security breaches. The CCPA also requires businesses subject to the law to provide new disclosures to California residents and to provide them with expanded rights with respect to their personal information, including the right to opt out of the sale of such information. Although there are limited exemptions for clinical trial and other research-related data under the CCPA, the CCPA and other similar laws could impact our business depending on how it will be interpreted by the new California Privacy Protection Agency. As we expand our operations, the CCPA may increase our compliance costs and potential liability. In addition, California voters approved the California Privacy Rights Act of 2020 (CPRA), which goes into effect on January 1, 2023. The CPRA will, among other things, give California residents the ability to limit the use of their sensitive information, opt out of certain types of profiling and automated processing activities, provide for penalties for CPRA violations concerning California residents under the age of 16, and establish a new California Privacy Protection Agency to implement and enforce the law. Additionally, Colorado and Virginia both signed privacy legislation, each of which go into effect in 2023, and multiple other states and the federal government are considering enacting similar legislation. Many states also have in place data security laws requiring companies to maintain certain safeguards with respect to the

processing of personal information, and all states require companies to notify individuals or government regulators in the event of a data breach impacting such information. New privacy laws add additional complexity, requirements, restrictions and potential legal risk. Accordingly, compliance programs may require additional investment in resources, and could impact availability of previously useful data.

Internationally, our operations abroad may also be subject to increased scrutiny or attention from foreign data protection authorities. For example, our clinical trial programs and research collaborations outside the US may implicate foreign data protection laws, including in the European Economic Area, Switzerland, and/or the UK (collectively, "Europe"). Many jurisdictions have established or are in the process of establishing privacy and data security legal frameworks with which we, our collaborators, service providers, including our CROs, and contractors must comply. For example, European data protection laws, including, without limitation, the EU GDPR, impose strict requirements for processing personal information (i.e., data which identifies an individual or from which an individual is identifiable), including clinical trial data and grant individuals' various data protection rights (e.g., the right to erasure of personal information). In turn, the EU GDPR and similar laws increase our obligations with respect to clinical trials conducted in Europe by expanding the definition of personal information to also include coded data and requiring (i) changes to informed consent practices and more detailed notices for clinical trial participants and investigators; (ii) consideration of data protection as any new products or services are developed, including to limit the amount of personal information processed; and (iii) implementation of appropriate technical and organizational measures to safeguard personal information and to report certain personal data breaches to the relevant supervisory authority without undue delay (for the EU GDPR no later than 72 hours where feasible). In the event of non-compliance, the EU GDPR provides for robust regulatory enforcement and fines of up to €20 million or 4% of the annual global revenue, whichever is greater. In addition, the EU GDPR confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the EU GDPR.

European data protection laws, including the EU GDPR, generally also prohibit the transfer of personal information from Europe to the US and most other countries that are not recognized as having "adequate" data protection laws unless the parties to the transfer have implemented specific safeguards to protect the transferred personal information. One of the primary safeguards allowing US companies to import personal information from Europe has been certification to the EU-US Privacy Shield and Swiss-US Privacy Shield frameworks administered by the US Department of Commerce. However, the Court of Justice of the European Union (CJEU) issued a decision in July 2020 invalidating the EU-US Privacy Shield framework as a data transfer mechanism (*Schrems II*) and imposing further restrictions on the use of standard contractual clauses (SCCs), including a requirement for companies to carry out a transfer privacy impact assessment, which, among other things, assesses laws governing access to personal information in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under the SCCs will need to be implemented to ensure an essentially equivalent level of data protection to that afforded in Europe. Following that decision, the Swiss Federal Data Protection and Information Commissioner (FDPIC) took a similar view and considered that data transfers based on the Swiss-US Privacy Shield framework are no longer lawful (despite the fact that *Schrems II* is not directly applicable in Switzerland (unless the Swiss based company is subject to the EU GDPR) and the Swiss-US Privacy Shield has not been officially invalidated). Further, the European Commission recently published new EU SCCs, which place onerous obligations on the contracting parties. At present, there are few, if any, viable alternatives to the SCCs. As such, any transfers by us or our third-party vendors, collaborators or others of personal information from Europe to the US or elsewhere may not comply with European data protection laws, may increase our exposure to European data protection laws' heightened sanctions for cross-border data transfer restrictions may restrict our clinical trial activities in Europe and may limit our ability to collaborate with CROs, service providers, contractors and other companies subject to European data protection laws. Loss of our ability to transfer personal information from Europe may also require us to increase our data processing capabilities in those jurisdictions at significant expense.

Following the UK's departure from the EU (Brexit), the EU GDPR's data protection obligations continue to apply to the UK in substantially unvaried form under the so-called "UK GDPR" (i.e., the EU GDPR as it continues to form part of law in the UK by virtue of section 3 of the European Union (Withdrawal) Act 2018, as amended (including by the various Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations)). The UK GDPR exists alongside the UK Data Protection Act 2018 that implements certain derogations in the UK GDPR into UK law. Under the UK GDPR, companies not established in the UK but that process personal information either in

relation to the offering of goods or services to individuals in the UK, or to monitor their behavior will be subject to the UK GDPR, the requirements of which are (at this time) largely aligned with those under the EU GDPR, and as such, may lead to similar compliance and operational costs with potential fines of up to £17.5 million or 4% of global turnover. As a result, we are potentially exposed to two parallel data protection regimes, each of which authorizes fines and the potential for divergent enforcement actions. It should also be noted that the new EU SCCs do not automatically apply in the UK since Brexit. However, on January 28, 2022, the UK Government laid before the UK Parliament its International Data Transfer Agreement (IDTA) and International Data Transfer Addendum (UK Addendum) to the new EU SCCs. If no objections are raised by the UK Parliament, the IDTA and the UK Addendum will come into force on March 21, 2022. The UK Information Commissioner's Office (ICO) is also expected to shortly publish its version of the transfer impact assessment.

Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, with strict requirements and limitations for processing personal information, which could increase the cost and complexity of delivering our services and operating our business. For example, Brazil enacted the General Data Protection Law, New Zealand enacted the New Zealand Privacy Act, China released its Personal Information Protection Law, which went into effect November 1, 2021, and Canada introduced the Digital Charter Implementation Act. As with the EU GDPR, these laws are broad and may increase our compliance burdens, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain, and process personal information about them.

We publish privacy policies and other documentation regarding our collection, processing, use and disclosure of personal information and/or other confidential information. Although we endeavor to comply with our published policies and other documentation, we may at times fail to do so or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our employees, collaborators, contractors, service providers or vendors fail to act in accordance with our published policies and documentation. Such failures can subject us to potential foreign, local, state and federal action if they are found to be deceptive, unfair, or misrepresentative of our actual practices. Moreover, trial participants or research subjects about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information or exercise their right to do so under applicable privacy legislation. Claims that we have violated individuals' privacy rights or failed to comply with data protection laws or applicable privacy policies and documentation, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

In addition to data privacy requirements, many jurisdictions impose mandatory clinical trial information obligations on sponsors. In the EU, such obligations arise under the Transparency Regulation No 1049/ 2001, EMA Policy 0043, EMA Policy 0070 and the Clinical Trials Regulation No 536/2014, all of which impose on sponsors the obligation to make publicly available certain information stemming from clinical studies. In the EU, the transparency framework provides EU-based parties the right to submit an access to documents request to the EMA for information included in the marketing authorization application dossier for approved medicinal products. Only very limited information is exempted from disclosure, i.e. commercially confidential information (which is construed increasingly narrowly) and protected personal data. It is possible for competitors to access and use this data in their own research and development programs anywhere in the world, once this data is in the public domain.

Enhanced governmental and public scrutiny over, or investigations or litigation involving, pharmaceutical manufacturer donations to patient assistance programs may require us to modify our programs and could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

To help patients afford our products, we have a patient assistance program that helps financially needy patients. This type of program has become the subject of enforcement scrutiny in recent years. For example, some pharmaceutical manufacturers have been named in class action lawsuits challenging the legality of their patient assistance programs under a variety of federal and state laws. Our patient assistance program could become the target of similar litigation. In addition, certain state and federal enforcement authorities and members of Congress have initiated inquiries about manufacturer-sponsored patient support programs, including, for example, manufacturer-sponsored patient assistance programs, co-pay assistance programs, and manufacturer contributions to independent charitable patient assistance programs. Some state legislatures have also been considering proposals that would restrict or ban co-pay coupons.

If we are deemed not to have complied with laws or regulations in the operation of, or our interactions with, these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. Further, numerous organizations, including pharmaceutical manufacturers, have been subject to ongoing litigation, enforcement activities and settlements related to their patient support programs and certain of these organizations have entered into, or have otherwise agreed to, significant civil settlements with applicable enforcement authorities. It is possible that future legislation may be proposed that would establish requirements with respect to these programs and/or support that would affect pharmaceutical manufacturers. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. A government investigation could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

If manufacturers obtain approval for generic versions of TAVALISSE, or of products with which we compete, our business may be harmed.

Under the FDCA, the FDA can approve an abbreviated new drug application (ANDA) for a generic version of a branded drug without the ANDA applicant undertaking the clinical testing necessary to obtain approval to market a new drug. Generally, in place of such clinical studies, an ANDA applicant usually needs only to submit data demonstrating that its product has the same active ingredient(s), strength, dosage form and route of administration and that it is bioequivalent to the branded product. In September 2019, the FDA published product-specific bioequivalence guidance on fostamatinib disodium to let potential ANDA applicants understand the data FDA would expect to see for approval of a generic version of TAVALISSE.

The FDCA requires that an applicant for approval of a generic form of a branded drug certify either that its generic product does not infringe any of the patents listed by the owner of the branded drug in the Orange Book or that those patents are not enforceable. This process is known as a paragraph IV challenge. Upon notice of a paragraph IV challenge, a patent owner has 45 days to bring a patent infringement suit in federal district court against the company seeking ANDA approval of a product covered by one of the owner's patents. If this type of suit is commenced, the FDCA provides a 30-month stay on the FDA's approval of the competitor's application. If the litigation is resolved in favor of the ANDA applicant or the challenged patent expires during the 30-month stay period, the stay is lifted, and the FDA may thereafter approve the application based on the standards for approval of ANDAs. Once an ANDA is approved by the FDA, the generic manufacturer may market and sell the generic form of the branded drug in competition with the branded medicine.

The ANDA process can result in generic competition if the patents at issue are not upheld or if the generic competitor is found not to infringe the owner's patents. If this were to occur with respect to TAVALISSE or products with which it competes, our business would be harmed. We have a number of patents listed in the Orange Book, the last of which is expected to expire in July 2032.

Unforeseen safety issues could emerge with TAVALISSE that could require us to change the prescribing information to add warnings, limit use of the product, and/or result in litigation. Any of these events could have a negative impact on our business.

Discovery of unforeseen safety problems or increased focus on a known problem could impact our ability to commercialize TAVALISSE and could result in restrictions on its permissible uses, including withdrawal of the medicine from the market.

If we or others identify additional undesirable side effects caused by TAVALISSE after approval:

- regulatory authorities may require the addition of labeling statements, specific warnings, contraindications, or field alerts to physicians and pharmacies;
- regulatory authorities may withdraw their approval of the product and require us to take our approved drugs off the market;

- we may be required to change the way the product is administered, conduct additional clinical trials, change the labeling of the product, or implement a Risk Evaluation and Mitigation Strategy, or REMS;
- we may have limitations on how we promote our drugs;
- third-party payers may limit coverage or reimbursement for TAVALISSE;
- sales of TAVALISSE may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of TAVALISSE and could substantially increase our operating costs and expenses, which in turn could delay or prevent us from generating significant revenue from sale of TAVALISSE.

If a safety issue emerges post-approval, we may become subject to costly product liability litigation by our customers, their patients or payers. Product liability claims could divert management's attention from our core business, be expensive to defend, and result in sizable damage awards against us that may not be covered by insurance. If we cannot successfully defend ourselves against claims that TAVALISSE caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

We currently hold $10.0 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to obtain insurance coverage at a reasonable cost or in amounts adequate to satisfy any liability or associated costs that may arise in the future. These events could harm our business and results of operations and cause our stock price to decline.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the US, we could be subject to additional reimbursement requirements, fines, sanctions and exposure under other laws which could have an adverse effect on our business, results of operations and financial condition.

We participate in the Medicaid Drug Rebate Program, as administered by CMS, and other federal and state government drug pricing programs in the US, and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payers in connection with drugs that are dispensed to beneficiaries/recipients of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing metrics that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing requirements and rebate/discount calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The requirements of these programs, including, by way of example, their respective terms and scope, change frequently. Responding to current and future changes may increase our costs, and the complexity of

compliance will be time consuming. Invoicing for rebates is provided in arrears, and there is frequently a time lag of up to several months between the sales to which rebate notices relate and our receipt of those notices, which further complicates our ability to accurately estimate and accrue for rebates related to the Medicaid program as implemented by individual states. Thus, there can be no assurance that we will be able to identify all factors that may cause our discount and rebate payment obligations to vary from period to period, and our actual results may differ significantly from our estimated allowances for discounts and rebates. Changes in estimates and assumptions may have an adverse effect on our business, results of operations and financial condition.

In addition, the Office of Inspector General of HHS and other Congressional enforcement and administrative bodies have recently increased their focus on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate average manufacturer price (AMP) and best price (BP) for compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payers. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the federal False Claims Act and other laws and regulations. Any required refunds to the US government or response to a government investigation or enforcement action would be expensive and time consuming and could have an adverse effect on our business, results of operations and financial condition. In addition, in the event that CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid for our covered outpatient drugs or under Medicare Part B for any of our products that may be reimbursed under Part B.

Even for those product candidates that have or may receive regulatory approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

For our product candidates that have or may receive regulatory approval, they may nonetheless fail to gain sufficient market acceptance by physicians, hospital administrators, patients, healthcare payors and others in the medical community. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including the following:

- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the willingness of physicians to change their current treatment practices;
- the willingness of hospitals and hospital systems to include our product candidates as treatment options;
- demonstration of efficacy and safety in clinical trials;
- the prevalence and severity of any side effects;
- the ability to offer product candidates for sale at competitive prices;
- the price we charge for our product candidates;
- the strength of marketing and distribution support; and
- the availability of third-party coverage and adequate reimbursement and the willingness of patients to pay out-of-pocket in the absence of such coverage and adequate reimbursement.

Efforts to educate the physicians, patients, healthcare payors and others in the medical community on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates are approved, if at all, but do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable on a sustained basis.

We will need additional capital in the future to sufficiently fund our operations and research.

We have consumed substantial amounts of capital to date as we continue our research and development activities, including preclinical studies and clinical trials and for the commercial launch of TAVALISSE. We may seek another collaborator or licensee in the future for further clinical development and commercialization of fostamatinib, as well as our other clinical programs, which we may not be able to obtain on commercially reasonable terms or at all. We believe that our existing capital resources will be sufficient to support our current and projected funding requirements, including the continued commercial launch of TAVALISSE in the US, through at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with commercial launch, the development of our product candidates and other research and development activities, we are unable to estimate with certainty our future product revenues, our revenues from our current and future collaborative partners, the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials and other research and development activities.

We will continue to need additional capital and the amount of future capital needed will depend largely on the success of our commercial launch of TAVALISSE and the success of our internally developed programs as they proceed in later and more expensive clinical trials, including any additional clinical trials that we may decide to conduct with respect to fostamatinib. While we intend to opportunistically seek access to additional funds through public or private equity offerings or debt financings, we do not know whether additional financing will be available when needed, or that, if available, we will obtain financing on reasonable terms. Our ability to raise additional capital, including our ability to secure new collaborations and continue to support existing collaboration efforts with our partners, may also be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the US and worldwide resulting from the ongoing COVID-19 pandemic. Unless and until we are able to generate a sufficient amount of product, royalty or milestone revenue, which may never occur, we expect to finance future cash needs through public and/or private offerings of equity securities, debt financings or collaboration and licensing arrangements, as well as through proceeds from the exercise of stock options and interest income earned on the investment of our cash balances and short-term investments. To the extent we raise additional capital by issuing equity securities in the future, our stockholders could at that time experience substantial dilution. In addition, we have a significant number of stock options outstanding. To the extent that outstanding stock options have been or may be exercised or other shares issued, our stockholders may experience further dilution. Further, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Our credit facility with MidCap includes certain covenants that may restrict our business, and any other debt financing that we are able to obtain in the future may involve operating covenants that restrict our business. To the extent that we raise additional funds through any new collaboration and licensing arrangements, we may be required to refund certain payments made to us, relinquish some rights to our technologies or product candidates or grant licenses on terms that are not favorable to us.

We have indebtedness in the form of a term loan pursuant to the Credit Agreement (as defined below) with MidCap, which could adversely affect our financial condition and our ability to respond to changes in our business. Further, if we are unable to satisfy certain conditions of the Credit Agreement, we will be unable to draw down the remainder of the facility.

On February 11, 2022, we entered into a Second Amendment (Second Amendment) to that certain Credit and Security Agreement, dated as of September 27, 2019, with MidCap (the initial Credit Agreement and, as modified by the Second Amendment, the Credit Agreement). Under the Credit Agreement, we are required to repay amounts due when there is an event of default for the term loans that results in the principal, premium, if any, and interest, if any, becoming due prior to the maturity date for the term loans. The Credit Agreement also contains a number of other affirmative and restrictive covenants. See “Note 10 – Debt” to our “Notes to Financial Statements” contained in “Part II, Item 8, Financial Statements and Supplementary Data” of this Annual Report on Form 10-K for additional details of the Credit Agreement. These and other terms in the Credit Agreement have to be monitored closely for compliance and could restrict our ability to grow our business or enter into transactions that we believe would be beneficial to our business. Our business may not generate cash flow from operations in the future sufficient to service our debt and support our growth strategies. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as restructuring our debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our

ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our current debt obligations. In addition, we cannot be sure that additional financing will be available when required or, if available, will be on terms satisfactory to us. Further, even if we are able to obtain additional financing, we may be required to use such proceeds to repay a portion of our debt.

Our indebtedness may have other adverse effects, such as:

- our vulnerability to adverse general economic conditions and heightened competitive pressures;
- dedication of a portion of our cash flow from operations to interest payments, limiting the availability of cash for other operational purposes;
- limited flexibility in planning for, or reacting to, changes in our business and industry; and
- our inability to obtain additional financing in the future.

Our Credit Agreement with MidCap contains a mandatory prepayment provision that gives MidCap and/or its Agent the right to demand payment of the outstanding principal and additional interest and fees in the event of default. We may not have enough available cash or be able to obtain financing at the time we are required to repay the term loan with additional interest and fees prior to maturity.

At closing, $10.0 million was funded to us in an initial tranche. The initial Credit Agreement also gave us the ability to access an additional $50.0 million at our option, of which $40.0 million may be drawn in two tranches subject to the achievement of certain customary conditions. In May 2020, our second tranche of $10.0 million was funded by MidCap. The Second Amendment, among other things, amended the applicable funding conditions, applicable commitments and certain other terms relating to available credit facilities (Tranches 3 and 4), added additional term loan credit facility (Tranche 5), and revised certain terms related to the financial covenants. Following the Second Amendment, the Credit Agreement gives us the ability to access the following available credit facilities: (i) on the closing date of the Second Amendment, $10.0 million term loan facility (Tranche 3), (ii) until August 31, 2022, an additional $10.0 million aggregate principal amount of term loan facility at our option (Tranche 4), and (iii) until March 31, 2023, an additional $20.00 million term aggregate principal amount of term loan facility subject to the satisfaction of applicable funding conditions which include minimum net revenue and compliance with financial covenants set forth in the Credit Agreement. On the closing of the Second Amendment, Tranche 3 of $10.0 million was funded by MidCap. If we are unable to satisfy these or other required conditions, we would not be able to draw down the remaining tranches of financing and may not be able to obtain alternative financing on commercially reasonable terms or at all, which could adversely impact our business.

We rely and may continue to rely on two distribution facilities for the sale of TAVALISSE and potential sale of any of our product candidates.

Our distribution operations for the sale of TAVALISSE is currently concentrated in two distribution centers owned by a third-party logistics provider. Additionally, our distribution operations, if and when we launch any of our product candidates in the future, may also be concentrated in such distribution centers owned by a third-party logistics provider. Any errors in inventory level management and unforeseen inventory shortage could adversely affect our business. In addition, any significant disruption in the operation of the facility due to natural disaster or severe weather, or events such as fire, accidents, power outages, system failures, or other unforeseen causes, could devalue or damage a significant portion of our inventories and could adversely affect our product distribution and sales until such time as we could secure an alternative facility. If we encounter difficulties with any of our distribution facilities, whether due to the impacts of the ongoing COVID-19 pandemic (including as a result of disruptions of global shipping and the transport of products) or otherwise, or other problems or disasters arise, we cannot ensure that critical systems and operations will be restored in a timely manner or at all, and this would have an adverse effect on our business. In addition, growth could require us to further expand our current facility, which could affect us adversely in ways that we cannot predict.

Forecasting potential sales for any of our product candidates will be difficult, and if our projections are inaccurate, our business may be harmed, and our stock price may be adversely affected.

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

- the efficacy and safety of any of our product candidates, including as relative to marketed products and product candidates in development by third parties;
- pricing (including discounting or other promotions), reimbursement, product returns or recalls, competition, labeling, adverse events and other items that impact commercialization;
- the rate of adoption in the particular market, including fluctuations in demand for various reasons;
- impacts due to the ongoing COVID-19 pandemic;
- lack of patient and physician familiarity with the drug;
- lack of patient use and physician prescribing history;
- lack of commercialization experience with the drug;
- actual sales to patients may significantly differ from expectations based on sales to wholesalers; and
- uncertainty relating to when the drug may become commercially available to patients and rate of adoption in other territories.

We expect that our revenues from sales of any of our product candidates will continue to be based in part on estimates, judgment and accounting policies. Any incorrect estimates or disagreements with regulators or others regarding such estimates or accounting policies may result in changes to our guidance, projections or previously reported results. Expected and actual product sales and quarterly and other results may greatly fluctuate, including in the near-term, and such fluctuations can adversely affect the price of our common stock, perceptions of our ability to forecast demand and revenues, and our ability to maintain and fund our operations.

We do not and will not have access to all information regarding fostamatinib and product candidates we licensed to Lilly, Kissei, Grifols and Medison.

We do not and will not have access to all information regarding fostamatinib and other product candidates, including potentially material information about commercialization plans, medical information strategies, clinical trial design and execution, safety reports from clinical trials, safety reports, regulatory affairs, process development, manufacturing and other areas known by Lilly, Kissei, Grifols and Medison. In addition, we have confidentiality obligations under our respective agreements with Lilly, Kissei, Grifols and Medison. Thus, our ability to keep our shareholders informed about the status of fostamatinib and other product candidates will be limited by the degree to which Lilly, Kissei, Grifols and/or Medison keep us informed and allows us to disclose such information to the public. If Lilly, Kissei, Grifols and/or Medison fail to keep us informed about commercialization efforts related to fostamatinib, or the status of the clinical development or regulatory approval pathway of other product candidates licensed to them, we may make operational and/or investment decisions that we would not have made had we been fully informed, which may adversely affect our business and operations.

Our future funding requirements will depend on many uncertain factors.

Our future funding requirements will depend upon many factors, many of which are beyond our control, including, but not limited to:

- the costs to commercialize fostamatinib for the treatment of ITP in the US, or any other future product candidates, if any such candidate receives regulatory approval for commercial sale;
- the progress and success of our clinical trials and preclinical activities (including studies and manufacture of materials) of our product candidates conducted by us;
- any current and future impacts of the ongoing and evolving COVID-19 pandemic;
- the costs and timing of regulatory filings and approvals by us and our collaborators;
- the progress of research and development programs carried out by us and our collaborative partners;
- any changes in the breadth of our research and development programs;
- the ability to achieve the events identified in our collaborative agreements that may trigger payments to us from our collaboration partners;
- our ability to acquire or license other technologies or compounds that we may seek to pursue;
- our ability to manage our growth;
- competing technological and market developments;
- the costs and timing of obtaining, enforcing and defending our patent and other intellectual property rights; and
- expenses associated with any unforeseen litigation, including any arbitration and securities class action lawsuits.

Insufficient funds may require us to delay, scale back or eliminate some or all of our commercial efforts and/or research and development programs, to reduce personnel and operating expenses, to lose rights under existing licenses or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose or may adversely affect our ability to operate as a going concern.

Our success as a company is uncertain due to our history of operating losses and the uncertainty of any future profitability.

We recognized loss from operations of $12.5 million in 2021 primarily due to higher operating expenses, partly offset by the revenue recognized from our product sales, the Lilly Agreement and the grant from the US Department of Defense. We have historically incurred losses from operations each year since we were incorporated in June 1996 other than in fiscal year 2010, due in large part to the significant research and development expenditures required to identify and validate new product candidates and pursue our development efforts, and the costs of our ongoing commercial efforts for TAVALISSE. We expect to continue to incur losses from operations, at least in the next 12 months, and there can be no assurance that we will generate annual operating income in the foreseeable future. Currently, our potential sources of revenues are our sales of TAVALISSE, upfront payments, research and development contingent payments and royalty payments pursuant to our collaboration arrangements, which may never materialize if our collaborators do not achieve certain events or generate net sales to which these contingent payments are dependent on. If our future drug candidates fail or do not gain regulatory approval, or if our drugs do not achieve sustainable market acceptance, we may not be profitable. As of December 31, 2021, we had an accumulated deficit of approximately $1.3 billion. The extent of our future losses or profitability, if any, especially due to the ongoing COVID-19 pandemic, is highly uncertain.

If our corporate collaborations or license agreements are unsuccessful, or if we fail to form new corporate collaborations or license agreements, our research and development efforts could be delayed.

Our strategy depends upon the formation and sustainability of multiple collaborative arrangements and license agreements with third parties now and in the future. We rely on these arrangements for not only financial resources, but also for expertise we need now and in the future relating to clinical trials, manufacturing, sales and marketing, and for licenses to technology rights. To date, we have entered into several such arrangements with corporate collaborators; however, we do not know if these collaborations or additional collaborations with third parties, if any, will dedicate sufficient resources or if any development or commercialization efforts by third parties will be successful. In addition, our corporate collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate or development program. Should a collaborative partner fail to develop or commercialize a compound or product to which it has rights from us for any reason, including corporate restructuring, such failure might delay our ongoing research and development efforts, because we might not receive any future payments, and we would not receive any royalties associated with such compound or product. We are conducting a Phase 3 clinical program to study fostamatinib in wAIHA on our own. We may seek another collaborator or licensee in the future for clinical development and commercialization of fostamatinib, as well as our other clinical programs, which we may not be able to obtain on commercially reasonable terms or at all. If we are unable to form new collaborations or enter into new license agreements, our research and development efforts could be delayed. In addition, the continuation of some of our partnered drug discovery and development programs may be dependent on the periodic renewal of our corporate collaborations.

Each of our collaborations could be terminated by the other party at any time, and we may not be able to renew these collaborations on acceptable terms, if at all, or negotiate additional corporate collaborations on acceptable terms, if at all. If these collaborations terminate or are not renewed, any resultant loss of revenues from these collaborations or loss of the resources and expertise of our collaborative partners could adversely affect our business.

Conflicts also might arise with collaborative partners concerning proprietary rights to particular compounds. While our existing collaborative agreements typically provide that we retain milestone payments, royalty rights and/or revenue sharing with respect to drugs developed from certain compounds or derivative compounds, any such payments or royalty rights may be at reduced rates, and disputes may arise over the application of payment provisions or derivative payment provisions to such drugs, and we may not be successful in such disputes. For example, in September 2018, BerGenBio served us with a notice of arbitration seeking declaratory relief related to the interpretation of provisions under our June 2011 license agreement, particularly as they relate to the rights and obligations of the parties in the event of the license or sale of a product in the program by BerGenBio and/or the sale of BerGenBio to a third party. The arbitration panel dismissed four of the six declarations sought by BerGenBio, and we thereafter consented to one of the remaining declarations requested by BerGenBio. On February 27, 2019, the arbitration panel issued a determination granting the declaration sought by BerGenBio on the remaining issue, and held that in the event of a sale of shares by BerGenBio's shareholders where there is no monetary benefit to BerGenBio, we would not be entitled to a portion of the proceeds from such a sale. In this circumstance where the revenue share provision is not triggered, the milestone and royalty payment provisions remain in effect. While we do not believe that the determination will have an adverse effect on our operations, cash flows or financial condition, we can make no assurance regarding any such impact. Additionally, the management teams of our collaborators may change for various reasons including due to being acquired. Different management teams or an acquiring company of our collaborators may have different priorities which may have adverse results on the collaboration with us.

We are also a party to various license agreements that give us rights to use specified technologies in our research and development processes. The agreements pursuant to which we have in-licensed technology permit our licensors to terminate the agreements under certain circumstances. If we are not able to continue to license these and future technologies on commercially reasonable terms, our product development and research may be delayed or otherwise adversely affected.

If conflicts arise between our collaborators or advisors and us, any of them may act in their self-interest, which may be adverse to our stockholders' interests.

If conflicts arise between us and our corporate collaborators or scientific advisors, the other party may act in its self-interest and not in the interest of our stockholders. Some of our corporate collaborators are conducting multiple product development efforts within each disease area that is the subject of the collaboration with us or may be acquired or merged with a company having a competing program. In some of our collaborations, we have agreed not to conduct, independently or with any third party, any research that is competitive with the research conducted under our collaborations. Our collaborators, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by our collaborators or to which our collaborators have rights, may result in their withdrawal of support for our product candidates.

If any of our corporate collaborators were to breach or terminate its agreement with us or otherwise fail to conduct the collaborative activities successfully and in a timely manner, the preclinical or clinical development or commercialization of the affected product candidates or research programs could be delayed or terminated. We generally do not control the amount and timing of resources that our corporate collaborators devote to our programs or potential products. We do not know whether current or future collaborative partners, if any, might pursue alternative technologies or develop alternative products either on their own or in collaboration with others, including our competitors, as a means for developing treatments for the diseases targeted by collaborative arrangements with us.

Our success is dependent on intellectual property rights held by us and third parties, and our interest in such rights is complex and uncertain.

Our success will depend to a large part on our own, our licensees' and our licensors' ability to obtain and defend patents for each party's respective technologies and the compounds and other products, if any, resulting from the application of such technologies. For example, fostamatinib is covered as a composition of matter in a US issued patent that has an expected expiration date of September 2031, after taking into account patent term adjustment and extension rules.

In the future, our patent position might be highly uncertain and involve complex legal and factual questions. For example, we may be involved in post-grant proceedings before the US Patent and Trademark Office. Post-grant proceedings are complex and expensive legal proceedings and there is no assurance we will be successful in any such proceedings. A post-grant proceeding could result in our losing our patent rights and/or our freedom to operate and/or require us to pay significant royalties. Additionally, third parties may challenge the validity, enforceability or scope of our issued patents, which may result in such patents being narrowed, invalidated or held unenforceable through interference, opposition or invalidity proceedings before the US Patent and Trademark Office or non-US patent offices. Any successful opposition to our patents could deprive us of exclusive rights necessary for the successful commercialization of fostamatinib or our other product candidates. Oppositions could also be filed to complementary patents, such as formulations, methods of manufacture and methods of use, that are intended to extend the patent life of the overall portfolio beyond the patent life covering the composition of matter. A successful opposition to any such complementary patent could impact our ability to extend the life of the overall portfolio beyond that of the related composition of matter patent.

Additional uncertainty may result because no consistent policy regarding the breadth of legal claims allowed in biotechnology patents has emerged to date. Accordingly, we cannot predict the breadth of claims allowed in our or other companies' patents.

Because the degree of future protection for our proprietary rights is uncertain, we cannot assure you that:

- we were the first to make the inventions covered by each of our pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;

- any of our pending patent applications will result in issued patents;
- any patents issued to us or our collaborators will provide a basis for commercially viable products or will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies that are patentable; or
- the patents of others will not have a negative effect on our ability to do business.

We rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable; however, trade secrets are difficult to protect. While we require employees, collaborators and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information.

We are a party to certain in-license agreements that are important to our business, and we generally do not control the prosecution of in-licensed technology. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology. Moreover, some of our academic institution licensors, research collaborators and scientific advisors have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, our ability to receive patent protection or protect our proprietary information may otherwise be impaired. In addition, some of the technology we have licensed relies on patented inventions developed using US government resources.

The US government retains certain rights, as defined by law, in such patents, and may choose to exercise such rights. Certain of our in-licenses may be terminated if we fail to meet specified obligations. If we fail to meet such obligations and any of our licensors exercise their termination rights, we could lose our rights under those agreements. If we lose any of our rights, it may adversely affect the way we conduct our business. In addition, because certain of our licenses are sublicenses, the actions of our licensors may affect our rights under those licenses.

If a dispute arises regarding the infringement or misappropriation of the proprietary rights of others, such dispute could be costly and result in delays in our research and development activities and partnering.

Our success will depend, in part, on our ability to operate without infringing or misappropriating the proprietary rights of others. There are many issued patents and patent applications filed by third parties relating to products or processes that are similar or identical to our licensors or ours, and others may be filed in the future. There may also be copyrights or trademarks that third parties hold. There can be no assurance that our activities, or those of our licensors, will not violate intellectual property rights of others. We believe that there may be significant litigation in the industry regarding patent and other intellectual property rights, and we do not know if our collaborators or we would be successful in any such litigation. Any legal action against our collaborators or us claiming damages or seeking to enjoin commercial activities relating to the affected products, our methods or processes could:

- require our collaborators or us to obtain a license to continue to use, manufacture or market the affected products, methods or processes, which may not be available on commercially reasonable terms, if at all;
- prevent us from using the subject matter claimed in the patents held by others;
- subject us to potential liability for damages;
- consume a substantial portion of our managerial and financial resources; and
- result in litigation or administrative proceedings that may be costly, whether we win or lose.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous US states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

Our ability to use net operating losses (NOLs) and certain other tax attributes is uncertain and may be limited.

Our ability to use our federal and state NOLs to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the NOLs, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our NOLs. Federal NOLs generated prior to 2018 will continue to be governed by the NOL carryforward rules as they existed prior to the adoption of the Tax Cuts and Jobs Act (Tax Act), which means that generally they will expire 20 years after they were generated if not used prior thereto. Many states have similar laws. Accordingly, our federal and state NOLs could expire unused and be unavailable to offset future income tax liabilities. Under the Tax Act as modified by the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), federal NOLs incurred in tax years beginning after December 31, 2017 and before January 1, 2021 may be carried back to each of the five tax years preceding such loss, and NOLs arising in tax years beginning after December 31, 2020 may not be carried back. Moreover, federal NOLs generated in tax years ending after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs may be limited to 80% of current year taxable income for tax years beginning after January 1, 2021. Under A.B. 85, the Company's California NOL carryforwards are suspended for tax years 2020, 2021, and 2022, but the period to use these carryovers was extended.

In addition, utilization of NOLs to offset potential future taxable income and related income taxes that would otherwise be due is subject to annual limitations under the "ownership change" provisions of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (Code) and similar state provisions, which may result in the expiration of NOLs before future utilization. In general, under the Code, if a corporation undergoes an "ownership change," 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 NOLs and other pre-change tax attributes (such as research and development credit carryforwards) to offset its post-change taxable income or taxes may be limited. Our equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. Although we have completed studies to provide reasonable assurance that an ownership change limitation would not apply, we cannot be certain that a taxing authority would reach the same conclusion. If, after a review or audit, an ownership change limitation were to apply, utilization of our domestic NOLs and tax credit carryforwards could be limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities. Moreover, our ability to utilize our NOLs is conditioned upon us achieving profitability and generating US federal taxable income.

Because we expect to be dependent upon collaborative and license agreements, we might not meet our strategic objectives.

Our ability to generate revenue in the near term depends on the timing of recognition of certain upfront payments, achievement of certain payment triggering events with our existing collaboration agreements and our ability to enter into additional collaborative agreements with third parties. Our ability to enter into new collaborations and the revenue, if any, that may be recognized under these collaborations is highly uncertain. If we are unable to enter into one or more new collaborations, our business prospects could be harmed, which could have an immediate adverse effect on our ability to continue to develop our compounds and on the trading price of our stock. Our ability to enter into a collaboration may be dependent on many factors, such as the results of our clinical trials, competitive factors and the fit of one of our programs with another company's risk tolerance, including toward regulatory issues, patent portfolio, clinical pipeline, the stage of the available data, particularly if it is early, overall corporate goals and financial position.

To date, a portion of our revenues have been related to the research or transition phase of each of our collaborative agreements. Such revenues are for specified periods, and the impact of such revenues on our results of operations is at least partially offset by corresponding research costs. Following the completion of the research or transition phase of each collaborative agreement, additional revenues may come only from payments triggered by milestones and/or the achievement of other contingent events, and royalties, which may not be paid, if at all, until certain conditions are met. This risk is heightened due to the fact that unsuccessful research efforts may preclude us from receiving any contingent payments under these agreements. Our receipt of revenues from collaborative arrangements is also significantly affected by the timing of efforts expended by us and our collaborators and the timing of lead compound identification. We have received payments from our collaborations with Lilly, Grifols, Kissei, Medison, Aclaris, Celgene, BMS, AZ, BerGenBio, Janssen Pharmaceutica N.V., a division of Johnson & Johnson, Novartis Pharma A.G., Daiichi, Merck & Co., Inc., Merck Serono and Pfizer. Under many agreements, future payments may not be earned until the collaborator has advanced product candidates into clinical testing, which may never occur or may not occur until sometime well into the future. If we are not able to generate revenue under our collaborations when and in accordance with our expectations or the expectations of industry analysts, this failure could harm our business and have an immediate adverse effect on the trading price of our common stock.

Our business requires us to generate meaningful revenue from royalties and licensing agreements. To date, we have not received any revenue from royalties for the commercial sale of drugs, and we do not know when we will receive any such revenue, if at all.

Securities class action lawsuits or other litigation could result in substantial damages and may divert management's time and attention from our business.

We have been subject to class action lawsuits in the past and we may be subject to lawsuits in the future, such as those that might occur if there was to be a change in our corporate strategy. These and other lawsuits are subject to inherent uncertainties, and the actual costs to be incurred relating to the lawsuit will depend upon many unknown factors. The outcome of litigation is necessarily uncertain, and we could be forced to expend significant resources in the defense of such suits, and we may not prevail. Monitoring and defending against legal actions is time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities. In addition, we may incur substantial legal fees and costs in connection with any such litigation. We have not established any reserves for any potential liability relating to any such potential lawsuits. It is possible that we could, in the future, incur judgments or enter into settlements of claims for monetary damages. A decision adverse to our interests on any such actions could result in the payment of substantial damages, or possibly fines, and could have an adverse effect on our cash flow, results of operations and financial position.

If our competitors develop technologies that are more effective than ours, our commercial opportunity will be reduced or eliminated.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Many of the drugs that we are attempting to discover will be competing with existing therapies. In addition, a number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. For example, the commercialization of new pharmaceutical products is highly competitive, and we face substantial competition with respect to TAVALISSE in which there are existing therapies and drug candidates in development for the treatment of ITP that may be alternative therapies to TAVALISSE. Many of our competitors, including a number of large pharmaceutical companies that compete directly with us, have significantly greater financial resources and expertise commercializing approved products than we do. Also, many of our competitors are large pharmaceutical companies that will have a greater ability to reduce prices for their competing drugs in an effort to gain market share and undermine the value proposition that we might otherwise be able to offer to payers. We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as from academic and research institutions and government agencies, both in the US and abroad. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions as our research programs. Our competitors including fully integrated pharmaceutical companies have extensive drug discovery efforts and are developing novel small-molecule pharmaceuticals. We also face significant competition from organizations that are pursuing the same or similar technologies, including the discovery of targets that are useful in compound screening, as the technologies used by us in our drug discovery efforts.

Competition may also arise from:

- new or better methods of target identification or validation;
- generic versions of TAVALISSE or of products with which we compete;
- other drug development technologies and methods of preventing or reducing the incidence of disease;
- new small molecules; or
- other classes of therapeutic agents.

Our competitors or their collaborative partners may utilize discovery technologies and techniques or partner with collaborators in order to develop products more rapidly or successfully than we or our collaborators are able to do. Many of our competitors, particularly large pharmaceutical companies, have substantially greater financial, technical and human resources and larger research and development staffs than we do. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies and may establish exclusive collaborative or licensing relationships with our competitors.

We believe that our ability to compete is dependent, in part, upon our ability to create, maintain and license scientifically-advanced technology and upon our and our collaborators' ability to develop and commercialize pharmaceutical products based on this technology, as well as our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary technology or processes, secure effective market access by ensuring competitive pricing and reimbursement in territories of interest, and secure sufficient capital resources for the expected substantial time period between technological conception and commercial sales of products based upon our technology. The failure by any of our collaborators or us in any of those areas may prevent the successful commercialization of our potential drug targets.

Many of our competitors, either alone or together with their collaborative partners, have significantly greater experience than we do in:

- identifying and validating targets;
- screening compounds against targets; and

- undertaking preclinical testing and clinical trials.

Accordingly, our competitors may succeed in obtaining patent protection, identifying or validating new targets or discovering new drug compounds before we do.

Our competitors might develop technologies and drugs that are more effective or less costly than any that are being developed by us or that would render our technology and product candidates obsolete and noncompetitive. In addition, our competitors may succeed in obtaining the approval of the FDA or other regulatory agencies for product candidates more rapidly. Companies that complete clinical trials, obtain required regulatory agency approvals and commence commercial sale of their drugs before us may achieve a significant competitive advantage, including certain patent and FDA marketing exclusivity rights that would delay or prevent our ability to market certain products. Any drugs resulting from our research and development efforts, or from our joint efforts with our existing or future collaborative partners, might not be able to compete successfully with competitors' existing or future products or obtain regulatory approval in the US or elsewhere.

We face and will continue to face intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology companies, for establishing relationships with academic and research institutions and for licenses to additional technologies. These competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective than ours.

Our ability to compete successfully will depend, in part, on our ability to:

- identify and validate targets;
- discover candidate drug compounds that interact with the targets we identify in a safe and efficacious way;
- attract and retain scientific and product development personnel;
- recruit subjects into our clinical trials;
- obtain and maintain required regulatory approvals;
- obtain patent or other proprietary protection for our new drug compounds and technologies; and
- enter commercialization agreements for our new drug compounds.

Our stock price may be volatile, and our stockholders' investment in our common stock could decline in value.

The market prices for our common stock and the securities of other biotechnology companies have been highly volatile and may continue to be highly volatile in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- the progress and success of our clinical trials and preclinical activities (including studies and manufacture of materials) of our product candidates conducted by us;
- our ability to continue to sell TAVALISSE in the US;
- our ability to enter into partnering opportunities across our pipeline;
- the receipt or failure to receive the additional funding necessary to conduct our business;
- selling of our common stock by large stockholders;
- presentations of detailed clinical trial data at medical and scientific conferences and investor perception thereof;
- announcements of technological innovations or new commercial products by our competitors or us;

- developments concerning proprietary rights, including patents;
- developments concerning our collaborations;
- publicity regarding actual or potential medical results relating to products under development by our competitors or us;
- regulatory developments in the US and foreign countries;
- changes in the structure of healthcare payment systems;
- litigation or arbitration;
- economic and other external factors or other disaster or crisis; and
- period-to-period fluctuations in financial results.

The withdrawal of the UK from the EU may adversely impact our ability to obtain regulatory approvals of our product candidates in the UK and the EU, result in restrictions or imposition of taxes and duties for importing our product candidates into the UK and the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the UK and the EU.

Following the result of a referendum in 2016, the UK left the EU on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement (Trade Agreement) that outlines the future trading relationship between the UK and the EU was agreed to in December 2020 and has been approved by each EU member state and the UK.

Since a significant proportion of the regulatory framework in the UK applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and will continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK or the EU. Great Britain (made up of England, Scotland, and Wales) is no longer covered by the EEA's procedures for the grant of marketing authorizations (Northern Ireland will be covered by such procedures). A separate marketing authorization will be required to market drugs in Great Britain. It is currently unclear whether the Medicines and Healthcare Products Regulatory Agency, or MHRA, in the UK is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals would delay or prevent us from commercializing our product candidates in the UK or the EU and restrict our ability to generate revenue and achieve and sustain profitability.

While the Trade Agreement provides for the tariff-free trade of medicinal products between the UK and the EU, there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU.

Orphan designation in Great Britain following Brexit is granted on an essentially identical basis as in the EU but is based on the prevalence of the condition in Great Britain. It is therefore possible that conditions that are currently designated as orphan conditions in Great Britain will no longer be, and conditions that are not currently designated as orphan conditions in the EU will be designated as such in Great Britain.

If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

The testing and marketing of medical products and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. We carry product liability insurance that is limited in scope and amount and may not be adequate to fully protect us against product liability claims. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with corporate collaborators. We, or our corporate collaborators, might not be able to obtain insurance at a reasonable cost, if at all. While under various circumstances we are entitled to be indemnified against losses by our corporate collaborators, indemnification may not be available or adequate should any claim arise.

We depend on various scientific consultants and advisors for the success and continuation of our research and development efforts.

We work extensively with various scientific consultants and advisors. The potential success of our drug discovery and development programs depends, in part, on continued collaborations with certain of these consultants and advisors. We, and various members of our management and research staff, rely on certain of these consultants and advisors for expertise in our research, regulatory and clinical efforts. Our scientific advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. We do not know if we will be able to maintain such consulting agreements or that such scientific advisors will not enter into consulting arrangements, exclusive or otherwise, with competing pharmaceutical or biotechnology companies, any of which would have a detrimental impact on our research objectives and could have an adverse effect on our business, financial condition and results of operations.

While we have a strong compliance effort in place to ensure we are complying with all requirements under anti-kickback laws, our consulting or advisory contracts with our scientific consultants and advisors may be scrutinized under the Anti-Kickback Statute, which prohibits, among other things, companies from transferring anything of value as remuneration for prescribing, purchasing, or recommending pharmaceutical and biological products. Although there are several statutory exceptions and regulatory safe harbors that may protect these arrangements from prosecution or regulatory sanctions, our consulting and advising contracts may be subject to scrutiny if they do not fit squarely within an exception or safe harbor.

If we use biological and hazardous materials in a manner that causes injury or violates laws, we may be liable for damages, penalties or fines.

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals, animals, and various radioactive compounds. We cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling or disposal of these animals and materials. In the event of contamination or injury, we could be held liable for damages that result or for penalties or fines that may be imposed, and such liability could exceed our resources. We are also subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. The cost of compliance with, or any potential violation of, these laws and regulations could be significant.

Our information technology systems, or those used by our CROs or other contractors or consultants, may fail or suffer other breakdowns, cyber-attacks, or information security breaches.

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business, particularly during the COVID-19 pandemic. We also rely on third party vendors and their information technology systems. Despite the implementation of security measures, our recovery systems, security protocols, network protection mechanisms and other security measures and those of our CROs and other contractors and consultants are

vulnerable to compromise from natural disasters; terrorism; war; telecommunication and electric failures; traditional computer hackers; malicious code (such as computer viruses or worms); employee error, theft or misuse; denial-of-service attacks; cyber-attacks by sophisticated nation-state and nation-state supported actors including ransomware; or other system disruptions. We receive, generate and store significant and increasing volumes of personal (including health), confidential and proprietary information. There can be no assurance that we, or our collaborators, CROs, third-party vendors, contractors and consultants will be successful in efforts to detect, prevent, protect against or fully recover systems or data from all break-downs, service interruptions, attacks or breaches. Any breakdown, cyber-attack or information security breach could result in a disruption of our drug development programs or other aspects of our business. For example, the loss of clinical trial data from completed or ongoing clinical trials for a product candidate could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability, incur significant remediation or litigation costs, result in product development delays, disrupt key business operations, cause loss of revenue and divert attention of management and key information technology resources.

Hackers and data thieves are increasingly sophisticated and operate large-scale and complex automated attacks, including on companies within the healthcare industry. As the cyber-threat landscape evolves, these threats are likely growing in frequency, sophistication and intensity and are increasingly difficult to detect. The costs of maintaining or upgrading our cyber-security systems at the level necessary to keep up with our expanding operations and prevent against potential attacks are increasing. Cyber threats may be generic, or they may be targeted against our information systems. Our network and storage applications and those of our contract manufacturing organizations, collaborators, contractors, CROs or vendors may be subject to unauthorized access or processing by hackers or breached due to operator or other human error, theft, malfeasance or other system disruptions. We may be unable to anticipate or immediately detect information security incidents and the damage caused by such incidents. These data breaches and any unauthorized access, processing or disclosure of our information or intellectual property could compromise our intellectual property and expose our sensitive business information. Such attacks, such as in the case of a ransomware attack, also may interfere with our ability to continue to operate and may result in delays and shortcomings due to an attack that may encrypt our or our service providers' or partners' systems unusable. Additionally, because our services involve the processing of personal information and other sensitive information about individuals we are subject to various laws, regulations, industry standards, and contractual requirements related to such processing. Any event that leads to unauthorized access, processing or disclosure of personal information, including personal information regarding our clinical study participants or employees, could harm our reputation and business, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to investigations and mandatory corrective action, and otherwise subject us to liability under laws, regulations or contracts that protect the privacy and security of personal information, which could disrupt our business, damage our reputation with our stakeholders, result in increased costs or loss of revenue, lead to negative publicity or result in significant financial exposure. The CCPA, in particular, includes a private right of action for California consumers whose personal information is impacted by a data security incident resulting from a company's failure to maintain reasonable security procedures, and hence may result in civil litigation in the event of a security breach impacting such information. In addition, legislators and regulators in the US have enacted and are proposing new and more robust privacy and cybersecurity laws and regulations in response to increasing broad-based cyberattacks, including the CCPA and New York SHIELD Act. New data security laws add additional complexity, requirements, restrictions and potential legal risk, and compliance programs may require additional investment in resources, and could impact strategies and availability of previously useful data.

The costs to respond to a security breach and/or to mitigate any identified security vulnerabilities could be significant, our efforts to address these issues may not be successful, and these issues could result in interruptions, delays, negative publicity, loss of customer trust, and other harms to our business and competitive position. Remediation of any potential security breach may involve significant time, resources, and expenses. We could be required to fundamentally change our business activities and practices in response to a security breach and our systems or networks may be perceived as less desirable, which could negatively affect our business and damage our reputation.

A security breach may cause us to breach our contracts with third parties. Our agreements with relevant stakeholders such as collaborators may require us to use legally required, industry-standard or reasonable measures to

safeguard personal information. A security breach could lead to claims by relevant stakeholders that we have failed to comply with such contractual obligations, or require us to cooperate with these stakeholders in their own compliance efforts related to the security breach. In addition, any non-compliance with our data privacy obligations in our contracts or our inability to flow down such obligations from relevant stakeholders to our vendors may cause us to breach our contracts. As a result, we could be subject to legal action or the relevant stakeholders could end their relationships with us. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages.

We may not have adequate insurance coverage for security incidents or breaches. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

Future equity issuances or a sale of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Because we will continue to need additional capital in the future to continue to expand our business and our research and development activities, among other things, we may conduct additional equity offerings. For example, we filed a universal shelf registration statement in March 2018 that was declared effective by the SEC in April 2018, and expired in April 2021, under which we sold 18,400,000 shares of common stock at a weighted-average price of $3.90 per share for net proceeds of $67.2 million, after deducting sale commissions. On August 3, 2021, we filed a new automatic shelf registration statement to register an additional $100.0 million of shares of our common stock for sale under our Open Market Sale Agreement with Jefferies. We may also in the future enter into underwriting or sales agreements with financial institutions for the offer and sale of any combination of common stock, preferred stock, debt securities and warrants in one or more offerings. If we or our stockholders sell, or if it is perceived that we or they will sell, substantial amounts of our common stock in the public market, the market price of our common stock could fall. A decline in the market price of our common stock could make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate. In addition, future sales by us of our common stock may be dilutive to existing stockholders. Furthermore, if we obtain funds through a credit facility or through the issuance of debt or preferred securities, these securities would likely have rights senior to the rights of our common stockholders, which could impair the value of our common stock.

Risks Related to Clinical Development and Regulatory Approval

Enacted or future legislation, and/or potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain regulatory approval of our product candidates and/or commercialize fostamatinib or our product candidates, once approved, and affect the prices we may set or obtain.

The regulations that govern, among other things, regulatory approvals, coverage, pricing and reimbursement for new drug products vary widely from country to country. In the US and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to successfully sell fostamatinib or any product candidates for which we obtain regulatory approval in the future. In particular, in March 2010, the Affordable Care Act was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and continues to significantly impact the US pharmaceutical industry. On June 17, 2021, the US Supreme Court dismissed the most recent judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the law. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. 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 Affordable Care Act. It is unclear how future actions before the Supreme Court, other such litigation, and the healthcare reform measures of the

Biden administration will impact the Affordable Care Act and our business.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce the costs of healthcare and/or impose price controls may adversely affect, for example:

- the demand for fostamatinib or our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Additionally, any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

In the US, the EU and other potentially significant markets for our current and future products, 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 has resulted in lower average selling prices. In the US, there have been several recent Congressional inquiries and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer-sponsored patient assistance programs, and reform government program reimbursement methodologies for drugs. The Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection under the federal Anti-Kickback Statute for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through PBMs, unless the price reduction is required by law. The implementation of the rule has been delayed by ongoing litigation and a Congress-passed moratorium on implementation before January 1, 2026. The rule also creates a new safe harbor manufacturer for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between PBMs and manufacturers, the implementation of which have also been delayed until January 1, 2026.

On November 20, 2020, the Centers for Medicare & Medicaid Services (CMS) also issued an interim final rule implementing former 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, effective January 1, 2021. On December 28, 2020, the US District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. CMS issued a final rule, effective February 28, 2022, rescinding the Most Favored Nation Model interim rule. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which, among other changes, eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacture price, for single source and innovator multiple source drugs, beginning January 1, 2024. The American Rescue Plan Act also temporarily increased premium tax credit assistance for individuals eligible for subsidies under the ACA for 2021 and 2022 and removed the 400% federal poverty level limit that otherwise applies for purposes of eligibility to receive premium tax credits. The Biden administration has begun taking executive actions to address drug pricing and other healthcare policy changes, including reversing certain measures by the Trump administration. For example, on July 9, 2021, President Biden signed an executive order to promote competition in the US economy that included several initiatives addressing prescription drugs. Among other provisions, the executive order directed the Secretary of HHS to issue a report to the White House within 45 days that includes a plan to, among other things, reduce prices for prescription drugs, including prices paid by the federal government for such drugs. In response to the Executive Order, on September 9, 2021, HHS issued a Comprehensive Plan for Addressing High Drug Prices that identified potential legislative policies and administrative tools that Congress

and the agency can pursue in order to make drug prices more affordable and equitable, improve and promote competition throughout the prescription drug industry, and foster scientific innovation.

Furthermore, the increased emphasis on managed healthcare in the US and on country and regional pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our 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. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

We cannot predict the likelihood, nature, or extent of health reform initiatives that may arise from future legislation or administrative action, particularly as a result of the new presidential administration. However, we expect these initiatives to increase pressure on drug pricing. Further, certain broader legislation that is not targeted to the health care industry may nonetheless adversely affect our profitability. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

See “Part I, Item 1 – Business – Government Regulation – Healthcare Reform” of this Annual Report on Form 10-K.

Regulatory approval for any approved product is limited by the FDA, the European Commission and other regulators to those specific indications and conditions for which clinical safety and efficacy have been demonstrated, and we may incur significant liability if it is determined that we are promoting the “off-label” use of TAVALISSE or any of our future product candidates if approved.

Any regulatory approval is limited to those specific diseases, indications and patient populations for which a product is deemed to be safe and effective by the FDA, the European Commission and other regulators. For example, the FDA-approved label for TAVALISSE is only approved for use in adults with ITP who have had an insufficient response to other treatments. In addition to the FDA approval required for new formulations, any new indication for an approved product also requires FDA approval. If we are not able to obtain FDA approval for any desired future indications for our products and product candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians may choose to prescribe drugs for uses that are not described in the product’s labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, our ability to promote the products is limited to those indications and patient populations that are specifically approved by the FDA. These “off-label” uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. We have implemented compliance and monitoring policies and procedures, including a process for internal review of promotional materials, to deter the promotion of TAVALISSE for off-label uses. We cannot guarantee that these compliance activities will prevent or timely detect off-label promotion by sales representatives or other personnel in their communications with health care professionals, patients and others, particularly if these activities are concealed from the Company. Regulatory authorities in the US generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on the subject of off-label use. If our promotional activities fail to comply with the FDA’s or other competent national authority’s regulations or guidelines, we may be subject to warnings from, or enforcement action by, these regulatory authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, suspend or withdraw an approved product from the market, require a recall or institute fines, which could result in the disgorgement of money, operating restrictions, injunctions or civil or criminal enforcement, and other consequences, any of which could harm our business.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading and non-promotional scientific exchange concerning their products. We engage in medical education activities and communicate with investigators and potential investigators

regarding our clinical trials. If the FDA or other regulatory or enforcement authorities determine that our communications regarding our marketed product are not in compliance with the relevant regulatory requirements and that we have improperly promoted off-label uses, or that our communications regarding our investigational products are not in compliance with the relevant regulatory requirements and that we have improperly engaged in pre-approval promotion, we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

Delays in clinical testing could result in increased costs to us.

We may not be able to initiate or continue clinical studies or trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials as required by the FDA or other regulatory authorities, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise. Even if we are able to enroll a sufficient number of patients in our clinical trials, if the pace of enrollment is slower than we expect, the development costs for our product candidates may increase and the completion of our clinical trials may be delayed, or our clinical trials could become too expensive to complete. For example, for our Phase 3 clinical trial to further evaluate fostamatinib in hospitalized patients with COVID-19 is currently enrolling but may experience delays. Significant delays in clinical testing could negatively impact our product development costs and timing. Our estimates regarding timing are based on a number of assumptions, including assumptions based on past experience with our other clinical programs. If we are unable to enroll the patients in these trials at the projected rate, the completion of the clinical program could be delayed and the costs of conducting the program could increase, either of which could harm our business.

Clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a study, delays from scaling up of a study, delays in reaching agreement on acceptable clinical trial agreement terms with prospective clinical sites, delays in obtaining institutional review board approval to conduct a study at a prospective clinical site or delays in recruiting subjects to participate in a study. In addition, we typically rely on third-party clinical investigators to conduct our clinical trials and other third-party organizations to oversee the operations of such trials and to perform data collection and analysis. The clinical investigators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. Failure of the third-party organizations to meet their obligations, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise, could adversely affect clinical development of our products. As a result, we may face additional delaying factors outside our control if these parties do not perform their obligations in a timely fashion. For example, any number of those issues could arise with our clinical trials causing a delay. Delays of this sort could occur for the reasons identified above or other reasons. If we have delays in conducting the clinical trials or obtaining regulatory approvals, our product development costs will increase. For example, we may need to make additional payments to third-party investigators and organizations to retain their services or we may need to pay recruitment incentives. If the delays are significant, our financial results and the commercial prospects for our product candidates will be harmed, and our ability to become profitable will be delayed. Moreover, these third-party investigators and organizations may also have relationships with other commercial entities, some of which may compete with us. If these third-party investigators and organizations assist our competitors at our expense, it could harm our competitive position.

Due to the evolving effects of the COVID-19 pandemic, for several of our development programs, we are experiencing a disruption or delay in our ability to enroll and assess patients, maintain patient enrollment, supply study drug, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in employee resources or otherwise. In addition, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 may adversely impact our clinical trial operations. In light of the evolving effects of the COVID-19 pandemic, we have taken, and will continue to take, measures to implement remote and virtual approaches to clinical development, including remote patient monitoring where possible, and if the COVID-19 pandemic continues and persists for an extended period of time, we could experience significant disruptions to our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

We may not be able to obtain Emergency Use Authorization (EUA) for fostamatinib for the treatment of hospitalized patients with COVID-19, and, even if we do, absent supplemental NDA approval for that indication, such EUA would be revoked when the COVID-19 emergency terminates.

Based on the results of the NIH/NHLBI-sponsored Phase 2 trial, in May 2021, we filed an EUA for the use of fostamatinib for the treatment of hospitalized patients with COVID-19. In August 2021, the FDA informed us that the clinical data submitted from the NIH/NHLBI-sponsored Phase 2 trial of fostamatinib to treat hospitalized patients suffering from COVID-19 was insufficient for EUA. We continue to focus on enrolling on our Rigel-led Phase 3 clinical trial, and we anticipate providing further safety and efficacy data from this larger trial of fostamatinib in COVID-19 patients. If this trial meets its endpoints, we plan to resubmit our EUA application with this additional data.

Section 564 of the FDCA allows the FDA to authorize the shipment of drugs, biological products, or medical devices that either lack required approval, licensure, or clearance (unapproved products), or are approved but are to be used for unapproved ways to diagnose, treat, or prevent serious diseases or conditions in the event of an emergency declaration by the HHS Secretary.

On February 4, 2020, then-HHS Secretary Alex M. Azar II declared a public health emergency for COVID-19, under 21 U.S.C. § 360bbb-3(b)(1), justifying the authorization of emergency use of unapproved therapeutic products, or unapproved uses of approved or cleared therapeutic products, to treat COVID-19. This determination was published in the Federal Register on February 7, 2020.

While this emergency declaration is effective, the FDA may authorize the use of an unapproved product or an unapproved use of an approved product if it concludes that:

- an agent referred to in the emergency declaration could cause a serious or life-threatening disease or condition;
- it is reasonable to believe that the authorized product may be effective in diagnosing, treating, or preventing that disease or condition or a serious or life-threatening disease or condition caused by an approved product or a product marketed under an EUA;
- the known and potential benefits of the authorized product, when used for that disease or condition, outweigh known and potential risks, taking into consideration the material threat of agents identified in the emergency declaration;
- there is no adequate, approved, and available alternative to the authorized product for diagnosing, preventing, or treating the relevant disease or condition;
- any other criteria prescribed by the FDA is satisfied.

Medical products that are granted an EUA are only permitted to commercialize their products under the terms and conditions provided in the authorization. The FDCA authorizes FDA to impose such conditions on an EUA as may be necessary to protect the public health. Consequently, postmarketing requirements will vary across EUAs. In addition, FDA has, on occasion, waived requirements for drugs marketed under an EUA.

Generally, EUAs for unapproved products or unapproved uses of approved products require that manufacturers distribute factsheets for healthcare providers, addressing significant known and potential benefits and risk, and the extent to which benefits and risks are unknown, and the fact that FDA has authorized emergency use; and, distribution of factsheets for recipients of the product, addressing significant known and potential benefits and risk, and the extent to which benefits and risks are unknown, the option to accept or refuse the product, the consequences of refusing, available alternatives and the fact that FDA has authorized emergency use.

Generally, EUAs for unapproved products and, per FDA's discretion, EUAs for unapproved uses of approved products, include requirements for adverse event monitoring and reporting, and other recordkeeping and reporting requirements. Note, however, that approved products are already subject to equivalent requirements.

In addition, the FDA may include various requirements in an EUA as a matter of discretion as deemed necessary to protect the public health, including restrictions on which entities may distribute the product, and how to perform distribution (including requiring that distribution be limited to government entities), restrictions on who may administer the product, requirements for collection and analysis of safety and effectiveness data, waivers of cGMP, and restrictions applicable to prescription drugs or restricted devices (including advertising and promotion restrictions).

The FDA may revoke an EUA when it is determined that the underlying health emergency no longer exists or warrants such authorization, if the conditions for the issuance of the EUA are no longer met, or if other circumstances make revocation appropriate to protect the public health or safety. We cannot predict how long, if ever, an EUA would remain in place.

We cannot predict with certainty whether the Phase 3 study will meet its primary endpoint, and we therefore cannot guarantee that we will submit a second application for an EUA for fostamatinib. Even if the Phase 3 study does meet its primary endpoint, we cannot predict whether FDA will grant an EUA for fostamatinib based on the study data. We also cannot predict how long, if ever, an EUA would remain in place.

Our COVID-19 product candidate may not successfully protect against variants of the SARS-CoV-2 virus.

As the SARS-CoV-2 virus continues to evolve, new strains of the virus or those that are already in circulation may prove more transmissible or cause more severe forms of COVID-19 disease than the predominant strains to date. There is a risk that any product candidates we develop will not be as effective against variant strains of the SARS-CoV-2 virus expressing variants of the spike protein, particularly strains with mutations in the receptor binding domain and N-terminal domain. Such failure could lead to significant reputational harm, in addition to adversely affecting our financial results.

Public perception of the risk-benefit balance for our COVID-19 product candidates may be affected by adverse events in clinical trials involving our product candidate or other COVID-19 treatments.

Negative perception of the efficacy, safety, or tolerability of any investigational medicines that we develop, or of other products similar to products we are developing, such as fostamatinib for the treatment of COVID-19, could adversely affect our ability to conduct our business, advance our investigational medicines, or obtain regulatory approvals.

Adverse events in clinical trials of our investigational medicines or in clinical trials of others developing similar products, including other COVID-19 treatments, could result in a decrease in the perceived benefit of one or more of our programs, increased regulatory scrutiny, decreased confidence by patients and clinical trial collaborators in our investigational medicines, and less demand for any product that we may develop. If and when they are used in clinical trials, our developmental candidates and investigational medicines could result in a greater quantity of reportable adverse events, including suspected unexpected serious adverse reactions, other reportable negative clinical outcomes, manufacturing reportable events or material clinical events that could lead to clinical delay or hold by the FDA or applicable regulatory authority or other clinical delays, any of which could negatively impact the perception of one or more of our programs, as well as our business as a whole. In addition, responses by US, state, or foreign governments to negative public perception may result in new legislation or regulations that could limit our ability to develop any investigational medicines or commercialize any approved products, obtain or maintain regulatory approval, or otherwise achieve profitability. More restrictive statutory regimes, government regulations, or negative public opinion would have an adverse effect on our business, financial condition, results of operations, and prospects and may delay or impair the development of our investigational medicines and commercialization of any approved products or demand for any products we may develop.

We lack the capability to manufacture compounds for clinical development, and we rely on and intend to continue relying on third parties for commercial supply, manufacturing and distribution if any of our product candidates which receive regulatory approval and we may be unable to obtain required material or product in a timely manner, at an acceptable cost or at a quality level required to receive regulatory approval.

We currently do not have the manufacturing capabilities or experience necessary to produce TAVALISSE or any product candidates for clinical trials, including fostamatinib in wAIHA, COVID-19, our IRAK inhibitor program

and our RIPK1 inhibitor program. We currently use one manufacturer of fostamatinib. We do not currently have, nor do we plan to acquire the infrastructure or capability to supply, manufacture or distribute preclinical, clinical or commercial quantities of drug substances or products. For each clinical trial of our unpartnered product candidates, we rely on third-party manufacturers for the active pharmaceutical ingredients, as well as various manufacturers to manufacture starting components, excipients and formulated drug products. Our ability to develop our product candidates, and our ability to commercially supply our products will depend, in part, on our ability to successfully obtain the APIs and other substances and materials used in our product candidates from third parties and to have finished products manufactured by third parties in accordance with regulatory requirements and in sufficient quantities for preclinical and clinical testing and commercialization. If we fail to develop and maintain supply relationships with these third parties, we may be unable to continue to develop or commercialize our product candidates.

We rely and will continue to rely on certain third parties, including those located outside the US, as our limited source of the materials they supply or the finished products they manufacture. The drug substances and other materials used in our product candidates are currently available only from one or a limited number of suppliers or manufacturers and certain of our finished product candidates are manufactured by one or a limited number of contract manufacturers. Any of these existing suppliers or manufacturers may:

- fail to supply us with product on a timely basis or in the requested amount due to unexpected damage to or destruction of facilities or equipment or otherwise;
- fail to increase manufacturing capacity and produce drug product and components in larger quantities and at higher yields in a timely or cost-effective manner, or at all, to sufficiently meet our commercial needs;
- be unable to meet our production demands due to issues related to their reliance on sole-source suppliers and manufacturers;
- supply us with product that fails to meet regulatory requirements;
- become unavailable through business interruption or financial insolvency;
- lose regulatory status as an approved source;
- be unable or unwilling to renew current supply agreements when such agreements expire on a timely basis, on acceptable terms or at all; or
- discontinue production or manufacturing of necessary drug substances or products.

Our current and anticipated future dependence upon these third-party manufacturers may adversely affect our ability to develop and commercialize product candidates on a timely and competitive basis, which could have an adverse effect on sales, results of operations and financial condition. If we were required to transfer manufacturing processes to other third-party manufacturers and we were able to identify an alternative manufacturer, we would still need to satisfy various regulatory requirements. Satisfaction of these requirements could cause us to experience significant delays in receiving an adequate supply of our products and products in development and could be costly. Moreover, we may not be able to transfer processes that are proprietary to the manufacturer, if any. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements and may also experience a shortage in qualified personnel, including due to the impacts of the COVID-19 pandemic. We may not be able to maintain or renew our existing third-party manufacturing arrangements, or enter into new arrangements, on acceptable terms, or at all. Our third-party manufacturers could terminate or decline to renew our manufacturing arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for the production of materials in sufficient quantity and of sufficient quality on acceptable terms, our planned clinical trials may be significantly delayed. Manufacturing delays could postpone the filing of our IND applications and/or the initiation or completion of clinical trials that we have currently planned or may plan in the future.

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration, the European Medicines Agency, national competent authorities in the EU and UK and

other federal and state government and regulatory agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards and they may not be able to comply. Switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly on acceptable terms, or at all. Additionally, if we are required to enter into new supply arrangements, we may not be able to obtain approval from the FDA of any alternate supplier in a timely manner, or at all, which could delay or prevent the clinical development and commercialization of any related product candidates. Failure of our third-party manufacturers or us to comply with applicable regulations, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise, could result in sanctions being imposed on us, including fines, civil penalties, delays in or failure to grant marketing approval of our product candidates, injunctions, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products and compounds, operating restrictions and criminal prosecutions, warning or similar letters or civil, criminal or administrative sanctions against the company, any of which could adversely affect our business.

Any product for which we have obtained regulatory approval, or for which we obtain approval in the future, is subject to, or will be subject to, extensive ongoing regulatory requirements by the FDA, EMA and other comparable regulatory authorities, and if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, we may be subject to penalties, we may be unable to generate revenue from the sale of such products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.

In April 2018, the FDA had approved TAVALISSE for the treatment of adult patients with chronic ITP who have had insufficient response to previous treatment. We launched fostamatinib in the US on our own in late May 2018. In January 2019, we entered into an exclusive commercialization license agreement with Grifols to commercialize fostamatinib for the treatment, palliation, or prevention of human diseases, including chronic or persistent immune ITP, AIHA, and IgAN in Europe and Turkey. In October 2018, we entered into an exclusive license and supply agreement with Kissei for the development and commercialization of fostamatinib in all indications in Japan, China, Taiwan, and the Republic of Korea. In October 2019, we also entered into two exclusive license agreements with Medison to commercialize fostamatinib in all potential indications in Canada and Israel. Any product for which we have obtained regulatory approval, or for which we obtain regulatory approval in the future, along with the manufacturing processes and practices, post-approval clinical research, product labeling, advertising and promotional activities for such product, are subject to continual requirements of, and review by, the FDA, the EMA and other comparable international regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current good manufacturing practices (cGMP) requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians, import and export requirements and recordkeeping. If we or our suppliers encounter manufacturing, quality or compliance difficulties with respect to TAVALISSE or any of our product candidates, when and if approved, whether due to the impacts of the ongoing COVID-19 pandemic (including as a result of disruptions of global shipping and the transport of products) or otherwise, we may be unable to obtain or maintain regulatory approval or meet commercial demand for such products, which could adversely affect our business, financial conditions, results of operations and growth prospects.

Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, the FDA often requires post-marketing testing and surveillance to monitor the effects of products. The FDA, the EMA and other comparable international regulatory agencies may condition approval of our product candidates on the completion of such post-marketing clinical studies. These post-marketing studies may suggest that a product causes undesirable side effects or may present a risk to the patient. Additionally, the FDA may require Risk Evaluation and Mitigation Strategies (REMS) to help ensure that the benefits of the drug outweigh its risks. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, limitations on who may prescribe or dispense the drug, requirements that patients enroll in a registry or undergo certain health evaluations or other measures that the FDA deems necessary to ensure the safe use of the drug.

Discovery after approval of previously unknown problems with any of our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on product manufacturing processes;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- untitled or warning letters or other adverse publicity;
- withdrawal of products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- refusal to permit the import or export of our products;
- product seizure;
- fines, restitution or disgorgement of profits or revenue;
- refusal to allow us to enter into supply contracts, including government contracts;
- injunctions; or
- imposition of civil or criminal penalties.

If such regulatory actions are taken, the value of our company and our operating results will be adversely affected. Additionally, if the FDA, the EMA or any other comparable international regulatory agency withdraws its approval of a product that is or may be approved, we will be unable to generate revenue from the sale of that product in the relevant jurisdiction, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased. Accordingly, we continue to expend significant time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, post-marketing studies and quality control.

If any of our third-party contractors fail to perform their responsibilities to comply with FDA rules and regulations, the marketing and sales of our products could be delayed and we may be subject to enforcement action, which could decrease our revenues.

Conducting our business requires us to manage relationships with third-party contractors. As a result, our success depends partially on the success of these third parties in performing their responsibilities to comply with FDA rules and regulations. Although we pre-qualify our contractors and we believe that they are fully capable of performing their contractual obligations, we cannot directly control the adequacy and timeliness of the resources and expertise that they apply to these activities.

If any of our partners or contractors fail to perform their obligations in an adequate and timely manner, or fail to comply with the FDA's rules and regulations, then the marketing and sales of our products could be delayed. The FDA may also take enforcement actions against us based on compliance issues identified with our contractors. If any of these events occur, we may incur significant liabilities, which could decrease our revenues. For example, sales and medical science liaison or MSL personnel, including contractors, must comply with FDA requirements for the advertisement and promotion of products.

Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process and does not assure FDA approval of our product candidates.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical need for this condition, the sponsor may apply for FDA fast track designation. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for more frequent interactions with the review team during product development, and the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

However, fast track designation does not change the standards for approval and does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. As a result, while the FDA has granted fast track designation to fostamatinib for the treatment of wAIHA and/or we may seek and receive fast track designation for our future product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

If we are unable to obtain regulatory approval to market products in the US and foreign jurisdictions, we will not be permitted to commercialize products we or our collaborative partners may develop.

We cannot predict whether regulatory clearance will be obtained for any product that we, or our collaborative partners, hope to develop. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Of particular significance to us are the requirements relating to research and development and testing.

Before commencing clinical trials in humans in the US, we, or our collaborative partners, will need to submit and receive approval from the FDA of an IND application. Clinical trials are subject to oversight by institutional review boards and the FDA and:

- must be conducted in conformance with the FDA's good clinical practices and other applicable regulations;
- must meet requirements for institutional review board oversight;
- must meet requirements for informed consent;
- are subject to continuing FDA and regulatory oversight;
- may require large numbers of test subjects; and
- may be suspended by us, our collaborators or the FDA at any time if it is believed that the subjects participating in these trials are being exposed to unacceptable health risks or if the FDA finds deficiencies in the IND or the conduct of these trials.

While we have stated that we intend to file additional INDs for future product candidates, this is only a statement of intent, and we may not be able to do so because we may not be able to identify potential product candidates. In addition, the FDA may not approve any IND we or our collaborative partners may submit in a timely manner, or at all.

Before receiving FDA approval to market a product, we must demonstrate with substantial clinical evidence that the product is safe and effective in the patient population and the indication that will be treated. Data obtained from preclinical and clinical activities are susceptible to varying interpretations that could delay, limit or prevent regulatory approvals. In addition, delays or rejections may be encountered based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or

injunction, adverse publicity, as well as other regulatory action against our potential products or us. Additionally, we have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approval.

If regulatory approval of a product is granted, this approval will be limited to those indications or disease states and conditions for which the product is demonstrated through clinical trials to be safe and efficacious. We cannot assure you that any compound developed by us, alone or with others, will prove to be safe and efficacious in clinical trials and will meet all of the applicable regulatory requirements needed to receive marketing approval.

Outside the US, our ability, or that of our collaborative partners, to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. This foreign regulatory approval process typically includes all of the risks and costs associated with FDA approval described above and may also include additional risks and costs, such as the risk that such foreign regulatory authorities, which often have different regulatory and clinical trial requirements, interpretations and guidance from the FDA, may require additional clinical trials or results for approval of a product candidate, any of which could result in delays, significant additional costs or failure to obtain such regulatory approval. There can be no assurance, however, that we or our collaborative partners will not have to provide additional information or analysis, or conduct additional clinical trials, before receiving approval to market product candidates.

We may be unable to expand our product pipeline, which could limit our growth and revenue potential.

Our business is focused on the development and commercialization of novel small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer and rare immune diseases. In this regard, we are pursuing internal drug discovery efforts with the goal of identifying new product candidates to advance into clinical trials. Internal discovery efforts to identify new product candidates require substantial technical, financial and human resources. These internal discovery efforts may initially show promise in identifying potential product candidates, yet ultimately fail to yield product candidates for clinical development for a number of reasons. For example, potential product candidates may, on later stage clinical study, be shown to have inadequate efficacy, harmful side effects, suboptimal pharmaceutical profiles or other characteristics suggesting that they are unlikely to be commercially viable products.

Apart from our internal discovery efforts, our strategy to expand our development pipeline is also dependent on our ability to successfully identify and acquire or in-license relevant product candidates. However, the in-licensing and acquisition of product candidates is a highly competitive area, and many other companies are pursuing the same or similar product candidates to those that we may consider attractive. In particular, larger companies with more well-established and diverse revenue streams may have a competitive advantage over us due to their size, financial resources and more extensive clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to in-license or acquire additional relevant product candidates on acceptable terms that would allow us to realize an appropriate return on our investment. If we are unable to develop suitable product candidates through internal discovery efforts, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise, or if we are unable to successfully obtain rights to additional suitable product candidates, our business and prospects for growth could suffer. Even if we succeed in our efforts to obtain rights to suitable product candidates, the competitive business environment may result in higher acquisition or licensing costs, and our investment in these potential products will remain subject to the inherent risks associated with the development and commercialization of new medicines. In certain circumstances, we may also be reliant on the licensor for the continued development of the in-licensed technology and their efforts to safeguard their underlying intellectual property.

With respect to acquisitions, we may not be able to integrate the target company successfully into our existing business, maintain the key business relationships of the target, or retain key personnel of an acquired business. Furthermore, we could assume unknown or contingent liabilities or incur unanticipated expenses. Any acquisitions or investments made by us also could result in our spending significant amounts, issuing dilutive securities, assuming or incurring significant debt obligations and contingent liabilities, incurring large one-time expenses and acquiring intangible assets that could result in significant future amortization expense and significant write-offs, any of which could harm our operating results.

We have obtained orphan drug designation from the FDA for fostamatinib for the treatment of ITP and wAIHA, but we may not be able to obtain or maintain orphan drug designation or exclusivity for fostamatinib for the treatment of ITP, wAIHA or our other product candidates, or we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

We have obtained orphan drug designation in the US for fostamatinib for the treatment of ITP and wAIHA. We may seek orphan drug designation for other product candidates in the future. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the US, or a patient population greater than 200,000 in the US where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the US. In the US, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. At this time, we do not have nor will we seek to apply for orphan drug designation in the EU or the UK in the foreseeable future.

We cannot assure you that any future application for orphan drug designation with respect to any other product candidate will be granted. If we are unable to obtain orphan drug designation with respect to other product candidates in the US, we will not be eligible to obtain the period of market exclusivity that could result from orphan drug designation or be afforded the financial incentives associated with orphan drug designation. Even though we have received orphan drug designation for fostamatinib for the treatment of ITP and wAIHA, we may not be the first to obtain marketing approval for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the US for fostamatinib for the treatment of ITP, wAIHA or any future product candidate may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Risks Related to Commercialization

Our prospects are highly dependent on our first commercial product, TAVALISSE. To the extent that the commercial success of TAVALISSE in the US is diminished or is not commercially successful, our business, financial condition and results of operations may be adversely affected, and the price of our common stock may decline.

TAVALISSE is our only drug that has been approved for sale in the US and Europe for patients with chronic ITP. We are focusing a significant portion of our activities and resources on fostamatinib, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to sustain successful commercialization of TAVALISSE in the US. We have entered into an exclusive commercialization agreement with Grifols to commercialize fostamatinib in Europe.

Sustained successful commercialization of TAVALISSE is subject to many risks and uncertainties, including the impact of the COVID-19 pandemic on the successful commercialization in the US, as well as the successful commercialization efforts for TAVLESSE in Europe through our collaborative partner, Grifols. Prior to TAVALISSE, we have never, as an organization, launched or commercialized a product, and there is no guarantee that we will be able to continue to do so successfully with fostamatinib for its approved indication. In addition, Grifols, is responsible for the commercial launch of TAVLESSE in Europe. Although Grifols has launched TAVLESSE in the UK, Germany, France, Italy, Spain, the Czech Republic and Norway and continues a phased rollout across the rest of Europe which is expected

to include Denmark, Finland and Sweden, we cannot be certain if Grifols will be successful in launching TAVLESSE in additional territories in Europe that it may pursue, or continue to be successful in commercializing and marketing in any such regions. There are numerous examples of unsuccessful product launches and failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us.

As we continue to build out our commercial team, there are many factors that could cause the commercialization of TAVALISSE to be unsuccessful, including a number of factors that are outside our control. The commercial success of TAVALISSE depends on the extent to which patients and physicians accept and adopt TAVALISSE for patients with chronic ITP who have had an insufficient response to a previous treatment. We also do not know how physicians, patients and payors will respond to our future price increases of TAVALISSE. Physicians may not prescribe TAVALISSE and patients may be unwilling to use TAVALISSE if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. TAVALISSE competes, and may in the future compete, with currently existing therapies, including generic drugs, and products currently under development. Our competitors, particularly large pharmaceutical companies, may deploy more resources to market, sell and distribute their products. If our efforts are not appropriately resourced to adequately promote our products, the commercial potential of our sales may be diminished. Additionally, any negative development for fostamatinib in clinical development in additional indications, such as in the clinical trials of fostamatinib in COVID-19 patients, may adversely impact the commercial results and potential of fostamatinib. Thus, significant uncertainty remains regarding the commercial potential of fostamatinib.

Market acceptance of fostamatinib will depend on a number of factors, including:

- the timing of market introduction of the product as well as competitive products;
- the clinical indications for which the product is approved;
- acceptance by physicians, the medical community and patients of the product as a safe and effective treatment;
- impacts due to the evolving effects of the COVID-19 pandemic;
- the ability to distinguish safety and efficacy from existing, less expensive generic alternative therapies, if any;
- the convenience of prescribing, administrating and initiating patients on the product and the length of time the patient is on the product;
- the potential and perceived value and advantages of the product over alternative treatments;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- pricing and the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the prevalence and severity of adverse side effects; and
- the effectiveness of sales and marketing efforts.

If we are unable to sustain anticipated level of sales growth from TAVALISSE, or if we fail to achieve anticipated product royalties and collaboration milestones, we may need to reduce our operating expenses, access other sources of cash or otherwise modify our business plans, which could have a negative impact on our business, financial condition and results of operations. For example, during 2021, we experienced lower than anticipated sales of TAVALISSE due to continuing impacts of physician and patient access issues created by the COVID-19 pandemic. From time to time, our net product sales are negatively impacted by the decrease in level of inventories remaining at our distribution channels.

We also may not be successful entering into arrangements with third parties to sell and market one or more of our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, including Kissei's development and commercialization of fostamatinib in all indications in Japan, China, Taiwan, and the Republic of Korea, Grifols' commercialization of fostamatinib in Europe and Turkey and Medison for future commercialization of fostamatinib in Canada and Israel. As a consequence of our license agreements with Kissei, Grifols and Medison, we rely heavily upon their regulatory, commercial, medical affairs, market access and other expertise and resources for commercialization of fostamatinib in their respective territories outside of the US. We cannot control the amount of resources that our partners dedicate to the commercialization of fostamatinib, and our ability to generate revenues from the commercialization of fostamatinib by our partners depends on their ability to achieve market acceptance of fostamatinib in its approved indications in their respective territories.

Furthermore, foreign sales of fostamatinib by our partners could be adversely affected by the imposition of governmental controls, political and economic instability, outbreaks of pandemic diseases, such as the COVID-19 pandemic, trade restrictions or barriers and changes in tariffs and escalating global trade and political tensions. For example, the ongoing COVID-19 pandemic has resulted in increased travel restrictions and extended shutdowns of certain businesses in the US and around the world. If our collaborators are unable to successfully complete clinical trials, delay commercialization of fostamatinib or do not invest the resources necessary to successfully commercialize fostamatinib in international territories where it has been approved, this could reduce the amount of revenue we are due to receive under these license agreements, resulting in harm to our business and operations. If we do not establish and maintain sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if we, or any of our collaborative partners, are able to continue to commercialize TAVALISSE or any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or labeling restrictions, all of which may vary from country to country and any of which could harm our business.

The commercial success of any product for which we have obtained regulatory approval, or for which we obtain regulatory approval in the future will depend substantially on the extent to which the costs of our product or product candidates are or will be paid by third-party payors, including government health care programs and private health insurers. There is a significant trend in the health care industry by public and private payers to contain or reduce their costs, including by taking the following steps, among others: decreasing the portion of costs payers will cover, ceasing to provide full payment for certain products depending on outcomes or not covering certain products at all. If payers implement any of the foregoing with respect to our products, it would have an adverse impact on our revenue and results of operations. If coverage is not available, or reimbursement is limited, we, or any of our collaborative partners, may not be able to successfully commercialize TAVALISSE or any of our product candidates in some jurisdictions. Even if coverage is provided, the approved reimbursement amount may not be at a rate that covers our costs, including research, development, manufacture, sale and distribution. In the US, no uniform policy of coverage and reimbursement for products exists among third-party payors; therefore, coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific, clinical or other support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed, which could delay market entry (or, if pricing is not approved, we may be unable to sell at all in a country where we have received regulatory approval for a product. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some countries, the proposed pricing for a drug must be approved before it may be lawfully marketed). In addition, authorities in some countries impose additional obligations, such as health technology assessments (HTAs), which assess the performance of a drug in comparison with its cost. The outcome of HTA assessments is judged on a national basis and some payers may not reimburse the use of our products or may reduce the rate of reimbursement for our products and as a result, revenue from such products may decrease.

In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any of our collaborative partners, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. In particular, we cannot predict to what extent the evolving effects of the COVID-19 pandemic, depending on its scale and duration, may continue to disrupt global healthcare systems and access to our products or result in a widespread loss of individual health insurance coverage due to unemployment, a shift from commercial payor coverage to government payor coverage, or an increase in demand for patient assistance and/or free drug programs, any of which would adversely affect access to and demand for our products and our net sales. Adverse pricing limitations may also hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval. Further, even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborative partners receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any of our collaborative partners, to successfully commercialize TAVALISSE or any of our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors.

Additionally, the labeling ultimately approved for any of our product candidates for which we have or may obtain regulatory approval may include restrictions on their uses and may be subject to ongoing FDA or international regulatory authority requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. If we or any of our collaborative partners do not timely obtain or comply with the labeling approval by the FDA or international regulatory authorities on any of our product candidates, it may delay or inhibit our ability to successfully commercialize our products and generate revenues.

If we are unable to successfully market and distribute TAVALISSE and retain experienced sales force, our business will be substantially harmed.

We currently have limited experience in marketing and selling pharmaceutical products. As a result, we will be required to expend significant time and resources to maintain a sales force that is credible and compliant with applicable laws in marketing TAVALISSE for patients with chronic ITP who have had an insufficient response to a previous treatment. In addition, we must continually train our sales force to ensure that an appropriate and compliant message about TAVALISSE is being delivered. If we are unable to effectively train our sales force and equip them with compliant and effective materials, including medical and sales literature to help them appropriately inform and educate health care providers regarding the potential benefits and proper administration of TAVALISSE, our efforts to successfully commercialize TAVALISSE could be put in jeopardy, which would negatively impact our ability to generate product revenues.

We have established our distribution, sales, marketing and market access capabilities, all of which will be necessary to successfully commercialize TAVALISSE. As a result, we will be required to expend significant time and resources to market, sell, and distribute TAVALISSE to hematologists and hematologists-oncologists. There is no guarantee that the marketing strategies we have developed, including our virtual strategies in response to the restrictions and limitations resulting from the COVID-19 pandemic, or the distribution, sales, marketing and market access capabilities that we have developed will be successful. Particularly, we are dependent on third-party logistics, specialty pharmacies and distribution partners in the distribution of TAVALISSE. If they are unable to perform effectively or if they do not provide efficient distribution of the medicine to patients, our business may be harmed. In addition, we actively participate in medical conferences and exhibits, such as the American Society of Clinical Oncology (ASCO) and ASH Annual Meeting & Exposition that are significant opportunities for us to educate physicians and key opinion leaders about TAVALISSE. In 2021, ASCO was held virtually in June 2021, and ASH was held in-person and virtually in December 2021. It is uncertain if in the future other key conferences will be held live, virtually, postponed or cancelled. Such disruptions may prevent us from effectively educating the prescribing physicians and key opinion leaders about TAVALISSE which would negatively impact utilization of TAVALISSE and our results of operations and

growth prospects could be adversely affected.

Maintaining our sales, marketing, market access and product distribution capabilities requires significant resources, and there are numerous risks involved with managing our commercial team, including our potential inability to successfully train, retain and incentivize adequate numbers of qualified and effective sales and marketing personnel. We are also competing for talent with numerous commercial and pre-commercial-stage oncology-focused biotechnology companies seeking to build out their commercial organizations, as well as other large pharmaceutical organizations that have extensive, well-funded and more experienced sales and marketing operations, and we may be unable to maintain or adequately scale our commercial organization as a result of such competition. If we cannot maintain effective sales, marketing, market access and product distribution capabilities, whether as a result of the ongoing COVID-19 pandemic or otherwise, we may be unable to realize the commercial potential of TAVALISSE. Also, to the extent that the commercial opportunities for TAVALISSE grow over time, we may not properly judge the requisite size and experience of our current commercialization teams or the level of distribution necessary to market and sell TAVALISSE, which could have an adverse impact on our business, financial condition and results of operations.

We may not be able to successfully develop or commercialize our product candidates if problems arise in the clinical testing and approval process.

The activities associated with the research, development and commercialization of fostamatinib and other product candidates in our pipeline must undergo extensive clinical trials, which can take many years and require substantial expenditures, subject to extensive regulation by the FDA and other regulatory agencies in the US and by comparable authorities in other countries. The process of obtaining regulatory approvals in the US and other foreign jurisdictions is expensive, and lengthy, if approval is obtained at all.

Our clinical trials may fail to produce results satisfactory to the FDA or regulatory authorities in other jurisdictions. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations. The FDA has substantial discretion in the approval process and may refuse to approve any NDA or sNDA and decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. Varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of fostamatinib for any individual, additional indications.

Due to the ongoing COVID-19 pandemic, it is also possible that we could experience delays in the timing of our interactions with regulatory authorities due to absenteeism by governmental employees or the diversion of regulatory authority efforts and attention to approval of other therapeutics or other activities related to COVID-19, which could delay or limit our ability to make planned regulatory submissions or develop and commercialize our product candidates on anticipated timelines.

In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review, which may cause delays in the approval or rejection of an application for fostamatinib or for our other product candidates.

Commercialization of our product candidates depends upon successful completion of extensive preclinical studies and clinical trials to demonstrate their safety and efficacy for humans. Preclinical testing and clinical development are long, expensive and uncertain processes.

In connection with clinical trials of our product candidates, we may face the following risks among others:

- the product candidate may not prove to be effective;
- the product candidate may cause harmful side effects;
- the clinical results may not replicate the results of earlier, smaller trials;
- we or third parties with whom we collaborate, may be significantly impacted by the evolving impacts of the ongoing COVID-19 pandemic;
- we, or the FDA or similar foreign regulatory authorities, may delay, terminate or suspend the trials;

- our results may not be statistically significant;
- patient recruitment and enrollment may be slower than expected;
- patients may drop out of the trials or otherwise not enroll; and
- regulatory and clinical trial requirements, interpretations or guidance may change.

We do not know whether we will be permitted to undertake clinical trials of potential products beyond the trials already concluded and the trials currently in process. It will take us or our collaborative partners several years to complete any such testing, and failure can occur at any stage of testing. Interim results of trials do not necessarily predict final results, and acceptable results in early trials may not be repeated in later trials. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after achieving promising results in earlier trials.

General Risk Factors

Shareholder activism could cause material disruption to our business.

Publicly traded companies have increasingly become subject to campaigns by activist investors advocating corporate actions such as actions related to environment, social and governance (ESG) matters, financial restructuring, increased borrowing, dividends, share repurchases and even sales of assets or the entire company. Responding to proxy contests and other actions by such activist investors or others in the future could be costly and time-consuming, disrupt our operations and divert the attention of our Board of Directors and senior management from the pursuit of our business strategies, which could adversely affect our results of operations and financial condition.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult.

Provisions of our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions:

- establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning a majority of our capital stock;
- authorize the issuance of "blank check" preferred stock that could be issued by our board of directors to increase the number of outstanding shares and thwart a takeover attempt;
- limit who may call a special meeting of stockholders;
- prohibit stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings;
- provide for a board of directors with staggered terms; and
- provide that the authorized number of directors may be changed only by a resolution of our board of directors.

In addition, Section 203 of the Delaware General Corporation Law, which imposes certain restrictions relating to transactions with major stockholders, may discourage, delay or prevent a third party from acquiring us.

Increasing use of social media could give rise to liability and may harm our business.

We and our employees are increasingly utilizing social media tools and our website as a means of communication. Despite our efforts to monitor evolving social media communication guidelines and comply with applicable laws and regulations, there is risk that the unauthorized use of social media by us or our employees to communicate about our products or business, sharing of publications in unintended audiences in other jurisdictions, or any inadvertent promotional activity or disclosure of material, nonpublic information through these means, may cause us to be found in violation of applicable laws and regulations, which may give rise to liability and result in harm to our business. In addition, there is also risk of inappropriate disclosure of sensitive information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse impact on our business, financial condition and results of operations. Furthermore, negative posts or comments about us or our products on social media could seriously damage our reputation, brand image and goodwill.

Our research and development efforts will be seriously jeopardized if we are unable to attract and retain key employees and relationships.

Our success depends on the continued contributions of our principal management and scientific personnel and on our ability to develop and maintain important relationships with leading academic institutions, scientists and companies in the face of intense competition for such personnel. In particular, our research programs depend on our ability to attract and retain highly skilled chemists, other scientists, and development, regulatory and clinical personnel. If we lose the services of any of our key personnel, our research and development efforts could be seriously and adversely affected. Our employees can terminate their employment with us at any time.

Global economic conditions could adversely impact our business.

The US government has indicated its intent to alter its approach to international trade policy and in some cases to renegotiate, or potentially terminate, certain existing bilateral or multi-lateral trade agreements and treaties with foreign countries. In addition, the US government has initiated or is considering imposing tariffs on certain foreign goods. Related to this action, certain foreign governments, including China, have instituted or are considering imposing tariffs on certain US goods. It remains unclear what the US Administration or foreign governments will or will not do with respect to tariffs or other international trade agreements and policies. A trade war or other governmental action related to tariffs or international trade agreements or policies has the potential to disrupt our research activities, affect our suppliers and/or the US economy or certain sectors thereof and, thus, could adversely impact our businesses.

The transition away from the London Interbank Offered Rate (LIBOR) could affect the value of certain short-term investments, outstanding debt from our existing credit facility as well as our ability to draw additional funds from our credit facility.

The UK's Financial Conduct Authority (FCA), which regulates LIBOR, has announced plans to phase out the use of LIBOR discontinued as a floating rate benchmark. The date of discontinuation will vary depending on the LIBOR currency and tenor. The FCA has announced that, after specified dates, LIBOR settings will cease to be provided by any administrator or will no longer be representative. Those dates are: (i) June 30, 2023, in the case of the principal US dollar LIBOR tenors (overnight and one, three, six and 12 months); and (ii) December 31, 2021, in all other cases (i.e., one-week and two-month U.S. dollar LIBOR and all tenors of non-US dollar LIBOR). LIBOR has been the principal floating rate benchmark in the financial markets, and its discontinuation has affected and will continue to affect the financial markets generally and may also affect our operations specifically.

The FCA and certain US regulators have stated that, despite expected publication of US dollar LIBOR through June 30, 2023, no new contracts using US dollar LIBOR should be entered into after December 31, 2021. Regulators have also stated that, for certain purposes, market participants should transition away from US. dollar LIBOR sooner. Regulatory authorities and legislative bodies have taken other actions related to the LIBOR discontinuation and are expected to continue to do so. There is no assurance as to the consequences of any such statements and other actions.

Although the foregoing reflects the likely timing of the LIBOR discontinuation and certain consequences, there is no assurance that LIBOR, of any particular currency or tenor, will continue to be published until any particular date or in any particular form, and there is no assurance regarding the consequences of the LIBOR discontinuation.

We have certain short-term investments which include financial instruments, as well an existing debt facility, subject to LIBOR. There remains uncertainty regarding the future utilization of LIBOR and the nature of any replacement rate, and any potential effects of the transition away from LIBOR on certain instruments into which we may enter in the future are not known. The transition process may involve, among other things, increased volatility or illiquidity in markets for instruments that currently rely on LIBOR. The transition may also result in reductions in the value of certain instruments or the effectiveness of related transactions such as hedges, increased borrowing costs, uncertainty under applicable documentation, or difficult and costly consent processes. Any such effects of the transition away from LIBOR, as well as other unforeseen effects, result in expenses, difficulties, complications or delays in connection with future financing efforts, which could have an adverse impact on our business, financial condition and results of operations.

Our facilities are located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail operations.

Our facilities are located in the San Francisco Bay Area near known earthquake fault zones and are vulnerable to significant damage from earthquakes. We are also vulnerable to damage from other types of disasters, including fires, floods, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our business at our facilities would be seriously, or potentially completely, impaired, and our research could be lost or destroyed. In addition, the unique nature of our research activities and of much of our equipment could make it difficult for us to recover from a disaster. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently lease facilities consisting of approximately 147,000 square feet of research and office space located at 1180 Veterans Boulevard, South San Francisco, California, which will expire in January 2023. In December 2014, we entered into a sublease agreement, amended in February 2017 and July 2017, with an unrelated third party to sublet a portion of our leased research and office space of approximately 66,000 square feet, which will expire in January 2023. We believe our facilities are in good operating condition and that the leased real property that we still occupy is adequate for all present and near term uses.

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

Market Information

Our common stock commenced trading publicly on the Nasdaq Global Market under the symbol "RIGL" on December 7, 2000.

Holders

As of February 24, 2022, there were approximately 91 stockholders of record of our common stock.

Dividends

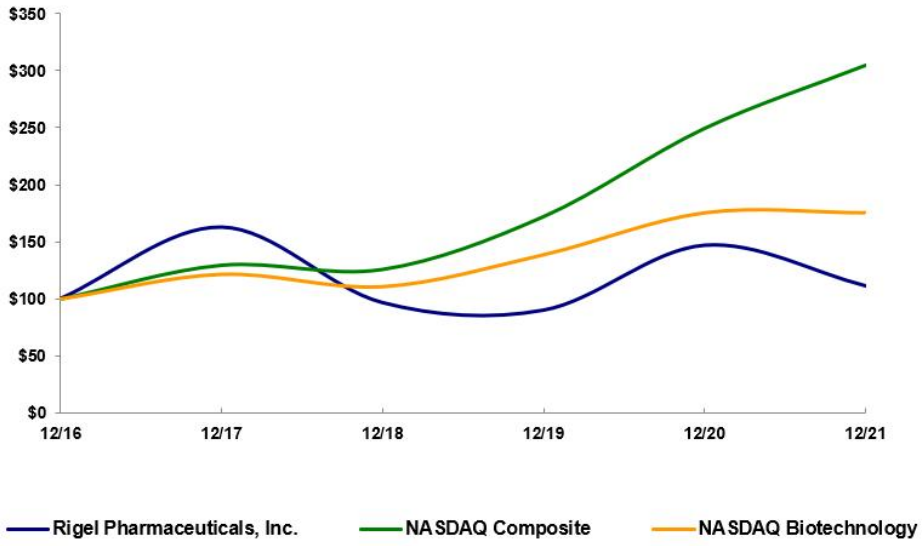
We have not paid any cash dividends on our common stock and currently do not plan to pay any cash dividends in the foreseeable future.

Performance Measurement Comparison

The graph below shows the cumulative total stockholder return of an investment of $100 (and the reinvestment of any dividends thereafter) on December 31, 2016 in (i) our common stock, (ii) the Nasdaq Composite Index and (iii) the Nasdaq Biotechnology Index. The Nasdaq Biotechnology Index is a modified-capitalization weighted index that includes securities of Nasdaq-listed companies classified according to the Industry Classification Benchmark as either Biotechnology or Pharmaceuticals and which also meet other eligibility criteria. Our stock price performance shown in the graph below is based upon historical data and is not indicative of future stock price performance.

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

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Rigel Pharmaceuticals, Inc., the Nasdaq Composite Index
and the Nasdaq Biotechnology Index



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

Item 6. [Reserved]

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

The following discussion should be read in conjunction with our "Notes to Financial Statements" contained in Part II, Item 8 of this Form 10-K. This section of this Form 10-K discusses 2021 and 2020 items and 2021 and 2020 year-to-year comparisons. This section does not discuss 2019 items and 2020 to 2019 year-to-year comparisons. Discussions of 2019 items and 2020 to 2019 year-to-year comparisons can be found in the "Part II, Item 7 Management's Discussion and Analysis of Financial Condition and Result of Operations" of the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

Overview

We are a biotechnology company dedicated to discovering, developing and providing novel small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer and rare immune diseases. Our pioneering research focuses on signaling pathways that are critical to disease mechanisms. Our first product approved by the FDA is TAVALISSE® (fostamatinib disodium hexahydrate) tablets, the only oral SYK inhibitor, for the treatment of adult patients with chronic ITP who have had an insufficient response to a previous treatment. The product is also commercially available in Europe, the UK (TAVLESSE) and Canada (TAVALISSE) for the treatment of chronic ITP in adult patients.

Fostamatinib is currently being studied in a Phase 3 trial for the treatment wAIHA; a Phase 3 clinical trial for the treatment of hospitalized high-risk patients with COVID-19; a NIH/NHLBI sponsored Phase 3 trial (ACTIV-4 Host Tissue Trial) for the treatment of COVID-19 in hospitalized patients; and a Phase 2 trial for the treatment of COVID-19 being conducted by Imperial College London.

Our other clinical programs include our IRAK inhibitor program and a RIPK1 inhibitor program in clinical development with partner Lilly. In addition, we have product candidates in clinical development with partners BerGenBio and Daiichi.

Business Update

For discussions of recent business updates, please refer to "Part I, Item 1, Business – Business Update" of this Annual Report on Form 10-K.

Product Development Programs

Our product portfolio features multiple novel, targeted drug candidates in the therapeutic areas of immunology, hematology, cancer and rare diseases. Please refer to "Part I, Item 1, Business - Product Portfolio" herein for a detailed discussion of our multiple product candidates in development.

Corporate Collaborations

For discussions of our Corporate Collaborations, see "Note 4 - Sponsored Research and License Agreements and Government Contract" to our "Notes to Financial Statements" contained in "Part II, Item 8, Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

Critical Accounting Estimates

The preparation of these financial statements requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are more fully described in "Note 1- Description of Business and Summary of Significant Accounting Policies", in the "Notes to Financial Statements" contained in "Part II, Item 8, Financial Statements and Supplementary Data" of this Annual Report on Form 10-K. We believe our critical accounting estimates which require subjective and complex judgments include estimates around our product sales allowances and discounts; estimates around accounting for collaboration arrangements; estimates around the fair value of our stock option awards and the probability of achievement of corporate performance-based milestones for our performance-based stock option awards; and estimates around research and development accruals.

Product Sales Allowances and Discounts

Our revenues from product sales are recognized at net sales price when our customers, the specialty distributors (SDs), obtain control of our product, which occurs at a point in time, upon delivery to such SDs. Under the revenue recognition guidance, we are required to estimate the transaction price, including variable consideration that is subject to a constraint, in our contracts with our customers. Variable considerations are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur. Revenue from product sales is recorded net of certain variable considerations which includes estimated government-mandated rebates and chargebacks, pharmacy benefit manager (PBM) rebates, distribution fees, estimated product returns and other deductions.

Provisions for sales discounts, returns and allowances are provided for in the period the related revenue is recorded. Our estimates are based on available customer and payer data received from the specialty pharmacies and distributors, as well as third-party market research data. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Contract Revenues from Collaborations

In the normal course of business, we conduct research and development programs independently and in connection with our corporate collaborators, pursuant to which we license certain rights to our intellectual property to third parties. The terms of these arrangements typically include payment to us for a combination of one or more of the following: upfront license fees; development, regulatory and commercial milestone payments; product supply services; and royalties on net sales of licensed products.

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

For arrangements that require us to share in the development costs but to which we do not participate in the co-development work, the portion of the upfront fee attributed to our share in the future development costs is excluded from the transaction price. If such share in the development costs is payable beyond 12 months from the delivery of the corresponding license, a significant financing component is deemed to exist. If a significant financing component is identified, we adjust the transaction price by reducing the upfront fee by the net present value of our share in future development costs over the expected commitment period. Such discounted amount will be reported as a liability in the balance sheet, with a corresponding interest expense being accreted based on a discount rate applied over the expected commitment period.

Development, Regulatory or Commercial Milestone Payments: At the inception of each arrangement that includes payments based the achievement of certain development, regulatory and commercial or launch events, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until uncertainty associated with the approvals has been resolved. The transaction price is then allocated to each performance obligation, on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such development and regulatory milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, and are recorded as part of contract revenues from collaborations during the period of adjustment.

Product Supply Services: Arrangements that include a promise for future supply of drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations.

Sales-based Milestone Payments and Royalties: For arrangements that include sales-based royalties, including milestone payments based on the volume of sales, we determine whether the license is deemed to be the predominant item to which the royalties or sales-based milestones relate to and if such is the case, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Stock-Based Compensation

The fair value of our stock option award is estimated on the date of grant using the Black-Scholes option pricing model which considered our stock price, as well as assumptions regarding a number of complex and subjective variables. These variables include, but are not limited to, volatility, expected term, risk-free interest rate and dividends. We estimate volatility over the expected term of the option using historical share price performance. For expected term, we take into consideration our historical data of options exercised, cancelled and expired. The risk-free rate is based on the US Treasury constant maturity rate. We have not paid and do not expect to pay dividends in the foreseeable future. We use the straight-line attribution method over the requisite employee service period for the entire award in recognizing stock-based compensation expense. We account for forfeitures as they occur.

We granted performance-based stock options to purchase shares of our common stock which will vest upon the achievement of certain corporate performance-based milestones. We determined the fair values of these performance-based stock options using the Black-Scholes option pricing model at the date of grant. For the portion of the performance-based stock options of which the performance condition is considered probable of achievement, we recognize stock-based compensation expense on the related estimated grant date fair values of such options on a straight-line basis from the date of grant up to the date when we expect the performance condition will be achieved. For the performance conditions that are not considered probable of achievement at the grant date or upon quarterly re-evaluation, prior to the event actually occurring, we recognize the related stock-based compensation expense when the event occurs or when we can determine that the performance condition is probable of achievement. In those cases, we recognize the change in estimate at the time we determine the condition is probable of achievement (by recognizing stock-based compensation expense as cumulative catch-up adjustment as if we had estimated at the grant date that the performance condition would have been achieved) and recognize the remaining compensation cost up to the date when we expect the performance condition will be achieved, if any.

Research and Development Accruals

We have various contracts with third parties related to our research and development activities. Costs that are incurred but not billed to us as of the end of the period are accrued. We make estimates of the amounts incurred in each period based on the information available to us and our knowledge of the nature of the contractual activities generating such costs. Clinical trial contract expenses are accrued based on units of activity. Expenses related to other research and development contracts, such as research contracts, toxicology study contracts and manufacturing contracts are estimated to be incurred generally on a straight-line basis over the duration of the contracts. Raw materials and study materials not related to our approved drug, purchased for us by third parties are expensed at the time of purchase.

We make significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, we adjust our accruals. Although we do not expect our estimates to be materially different from amounts actually incurred, such estimates for the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. Variations in assumptions used to estimate accruals including, but not limited to, the number of patients enrolled, the rate of patient enrollment and the actual services performed may result in adjustments in research and development accruals in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our financial condition and results of operations.

Recent Accounting Pronouncements

For a discussion of new accounting pronouncements, see "Note 1- Description of Business and Summary of Significant Accounting Policies", in the "Notes to Financial Statements" contained in "Part II, Item 8, Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

Results of Operations

Years Ended December 31, 2021, 2020 and 2019

Revenues

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
			(in thousands)		
Product sales, net	$ 63,010	$ 61,696	$ 43,772	$ 1,314	$ 17,924
Contract revenues from collaborations	75,726	46,925	15,516	28,801	31,409
Government contract	10,500	—	—	10,500	—
Total revenues	$ 149,236	$ 108,621	$ 59,288	$ 40,615	$ 49,333

The following table summarizes revenues from each of our customers who individually accounted for 10% or more (wherein * denotes less than 10%) of our gross revenues (as a percentage of gross revenues):

	Year Ended December 31,		
	2021	2020	2019
Lilly	48%	—	—
McKesson Specialty Care Distribution Corporation	20%	23%	30%
ASD Healthcare and Oncology Supply	17%	30%	37%
Grifols	*	41%	*

Net product sales during the periods presented pertained to sales of TAVALISSE in the US, net of chargebacks, discounts and fees, government and other rebates and returns. The increase in our net product sales in 2021 compared to 2020 was primarily driven by the increase in quantities sold as well as the increase in price per bottle of TAVALISSE. The increase in our net product sales resulting from the increase in quantities sold and price per bottle were partially offset by the increase in revenue reserves mainly due to higher government program rebates.

Following table summarizes our revenues by collaborative partners for the periods presented:

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
	(in thousands)				
Lilly	$ 66,555	$ —	$ —	$ 66,555	$ —
Grifols	2,955	44,825	4,712	(41,870)	40,113
Daiichi	1,800	2,100	—	(300)	2,100
Medison	75	—	—	75	—
Kissei	341	—	1,554	341	(1,554)
Aclaris	—	—	5,500	—	(5,500)
Celgene	—	—	3,750	—	(3,750)
Other third party	4,000	—	—	4,000	—
Total revenues from collaborations	$ 75,726	$ 46,925	$ 15,516	$ 28,801	$ 31,409

Contract revenues from collaborations in 2021 comprised of $66.6 million revenue related to our license agreement with Lilly, $4.0 million revenue related to grant of non-exclusive license of a certain patent to an unrelated third-party company, $1.8 million in revenue related to the achievement of milestone under our collaboration agreement with Daiichi, $3.0 million related to our performance of research and development services and delivery of drug supply under our collaboration agreement with Grifols, $0.3 million related delivery of drug supply to Kissei, and $0.1 million milestone payment under our commercial and license agreement with Medison. Contract revenues from collaborations in 2020 were comprised of revenue of $44.9 million from Grifols related to the upfront fee previously received, as well as the milestone payment received in the 2020 upon EC approval of the MAA for fostamatinib in Europe, and $2.1 million milestone payment under our collaboration agreement with Daiichi.

Government contract revenue in 2021 of $10.5 million was related to the income we recognized from the $16.5 million government award granted to us, pursuant to the agreement we entered in January 2021 with the US Department of Defense to support our ongoing Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients. We expect to receive the remaining award of $6.0 million and will recognize as income throughout the period we conduct our clinical trial, when there is reasonable assurance that the conditions of the grant will be met, and the grant will be received.

Our potential future revenues may include product sales from TAVALISSE; payments from our collaboration partners and from new collaboration partners with whom we enter into agreements in the future, if any; and from existing government grants and any future grants we may be entitled to, if any; the timing and amount of which is unknown at this time. We cannot currently fully forecast the extent of the impacts that the COVID-19 pandemic may have on our revenues. Our net product sales may be impacted by changes to the government program rebates and new private payer rebate contracts we entered or may enter in the future. As of December 31, 2021, we had deferred revenues of $2.6 million, which we will recognize as revenue upon satisfaction of our remaining performance obligations under our respective collaboration agreements.

Cost of Product Sales

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
	(in thousands)				
Cost of product sales	$ 1,083	$ 895	$ 906	$ 188	$ (11)

The cost of product sales for the periods presented was related to our product, TAVALISSE. Prior to the FDA approval in May 2018, manufacturing and related costs were charged to research and development expense. Therefore, these costs were not capitalized and as a result, are not fully reflected in the cost of product sales during the periods presented. We expect we will continue to have a lower cost of product sales that excludes the cost of the active

pharmaceutical ingredient (API) that was produced prior to FDA approval until we sell TAVALISSE that includes newly manufactured API. We expect that this will be the case for the near-term and as a result, our cost of product sales will be less than we anticipate it will be in future periods. As we produce TAVALISSE in the future, our inventory cost in the Balance Sheet and cost of product sales will increase reflecting the full cost of manufacturing. The cost of product sales remained relatively flat for 2021 compared to 2020.

Research and Development Expenses

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
	(in thousands)				
Research and development expense	$ 65,237	$ 60,101	$ 52,885	$ 5,136	$ 7,216
Stock-based compensation expense included in research and development expense	$ 1,700	$ 2,072	$ 2,662	$ (372)	$ (590)

The increase in research and development expense in 2021 compared to 2020 was primarily due to higher research and development costs of $10.9 million related to our ongoing Phase 3 clinical trial on hospitalized COVID-19 patients, increase in our research and development of our IRAK 1/4 inhibitor program of $1.0 million, and increase in our other research and development costs in our other clinical studies of $0.5 million. These increases were partially offset by a decrease in research and development costs of $6.1 million due to the completion of a clinical trial in our RIPK1 inhibitor program, and decrease in personnel- related costs of $1.2 million mainly due to decrease in headcount as a result of the restructuring of the research department in November 2021.

Our research and development expenditures include costs related to preclinical and clinical trials, scientific personnel, supplies, equipment, consultants, sponsored research, stock-based compensation, and allocated facility costs. We expect to continue to incur significant research and development expense as we continue our activities in our Phase 3 wAIHA, COVID-19 and other clinical studies. In November 2021, we completed enrollment of the wAIHA study. Following the six-month treatment period after the last patient enrollment, we expect to report topline data from the 24-week study in mid-2022 and proceed with regulatory filings if the data is positive. If approved, fostamatinib has the potential to be the first to market therapy for patients with wAIHA. We also continue to enroll patients in our Phase 3 clinical trial of fostamatinib for the treatment of hospitalized high-risk patients with COVID-19. In January 2021, the US Department of Defense awarded us a total of $16.5 million grant that will partially fund our Phase 3 clinical trial for hospitalized COVID-19 patients. Currently, we cannot fully forecast the scope the evolving effects of COVID-19 pandemic may have on our ability to continue to treat patients enrolled in our trials, enroll and assess new patients, supply study drug, obtain complete data points in accordance with the study protocol, and overall impact on, and timing of, clinical study results. We expect cost savings on our research and development costs because of reduction in workforce, primarily in the research organization. In November 2021, we announced our plans to exit early-stage research and focus resources on our mid to late-stage development programs and our commercialization efforts. The strategy will strengthen our ability to execute or near-term value drivers, such as growing ITP sales, expanding the addressable market for fostamatinib with wAIHA and COVID-19, advancing our wholly-owned IRAK1/4 program in hematology and immunology.

We do not track fully burdened research and development costs separately for each of our drug candidates. We review our research and development expenses by focusing on three categories: research, development, and other. Our research team is focused on identifying and evaluating product candidates in our focused range of therapeutic indications that can be developed into small molecule therapeutics in our own proprietary programs or with potential collaborative partners. “Research” expenses relate primarily to personnel expenses, lab supplies, fees to third party research consultants and compounds. Our development group leads the implementation of our clinical and regulatory strategies and prioritizes disease indications in which our compounds may be studied in clinical trials. “Development” expenses relate primarily to clinical trials, personnel expenses, costs related to our regulatory filings, lab supplies and fees to third party research consultants. “Other” expenses primarily consist of allocated facilities costs and allocated stock-based compensation expense relating to personnel in research and development groups.

In addition to reviewing the three categories of research and development expenses described in the preceding paragraph, we principally consider qualitative factors in making decisions regarding our research and development programs, which include enrollment in clinical trials and the results thereof, the clinical and commercial potential for our drug candidates and competitive dynamics. We also make our research and development decisions in the context of our overall business strategy, which includes the evaluation of potential collaborations for the development of our drug candidates.

We do not have reliable estimates regarding the timing of our clinical trials. Preclinical testing and clinical development are long, expensive and uncertain processes. In general, biopharmaceutical development involves a series of steps, beginning with identification of a potential target and including, among others, proof of concept in animals and Phase 1, 2 and 3 clinical trials in humans. Significant delays in clinical testing could materially impact our product development costs and timing of completion of the clinical trials. We do not know whether planned clinical trials will begin on time, will need to be halted or revamped or will be completed on schedule, or at all. Clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a trial, delays from scale up, delays in reaching agreement on acceptable clinical trial agreement terms with prospective clinical sites, delays in obtaining institutional review board approval to conduct a clinical trial at a prospective clinical site or delays in recruiting subjects to participate in a clinical trial.

We currently do not have reliable estimates of total costs for a particular drug candidate to reach the market. Our potential products are subject to a lengthy and uncertain regulatory process that may involve unanticipated additional clinical trials and may not result in receipt of the necessary regulatory approvals. Failure to receive the necessary regulatory approvals would prevent us from commercializing the product candidates affected. In addition, clinical trials of our potential products may fail to demonstrate safety and efficacy, which could prevent or significantly delay regulatory approval.

The following table presents our total research and development expenses by category:

	Year Ended December 31,			From January 1, 2007* to December 31, 2021
	2021	2020	2019	
Categories:				
Research	$ 8,195	$ 9,307	$ 10,063	$ 264,232
Development	49,557	42,758	34,142	497,319
Other	7,485	8,036	8,680	262,436
	$ 65,237	$ 60,101	$ 52,885	$ 1,023,987

* We started tracking research and development expenses by category on January 1, 2007.

"Other" expenses in 2021, 2020 and 2019 consisted of allocated facilities costs of $5.8 million, $6.0 million and $6.0 million, respectively, and allocated stock-based compensation expense of $1.7 million, $2.1 million and $2.6 million, respectively.

In 2021, a major portion of our total research and development expense was associated with our COVID-19, AIHA and IRAK programs, personnel-related costs of our research and development personnel and allocated facilities costs. In 2020 and 2019, a major portion of our total research and development expense was associated with our AIHA, RIPK1, and IRAK programs, personnel-related costs of our research and development personnel and allocated facilities costs.

Selling, General and Administrative Expense

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
	(in thousands)				
Selling, general and administrative expense	$ 91,891	$ 76,598	$ 74,588	$ 15,293	$ 2,010
Stock-based compensation expense included in selling, general and administrative expense	$ 7,337	$ 5,223	$ 6,453	$ 2,114	$ (1,230)

The increase in selling, general and administrative expense in 2021 compared to 2020 was primarily due to the increases in costs of commercial activities of $4.8 million, costs of consultants and third-party services of $2.8 million, personnel-related costs of $2.7 million, stock-based compensation expense of $2.1 million, recruitment fees of $0.6 million, and other various sales, general and administrative costs of $2.3 million. These increases were primarily impacted by the expansion of our commercial operations.

We expect our selling, general and administrative expense in 2022 to increase as we continue to expand our commercial activities, including the effect of the recent sales force expansion. In response to the limitations on in-person office visits during the ongoing COVID-19 pandemic, we continue to deploy resources to enable our field-based employees to continue to engage virtually with healthcare providers. These virtual engagements have enabled our field team to support existing prescribers as well as partner with new prescribers to identify appropriate patients for our product. However, we are not currently able to fully forecast the scope of impacts that the COVID-19 pandemic may have on our commercial activities and sales of our product.

Restructuring charges

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
	(in thousands)				
Restructuring charges	$ 3,521	$ —	$ —	$ 3,521	$ —
Stock-based compensation expense included in restructuring charges	$ 449	$ —	$ —	$ 449	$ —
Deprecation expense included in restructuring charges	$ 145	$ —	$ —	$ 145	$ —

In November 2021, we announced a reduction in our workforce resulting in the elimination of positions primarily in the research organization. We recorded restructuring charges of $3.5 million in the statements of operations in 2021, comprised of $2.9 million cash severance, bonus and related taxes of affected employees, $0.4 million of stock-based compensation expense related to modification of stock options and $0.1 million impairment of certain property and equipment which was recorded within depreciation expense

Interest Income

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
	(in thousands)				
Interest income	$ 47	$ 582	$ 2,532	$ (535)	$ (1,950)

Interest income results from our interest-bearing cash and investment balances. The decreases in interest income in 2021 compared to 2020 were primarily due to a decrease in interest rates on our investments.

Interest Expense

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
			(in thousands)		
Interest expense	$ (4,860)	$ (1,353)	$ (335)	$ (3,507)	$ (1,018)

Interest expense in 2021 was comprised of interest on the financing liability from our collaboration partners Lilly and Medison, and interest on outstanding balance on our term loan from Midcap. Interest expense in 2020 and 2019 was related to the outstanding balance on our term loan from Midcap. The increase in interest expense in 2021 compared to 2020 was mainly due to the interest expense associated with the financing liability from our collaboration partners amounting to $3.1 million. Incrementally, interest expense increased due to the increase in the outstanding term loan credit balance. The principal balance of loan prior to May 2020 was the initial $10.0 million under Tranche 1. In May 2020, we accessed the Tranche 2 for an additional $10.0 million loan. See “Note 10 - Debt” to our “Notes to Financial Statements” contained in “Part II, Item 8, Financial Statements and Supplementary Data” of this Annual Report on Form 10-K.

Provision for Income Taxes

	Year Ended December 31,			Aggregate Change	Aggregate Change
	2021	2020	2019	2021 from 2020	2020 from 2019
			(in thousands)		
Provision for income taxes	$ 605	$ —	$ —	$ 605	$ —

The provision for income taxes in 2021 was related to the state tax liability primarily due to revenue recognized for the Lilly Agreement. We do not expect to owe federal income taxes due to the sufficient NOL carryforwards that were generated prior to the enactment of the Tax Act, as well as significant research and development credit carryforwards. We continue to record a full valuation allowance on our deferred tax assets considering our cumulative losses in prior years and forecasted losses in the future.

Liquidity and Capital Resources

Liquidity

As of December 31, 2021, we had approximately $125.0 million in cash, cash equivalents and short-term investments, as compared to approximately $57.3 million as of December 31, 2020. The increase of approximately $67.6 million was primarily attributable to the upfront cash payment of $125.0 million from Lilly, partially offset by cash used in our other operating activities. As of December 31, 2021 and 2020, we maintained investment portfolios primarily in money market funds, US treasury bills, government-sponsored enterprise securities, and corporate bonds and commercial paper. Cash in excess of immediate requirements is invested with regard to liquidity and capital preservation. We view our investments portfolio as available-for-sale and are available for use in current operations. Wherever possible, we seek to minimize the potential effects of concentration and degrees of risk. We continue to monitor the impact of the changes in the conditions of the credit and financial markets to our investment portfolio and assess if future changes in our investment strategy are necessary.

Following summarizes our cash flow activity for the periods presented:

	Year Ended December 31,		
	2021	2020	2019
		(in thousands)	
Net cash provided by (used in):			
Operating activities	$ 5,878	$ (52,185)	$ (41,510)
Investing activities	(80,036)	47,466	(23,656)
Financing activities	62,675	12,571	11,365
Net (decrease) increase in cash and cash equivalents	$ (11,483)	$ 7,852	$ (53,801)

Net cash provided by operating activities in 2021 was primarily due to the cash received from Lilly for the portion allocated as net transaction price of $67.1 million, proceeds from sales of TAVALISSE, cash received from the awards granted by the US Department of Defense, and cash received from our other collaboration partners. These increases were partially offset by payments of our research and development programs and other operating expenses. Net cash used in operating activities in 2020 was related to our research and development programs and our continued commercialization of TAVALISSE, partially offset by the $20.0 million payment received from Grifols, proceeds from sale of TAVALISSE, and other cash received from our other collaboration partners.

Net cash used in investing activities in 2021 was due to net purchases of short-term investments of $79.4 million and capital expenditures of $0.6 million. Net cash provided by investing activities in 2020 was related to net maturities of short-term investments of $48.7 million, partially offset by capital expenditures of $1.3 million.

Net cash provided by financing activities in 2021 was primarily due to the cash received from Lilly for the portion allocated as financing component amounting to $57.9 million and proceeds from exercise of stock options and participation in the Purchase Plan of $4.8 million. Net cash provided by financing activities in 2020 consisted of proceeds from funding of the second $10.0 million tranche from our term loan credit facility with MidCap and $2.6 million from the exercise of stock options and participation in the Purchase Plan.

We believe that our existing capital resources will be sufficient to support our current and projected funding requirements, including the continued commercialization of TAVALISSE, through at least the next 12 months from the Annual Report on Form 10-K filing date. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with commercializing a product, the development of our product candidates and other research and development activities, we are unable to estimate with certainty our future product revenues, our revenues from our current and future collaborative partners, the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials and other research and development activities.

Capital Resources

Since inception, we have financed our operations primarily through sales of equity securities, contract payments under our collaboration agreements and from sales of TAVALISSE beginning in May 2018. We have consumed substantial amounts of capital resources to date as we continue our research and development activities, including preclinical studies and clinical trials and our ongoing commercial launch of TAVALISSE.

In addition to the upfront cash payment we received from Lilly under the Lilly Agreement, we may also be eligible for potential development, regulatory, and commercial milestone payments totaling up to an additional $835.0 million, as well as tiered royalties on net sales of non-CNS and CNS disease products up to low-double digits that will vary depending upon our clinical development investment. Further, under our other sponsored research and license agreements with Grifols, Kissei, Medison, BerGenBio and Daiichi, we may be entitled to receive future payments contingent upon specified events achieved by such partners. Total future contingent payments to us under such agreements (excluding Lilly) could exceed $500.0 million if all potential product candidates achieved all of the payment triggering events under such agreements (based on a single product candidate under each agreement). See further discussions of our Sponsored Research and License Agreements and Government Contract in “Note 4 - Sponsored Research and License Agreements and Government Contract” to our “Notes to Financial Statements” contained in “Part II, Item 8, Financial Statements and Supplementary Data” of this Annual Report on Form 10-K.

In January 2021, we were awarded $16.5 million by the US Department of Defense to support our ongoing Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients. Under the agreement with the US Department of Defense, we are entitled to receive such award based on the agreed-upon payment schedule, subject to submission of proper documentation as evidence of completion of certain clinical trial events or milestones as specified in the agreement, and approval by the US Department of Defense that such events or milestones have been met. In 2021, we recognized income from the awards from the US Department of Defense of $10.5 million, of which $9.5 million was collected as of December 31, 2021. We expect to bill the remaining awards of $6.0 million throughout the period of which we conduct our clinical trial, subject to us meeting certain clinical trial events or milestones and approval by the US Department of Defense as specified in the agreement.

In August 2020, we entered into an Open Market Sale Agreement with Jefferies LLC, as a sole agent, pursuant to which we may sell from time to time, through Jefferies, shares of our common stock in sales deemed to be "at-the-market offerings" as defined in Rule 415 under the Securities Act, subject to conditions specified in the Open Market Sale Agreement, including maintaining an effective registration statement covering the sale of shares under the Open Market Sale Agreement. In April 2021, the registration statement registering the sale of shares under the Open Market Sale Agreement expired. From the time of implementation of the Open Market Sale Agreement through expiration of the registration statement, no sales of shares occurred. A new automatic shelf registration statement was filed on August 3, 2021 to register the sale of up to a maximum aggregate offering price of $100.0 million of shares of our common stock that may be issued and sold from time to time under the Open Market Sale Agreement.

As of December 31, 2021, we have a principal term loan outstanding with MidCap amounting to $20.0 million, pursuant to the Credit and Security Agreement (Credit Agreement) we entered in September 2019. The Credit Agreement provides for $60.0 million term loan credit facility. As of December 31, 2021, the credit facility provides us with access for an additional $40.0 million term loan subject to the achievement of certain customary conditions. On February 11, 2022, we entered into Second Amendment to our Credit Agreement with MidCap which, among other things, amend the applicable funding conditions, applicable commitments and certain other terms relating to available credit facilities (Tranches 3 and 4), add additional term loan credit facility (Tranche 5), and revise certain terms related to the financial covenants. See "Note 15 – Subsequent Events" to our "Notes to Financial Statements" for further discussions.

We have a sublease agreement originally entered in December 2014 with an unrelated third party to occupy a portion of our research and office space which will expire in January 2023. As of December 31, 2021, we expect to receive approximately $5.1 million in future sublease income (excluding our subtenant's share of the facility's operating expenses) through January 2023.

Our operations will require significant additional funding for the foreseeable future. Unless and until we are able to generate a sufficient amount of product, royalty or milestone revenue, we expect to opportunistically finance future cash needs through public and/or private offerings of equity securities, debt financings and/or collaboration and licensing arrangements, and to a much lesser extent through the proceeds from exercise of stock options and interest income earned on the investment of our excess cash balances and short-term investments. However, the COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. Our ability to raise additional capital may be adversely impacted by potential worsening of global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the US 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 for certain corporate development transactions or our ability to make important, opportunistic investments. In addition, any additional capital we raise by issuing equity securities, our stockholders could at that time experience substantial dilution. Our current credit facility with MidCap and any debt financing that we are able to obtain in the future may involve operating covenants that may restrict our business. To the extent that we raise additional funds through collaboration and licensing arrangements, we may be required to relinquish some of our rights to our technologies or product candidates or grant licenses on terms that are not favorable to us.

Our future funding requirements will depend upon many factors, including, but not limited to:

- the ongoing costs to commercialize TAVALISSE for the treatment of ITP in the US, or any other future product candidates, if any such candidate receives regulatory approval for commercial sale;
- our ability to generate expected revenue from our commercialization efforts;
- the progress and success of our clinical trials and preclinical activities (including studies and manufacture of materials) of our product candidates conducted by us;
- our ability to meet operating covenants under our current and future credit facilities, if any;
- our ability to enter into partnering opportunities across our pipeline within and outside the US;
- the costs and timing of regulatory filings and approvals by us and our collaborators;
- the progress of research and development programs carried out by us and our collaborative partners;

- any changes in the breadth of our research and development programs;
- the ability to achieve the events identified in our collaborative agreements that may trigger payments to us from our collaboration partners;
- our ability to acquire or license other technologies or compounds that we may seek to pursue;
- our ability to manage our growth;
- competing technological and market developments;
- the costs and timing of obtaining, enforcing and defending our patent and other intellectual property rights; and
- expenses associated with any unforeseen litigation, including any arbitration and securities class action lawsuits.

Insufficient funds may require us to delay, scale back or eliminate some or all of our commercial efforts and/or research or development programs, to lose rights under existing licenses or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose or may adversely affect our ability to operate as a going concern.

Material Cash Requirements

We conduct our commercial activities and research and development programs internally and through third parties that include, among others, arrangements with vendors, consultants, contract research organizations (CRO) and universities. We have contractual arrangements with these parties, however our contracts with them are cancelable generally on reasonable notice within one year and our obligations under these contracts are primarily based on services performed. We do not have any purchase commitments under any collaboration arrangements.

We have agreements with certain clinical research organizations to conduct our clinical trials and with third parties relative to our commercialization of TAVALISSE. The timing of payments for any amounts owed under the respective agreements will depend on various factors including, but not limited to, patient enrollment and other progress of the clinical trial and various activities related to commercial launch. We expect we will continue to enter into contracts in the normal course of business with various third parties who support our clinical trials, support our preclinical research studies, and provide other services related to our operating purposes as well as our commercial launch of TAVALISSE. We can terminate these agreements at any time, and if terminated, we would not be liable for the full amount of the respective agreements. Instead, we will be liable for services provided through the termination date plus certain cancellation charges, if any, as defined in each of the respective agreements. In addition, these agreements may, from time to time, be subjected to amendments as a result of any change orders executed by the parties.

As discussed in detail in “Note 4 – Sponsored Research and License Agreements and Government Contract” of our “Notes to Financial Statements” contained in “Part II, Item 8, Financial Statements and Supplementary Data” of this Annual Report on Form 10-K, pursuant to our global exclusive license agreement and strategic collaboration agreement with Lilly, we are responsible for funding the development costs for R552 in the US, Europe, and Japan, up to $65.0 million through April 1, 2024. As of and for the year ended December 31, 2021, Lilly billed us $2.1 million of the funding development costs, which was subsequently paid in the first quarter of 2022. We have the right to opt-out of co-funding of development costs at two different specified times. If we decide not to exercise our opt-out rights, we will be required to share in global development costs up to certain amounts at a specified cap, as set forth in the agreement.

As of December 31, 2021, we have a contractual commitment related to our facilities lease which will expire in January 2023 amounting to $11.4 million, with $10.5 million payable within 12 months. This amount excludes the expected sublease income as discussed above.

We also have a contractual commitment with respect to our credit facility with Midcap. Under our Credit Agreement with MidCap, we are obligated to make interest payments at an annual rate of one-month LIBOR (or a comparable applicable index rate determined pursuant to the Credit Agreement if the LIBOR is no longer available) plus 5.65%, subject to a LIBOR floor of 1.50% and payable monthly in arrears, originally for the first 24 months and the interest plus principal amortization for the next 36 months. Our Credit Agreement provides us an option to extend the interest-only period to 36 months (first interest-only extension) and again to 48 months (second interest-only extension) upon the satisfaction of certain conditions set forth in the Credit Agreement. In June 2021, we satisfied the first interest-only extension conditions under the Initial Credit Agreement which effectively extended the interest-only period to 36 months or through October 1, 2022. As of December 31, 2021, the outstanding principal amount of the loan was $20.0 million, with $2.5 million payable within 12 months. As of December 31, 2021, we deemed that it is probable that we will satisfy the second interest-only criteria. Accordingly, we classified our outstanding loan as long-term liabilities in the Balance Sheet. We are also obligated to pay annual administrative fees and a final fee due at maturity. Future interest and final fee payments associated with the credit facility amounted to $2.8 million, with $1.4 million payable within 12 months.

We are also subject to claims related to the patent protection of certain of our technologies, as well as purported securities class action lawsuit, other litigations, and other contractual agreements. We are required to assess the likelihood of any adverse judgments or outcomes to these matters as well as potential ranges of probable losses. A determination of the amount of reserves required, if any, for these contingencies is made after careful analysis of each individual matter.

We do not have other material contractual commitments with respect to matters discussed above.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities related to our investments and borrowings. As of December 31, 2021, we have approximately $125.0 million of cash, cash equivalents and short-term investments. Our cash equivalents and short-term investments consists of money market funds, US treasury bills, government-sponsored enterprise securities, and corporate bonds and commercial paper. Our cash equivalents and short-terms investments are invested in high-grade securities, and as a result, we believe represent a minimal credit risk. The goals of our investment policy are liquidity and capital preservation; we do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate exposure. If interest rates were to increase or decrease by 100 basis points, the fair value of our cash equivalents and short-term investments would increase or decrease by an immaterial amount.

As of December 31, 2021, our outstanding principal loans consist of $20.0 million from MidCap. The outstanding principal balance of the loan bears interest at an annual rate of one-month LIBOR (or a comparable applicable index rate determined pursuant to the Credit Agreement if the LIBOR is no longer available) plus 5.65%, subject to a LIBOR floor of 1.50% and is payable monthly in arrears. Accordingly, our interest expense under the MidCap Credit Agreement is subject to changes in the one-month LIBOR rate. Given that the contractual LIBOR floor rate is significantly higher than the current LIBOR rate, fluctuations in such LIBOR rate would not have a material effect on our interest payment obligation.

Item 8. Financial Statements and Supplementary Data

INDEX TO FINANCIAL STATEMENTS
Rigel Pharmaceuticals, Inc.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Rigel Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Rigel Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations, comprehensive loss, stockholders' 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 "financial statements"). In our opinion, the 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 March 1, 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 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.

Product Sales Allowances and Discounts

Description of the Matter	As described in Note 1 to the financial statements, revenue from product sales is recorded net of adjustments for estimated government-mandated rebates and chargebacks, distribution fees, estimated product returns, and other deductions. Provisions for these adjustments are recorded in the period in which the related revenue is recorded and are presented either as a reduction of accounts receivable or as an accrued liability in the Company's balance sheet. As of December 31, 2021, the Company has recorded net liabilities for product sales allowances and discounts of $7.9 million.

Auditing product sales allowances and discounts involved evaluation of management's subjective judgments regarding the reasonableness of estimated payor and channel mix applied to product sales during the period. These estimates are based on available customer and payor data received from specialty pharmacies and distributors and reflect management's judgments regarding adjustments to historical trends. The Company has a limited history upon which to base such estimates, and changes in the estimated payor and channel mix can have a material effect on the amount of variable consideration recognized.

How We Addressed the Matter in Our Audit

We tested the Company's internal controls over the process for estimating and recording product sales allowances and discounts. Our testing included controls over management's review of significant assumptions, such as payor mix and channel mix, and other inputs such as product sold, contractual terms, discount rates, historical data and expected channel inventory levels, used in the estimates.

To test the Company's provisions for allowances and discounts, our audit procedures included, among others, evaluating the methodologies and assumptions used and the underlying data used by the Company. We evaluated the assumptions used by management against historical trends, evaluated the change in estimated accruals from prior periods, and assessed the historical accuracy of the Company's estimates against actual results. We performed substantive analytical procedures on material ending accrual balances by assessing whether the accrued balance is reasonable relative to historical payment lag and sales activity.

/s/ Ernst & Young LLP
We have served as the Company's auditor since 1998.
San Francisco, California
March 1, 2022

RIGEL PHARMACEUTICALS, INC.
BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 18,890	$ 30,373
Short-term investments	106,077	26,954
Accounts receivable, net	15,472	15,973
Inventories	6,616	1,638
Prepaid and other current assets	7,412	14,045
Total current assets	154,467	88,983
Property and equipment, net	2,184	2,676
Operating lease right-of-use asset	9,703	17,895
Other assets	974	824
	$ 167,328	$ 110,378
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,795	$ 3,707
Accrued compensation	10,690	9,592
Accrued research and development	10,384	4,889
Other accrued liabilities	12,691	11,014
Lease liabilities, current portion	9,892	8,621
Deferred revenue	2,596	3,018
Other long-term liabilities, current portion	13,506	—
Total current liabilities	63,554	40,841
Long-term portion of lease liabilities	759	10,651
Loans payable, net of discount	19,914	19,815
Other long-term liabilities	52,727	5,045
Commitments		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; none issued and outstanding as of December 31, 2021 and 2020	—	—
Common stock, $0.001 par value; 400,000,000 shares authorized; 171,602,226 and 169,316,782 shares issued and outstanding as of December 31, 2021 and 2020, respectively	172	169
Additional paid-in capital	1,354,190	1,339,833
Accumulated other comprehensive income (loss)	(102)	(4)
Accumulated deficit	(1,323,886)	(1,305,972)
Total stockholders' equity	30,374	34,026
	$ 167,328	$ 110,378

See Accompanying Notes to Financial Statements.

RIGEL PHARMACEUTICALS, INC.
STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)

	Year Ended December 31,		
	2021	2020	2019
Revenues:			
Product sales, net	$ 63,010	$ 61,696	$ 43,772
Contract revenues from collaborations	75,726	46,925	15,516
Government contract	10,500	—	—
Total revenues	149,236	108,621	59,288
Costs and expenses:			
Cost of product sales	1,083	895	906
Research and development	65,237	60,101	52,885
Selling, general and administrative	91,891	76,598	74,588
Restructuring charges	3,521	—	—
Total costs and expenses	161,732	137,594	128,379
Loss from operations	(12,496)	(28,973)	(69,091)
Interest income	47	582	2,532
Interest expense	(4,860)	(1,353)	(335)
Loss before income taxes	(17,309)	(29,744)	(66,894)
Provision for income taxes	605	—	—
Net loss	$ (17,914)	$ (29,744)	$ (66,894)
Net loss per share, basic and diluted	$ (0.11)	$ (0.18)	$ (0.40)
Weighted average shares used in computing net loss per share, basic and diluted	170,492	168,754	167,400

See Accompanying Notes to Financial Statements.

RIGEL PHARMACEUTICALS, INC.
STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,		
	2021	2020	2019
Net loss	$ (17,914)	$ (29,744)	$ (66,894)
Other comprehensive income (loss):			
Net unrealized gain (loss) on short-term investments	(98)	(27)	47
Comprehensive loss	$ (18,012)	$ (29,771)	$ (66,847)

See Accompanying Notes to Financial Statements.

RIGEL PHARMACEUTICALS, INC.
STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share amounts)

	Common Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of January 1, 2019	167,171,505	$ 167	$ 1,319,068	$ (24)	$ (1,209,334)	$ 109,877
Net loss	—	—	—	—	(66,894)	(66,894)
Net change in unrealized gain (loss) on short-term investments	—	—	—	47		47
Issuance of common stock upon exercise of options and participation in Purchase Plan	816,345	1	1,575	—		1,576
Stock compensation expense	—	—	9,209	—		9,209
Balance as of December 31, 2019	167,987,850	168	1,329,852	23	(1,276,228)	53,815
Net loss	—	—	—	—	(29,744)	(29,744)
Net change in unrealized gain (loss) on short-term investments	—	—	—	(27)	—	(27)
Issuance of common stock upon exercise of options and participation in Purchase Plan	1,328,932	1	2,595	—	—	2,596
Stock compensation expense	—	—	7,386	—	—	7,386
Balance as of December 31, 2020	169,316,782	169	1,339,833	(4)	(1,305,972)	34,026
Net loss	—	—	—	—	(17,914)	(17,914)
Net change in unrealized gain (loss) on short-term investments	—	—	—	(98)	—	(98)
Issuance of common stock upon exercise of options and participation in Purchase Plan	2,285,444	3	4,772	—	—	4,775
Stock compensation expense	—	—	9,585	—	—	9,585
Balance as of December 31, 2021	171,602,226	$ 172	$ 1,354,190	$ (102)	$ (1,323,886)	$ 30,374

See Accompanying Notes to Financial Statements.

RIGEL PHARMACEUTICALS, INC.
STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2021	2020	2019
Operating activities			
Net loss	$ (17,914)	$ (29,744)	$ (66,894)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Stock-based compensation expense	9,486	7,297	9,115
Depreciation and amortization	1,162	706	683
Non-cash interest expense	3,139	—	—
Net amortization and accretion of discount on short-term investments and term loan	287	(122)	(1,073)
Changes in assets and liabilities:			
Accounts receivable, net	501	(5,862)	(6,034)
Inventories	(4,875)	(126)	(366)
Prepaid and other current assets	6,633	(4,583)	(5,673)
Other assets	(150)	(128)	39
Right-of-use assets	8,192	7,814	7,118
Accounts payable	41	(331)	(2,239)
Accrued compensation	1,098	773	(1,133)
Accrued research and development	5,495	(1,071)	(803)
Other accrued liabilities	1,826	4,051	3,122
Lease liability	(8,621)	(7,230)	(6,725)
Deferred revenue	(422)	(23,629)	24,255
Other long-term liabilities	—	—	5,098
Net cash provided by (used in) operating activities	5,878	(52,185)	(41,510)
Investing activities			
Purchases of short-term investments	(141,459)	(81,706)	(145,327)
Maturities of short-term investments	62,050	130,434	123,126
Capital expenditures	(627)	(1,262)	(1,455)
Net cash (used in) provided by investing activities	(80,036)	47,466	(23,656)
Financing activities			
Cost share advance from collaboration partner	57,900	—	—
Net proceeds from issuances of common stock upon exercise of options and participation in Purchase Plan	4,775	2,596	1,576
Net proceeds from term loan financing	—	9,975	9,789
Net cash provided by financing activities	62,675	12,571	11,365
Net increase (decrease) in cash and cash equivalents	(11,483)	7,852	(53,801)
Cash and cash equivalents at beginning of period	30,373	22,521	76,322
Cash and cash equivalents at end of period	$ 18,890	$ 30,373	$ 22,521
Supplemental disclosure of cash flow information			
Interest paid	$ 1,500	$ 1,180	$ 137

See Accompanying Notes to Financial Statements.

RIGEL PHARMACEUTICALS, INC.
NOTES TO FINANCIAL STATEMENTS

In this Annual Report on Form 10-K, "Rigel," "we," "us" and "our" refer to Rigel Pharmaceuticals, Inc. and "common stock" refers to Rigel's common stock, par value $0.001 per share.

1. DESCRIPTION OF BUSINESS AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Description of Business

We are a biotechnology company dedicated to discovering, developing and providing novel small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer and rare immune diseases. Our pioneering research focuses on signaling pathways that are critical to disease mechanisms. Our first product approved by the US Food and Drug Administration (FDA) is TAVALISSE® (fostamatinib disodium hexahydrate) tablets, the only approved oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. The product is also commercially available in Europe, United Kingdom (UK) (TAVLESSE) and Canada (TAVALISSE) for the treatment of chronic ITP in adult patients.

Fostamatinib is currently being studied in a Phase 3 trial for the treatment of warm autoimmune hemolytic anemia (wAIHA); a Phase 3 clinical trial for the treatment of hospitalized high-risk patients with COVID-19; a National Institute of Health (NIH)/National Heart, Lung, and Blood Institute (NHLBI) sponsored Phase 3 trial (ACTIV-4 Host Tissue Trial) for the treatment of COVID-19 in hospitalized patients; and a Phase 2 trial for the treatment of COVID-19 being conducted by Imperial College London.

Our other clinical programs include our interleukin receptor-associated kinase (IRAK) inhibitor program and a receptor-interacting serine/threonine-protein kinase (RIPK1) inhibitor program in clinical development with partner Eli Lilly and Company (Lilly). In addition, we have product candidates in clinical development with partners BerGenBio ASA (BerGenBio) and Daiichi Sankyo (Daiichi).

Basis of presentation

The accompanying financial statements have been prepared in accordance with United States generally accepted accounting principles (US GAAP). Any reference in these notes to applicable accounting guidance is meant to refer to the authoritative US GAAP included in the Accounting Standards Codification (ASC), and Accounting Standards Update (ASU) issued by the Financial Accounting Standards Board (FASB).

Liquidity

As of December 31, 2021, we had approximately $125.0 million in cash, cash equivalents and short-term investments. Since inception, we have financed our operations primarily through sales of equity securities, debt financing arrangement, contract payments under our collaboration agreements and from product sales. Based on our current operating plan, we believe that our existing cash, cash equivalents, and short-term investments will be sufficient to fund our expenses and capital expenditure requirements for at least the next 12 months from the date of issuance of this Annual Report on Form 10-K.

Use of estimates

The preparation of financial statements in conformity with US GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Significant estimates and assumptions made by management include those relating to revenue recognition on product sales and collaboration agreements, recoverability of our assets, including accounts receivables and inventories, stock-based compensation and the probability of achievement of corporate performance-based milestones for our performance-based stock option awards, impairment issues, the weighted average incremental borrowing rate for our lease, estimated interest rate for our financing liability, the estimated useful life of assets, and estimated accruals, particularly research and development accruals, on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. To the extent there are material differences between these estimates and actual results, our financial statements will be affected.

Inventories

Inventories are stated at the lower of cost or estimated net realizable value. We determine the cost of inventories using the standard cost method, which approximates actual cost based on a first-in, first-out basis. Inventories consist primarily of third-party manufacturing costs and allocated internal overhead costs. We began capitalizing inventory costs associated with our product upon regulatory approval when, based on management's judgment, future commercialization was considered probable and the future economic benefit was expected to be realized.

Prior to FDA approval of TAVALISSE, all manufacturing costs were charged to research and development expense in the period incurred. As of December 31, 2021 and 2020, our physical inventory included active pharmaceutical product for which costs have been previously charged to research and development expense. However, manufacturing of drug product, finished bottling and other labeling activities that occurred post FDA approval are included in the inventory value at each balance sheet date.

We provide reserves for potential excess, dated or obsolete inventories based on an analysis of forecasted demand compared to quantities on hand and any firm purchase orders, as well as product shelf life.

Cost of Product Sales

Cost of product sales consists of third-party manufacturing costs, transportation and freight, and indirect overhead costs associated with the manufacture and distribution of TAVALISSE. A portion of the cost of producing the product sold to date was expensed as research and development prior to the Company's New Drug Application approval for TAVALISSE and therefore is not included in the cost of product sales during this period.

Accounts Receivable

Accounts receivable are recorded net of customer allowances for prompt payment discounts and any allowance for doubtful accounts. We estimate the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of our customers and individual customer circumstances. To date, we have determined that an allowance for doubtful accounts is not required.

The following table summarizes the activity of our customer allowances for prompt payment discounts for the periods presented (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Balance at the beginning of the year	$ 171	$ 109	$ 50
Provision for prompt payment discount	609	807	540
Reduction in prompt payment discount	(674)	(745)	(481)
Balance at end of the year	$ 106	$ 171	$ 109

Revenue Recognition

We recognize revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers (ASC 606), when a customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine whether arrangements are within the scope of ASC 606, 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 Company satisfies its performance obligation. We 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 to the customer. At contract inception, once the contract is determined to be within the scope of this new guidance, we assess the goods or services promised within each contract and identify, as a performance obligation, 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.

Product Sales

Revenues from product sales are recognized when the specialty distributors (SDs), who are our customers, obtain control of our product, which occurs at a point in time, upon delivery to such SDs. These SDs subsequently resell our products to specialty pharmacy providers, health care providers, hospitals and clinics. In addition to distribution agreements with these SDs, we also enter into arrangements with specialty pharmacy providers, in-office dispensing providers, group purchasing organizations, and government entities that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of our products.

Under ASC 606, we are required to estimate the transaction price, including variable consideration that is subject to a constraint, in our contracts with our customers. Variable consideration is included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur. Revenue from product sales is recorded net of certain variable consideration which includes estimated government-mandated rebates and chargebacks, distribution fees, estimated product returns and other deductions.

Provisions for returns and other adjustments are provided for in the period the related revenue is recorded. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

The following are our significant categories of sales discounts and allowances:

Sales Discounts. We provide certain customer a prompt payment discount that is explicitly stated in our contract. The sales discount is recorded as a reduction of revenue in the period the related product revenue is recognized.

Product Returns. We offer our SDs a right to return product purchased directly from us, which is principally based upon the product's expiration date. Product return allowances are estimated and recorded at the time of sale.

Government and Private Payor Rebates: We are subject to discount obligations under the state Medicaid programs and Medicare prescription drug coverage gap program. We estimate our Medicaid and Medicare prescription drug coverage gap rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. In December 2021 and beginning of 2022, we entered into rebate program agreements with Pharmacy Benefit Managers (PBMs), pursuant to which rebates will be paid in accordance with the respective agreements. The rebate reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and related liability is recorded as revenue reserves within other accrued liabilities in the balance sheet. Our liability for these rebates consists primarily of estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but remains in the distribution channel inventories at the end of each reporting period.

Chargebacks and Discounts: Chargebacks for fees and discounts represent the estimated obligations resulting from contractual commitments to sell products to certain specialty pharmacy providers, in-office dispensing providers, group purchasing organizations, and government entities at prices lower than the list prices charged to our SDs who directly purchase the product from us. These SDs charge us for the difference between what they pay for the product and our contracted selling price to these specialty pharmacy providers, in-office dispensing providers, group purchasing organizations, and government entities. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue. Actual chargeback amounts are generally determined at the time of resale to the specialty pharmacy providers, in-office dispensing providers, group purchasing organizations, and government entities by our SDs. The estimated obligations arising from these chargebacks and discounts are recorded as revenue reserves within other accrued liabilities in the balance sheet.

Co-Payment Assistance: We offer co-payment assistance to commercially insured patients meeting certain eligibility requirements. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue.

Contract Revenues from Collaborations

In the normal course of business, we conduct research and development programs independently and in connection with our corporate collaborators, pursuant to which we license certain rights to our intellectual property to third parties. The terms of these arrangements typically include payment to us for a combination of one or more of the following: upfront license fees; development, regulatory and commercial milestone payments; product supply services; and royalties on net sales of licensed products.

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

For arrangements that require us to share in the development costs but to which we do not participate in the co-development work, the portion of the upfront fee attributed to our share in the future development costs is excluded from the transaction price. If such share in the development costs is payable beyond 12 months from the delivery of the corresponding license, a significant financing component is deemed to exist. If a significant financing component is identified, we adjust the transaction price by reducing the upfront fee by the net present value of our share in future development costs over the expected commitment period. Such discounted amount will be reported as a liability in the balance sheet, with a corresponding interest expense being accreted based on a discount rate applied over the expected commitment period.

Development, Regulatory or Commercial Milestone Payments: At the inception of each arrangement that includes payments based on the achievement of certain development, regulatory and commercial or launch events, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until uncertainty associated with the approvals has been resolved. The transaction price is then allocated to each performance obligation, on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such development and regulatory milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, and recorded as part of contract revenues from collaborations during the period of adjustment.

Product Supply Services: Arrangements that include a promise for future supply of drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations.

Sales-based Milestone Payments and Royalties: For arrangements that include sales-based royalties, including milestone payments based on the volume of sales, we determine whether the license is deemed to be the predominant item to which the royalties or sales-based milestones relate to and if such is the case, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Government Contract

In January 2021, we were awarded up to $16.5 million by the US Department of Defense's Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (referred to here as the US Department of Defense) to support our ongoing Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib for the treatment of hospitalized high-risk patients with COVID-19. We determined that the government award should be accounted for under IAS 20, *Accounting for Government Grants and Disclosure of Government Assistance,* which is outside the scope of Topic 606, as the US Department of Defense is not receiving reciprocal value for their contributions. Revenue is recognized when there is reasonable assurance that the conditions of the grant will be met, and the grant will be received. For the US Department of Defense's contract, this occurs when either each milestone has been accepted by the US Department of Defense or management has concluded that the conditions of the grant have been substantially met. See "Note 4 – Sponsored Research and License Agreements and Government Contract" for further discussion.

Stock-based Compensation

Share-based awards are valued at fair value on the date of grant and that fair value is recognized over the requisite service period, which is generally the vesting period of the respective award. We use the straight-line attribution method over the requisite employee service period for the entire award in recognizing stock-based compensation expense. We account for forfeitures as they occur.

The fair value of each option award is estimated on the date of grant using the Black-Scholes option pricing model. The model requires management to make a number of assumptions including expected volatility, expected term, risk-free interest rate and expected dividends. A number of these assumptions are subjective, and their determination generally require judgment. We segregate option awards into the following three homogenous groups for the purposes of determining fair values of options: officers and directors, all other employees, and consultants. We determine the weighted-average valuation assumptions separately for each of these groups as follows:

- Volatility – We estimate volatility using the historical share price performance over the expected life of the option up to the point where we have historical market data. We also consider other factors, such as implied volatility, our current clinical trials and other company activities that may affect the volatility of our stock in the future. We determined that at this time historical volatility is more indicative of our expected future stock performance than implied volatility.

- Expected term – We analyze various historical data to determine the applicable expected term for each of the other option groups. This data includes: (1) for exercised options, the term of the options from option grant date to exercise date; (2) for cancelled options, the term of the options from option grant date to cancellation date, excluding non-vested option forfeitures; and (3) for options that remained outstanding at the balance sheet date, the term of the options from option grant date to the end of the reporting period and the estimated remaining term of the options. The consideration and calculation of the above data gives us reasonable estimates of the expected term for each employee group. We also consider the vesting schedules of the options granted and factors surrounding exercise behavior of the option groups, our current market price and company activity that may affect our market price. In addition, we consider the optionee type (i.e., officers and directors or all other employees) and other factors that may affect the expected term of the option. For options granted to consultants, we use the contractual term of the option, which is generally

10 years, for the initial valuation of the option and the remaining contractual term of the option for the succeeding periods.

- Risk-free interest rate – The risk-free interest rate is based on US Treasury constant maturity rates with similar terms to the expected term of the options for each option group.

- Dividend yield – The expected dividend yield is 0% as we have not paid and do not expect to pay dividends in the future.

We grant performance-based stock options to purchase shares of our common stock which will vest upon the achievement of certain corporate performance-based milestones. We determine the fair values of these performance-based stock options using the Black-Scholes option pricing model at the date of grant. For the portion of the performance-based stock options of which the performance condition is considered probable of achievement, we recognize stock-based compensation expense on the related estimated grant date fair values of such options on a straight-line basis from the date of grant up to the date when we expect the performance condition will be achieved. For the performance conditions that are not considered probable of achievement at the grant date or upon re-evaluation at each reporting date, prior to the event actually occurring, we recognize the related stock-based compensation expense when the event occurs or when we can determine that the performance condition is probable of achievement. In those cases, we recognize the change in estimate at the time we determine the condition is probable of achievement (by recognizing stock-based compensation expense as cumulative catch-up adjustment as if we had estimated at the grant date that the performance condition would have been achieved) and recognize the remaining compensation cost up to the date when we expect the performance condition will be achieved, if any.

The fair value of a restricted stock unit grant is based on the market price of our common stock on the date of grant.

Cash, cash equivalents and short-term investments

Our investment in debt securities consists of money market funds, US treasury bills, government- sponsored enterprise securities, and corporate bonds and commercial paper. All of our investment in debt securities are available-for-sale and are classified based on their maturities. We consider all highly liquid investments in debt securities with maturity of 90 days or less from the date of purchase to be cash equivalents. All other investments with maturity greater than 90 days from the date of purchase are classified as short-term investments. Unrealized gains (losses) are reported within the statements of stockholders' equity and comprehensive loss. The cost of securities sold is based on the specific identification method.

Fair value of financial instruments

The carrying amounts of our financial instruments, including cash, accounts receivable, accounts payable and accrued liabilities, approximate fair value due to their relatively short maturities. The carrying value of our loans payable and other long-term debt approximates fair value based on management's estimation that a current interest rate would not differ materially from the stated rate, or the discount rate applied.

The fair value of our cash equivalents and short-term investments measured at fair value on a recurring basis and are categorized based upon the lowest level of significant input to the valuations.

Assets and liabilities recorded at fair value in our financial statements are categorized based upon the level of judgment associated with the inputs used to measure their fair value. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. Hierarchical levels directly related to the amount of subjectivity associated with the inputs to fair valuation of these assets and liabilities, are as follows:

- Level 1 – Inputs are unadjusted, quoted prices in active markets for identical assets at the reporting date. Active markets are those in which transactions for the asset or liability occur in sufficient frequency and volume to provide pricing information on an ongoing basis.

  The fair valued assets we hold that are generally included under this Level 1 are money market securities where fair value is based on publicly quoted prices.

- Level 2 – Inputs, other than quoted prices included in Level 1, that are either directly or indirectly observable for the asset or liability through correlation with market data at the reporting date and for the duration of the instrument's anticipated life.

  The fair valued assets we hold that are generally assessed under Level 2 included government-sponsored enterprise securities, US treasury bills and corporate bonds and commercial paper. We utilize third party pricing services in developing fair value measurements where fair value is based on valuation methodologies such as models using observable market inputs, including benchmark yields, reported trades, broker/dealer quotes, bids, offers and other reference data. We use quotes from external pricing service providers and other on-line quotation systems to verify the fair value of investments provided by our third-party pricing service providers. We review independent auditor's reports from our third-party pricing service providers particularly regarding the controls over pricing and valuation of financial instruments and ensure that our internal controls address certain control deficiencies, if any, and complementary user entity controls are in place.

- Level 3 – Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities and which reflect management's best estimate of what market participants would use in pricing the asset or liability at the reporting date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model. We do not have fair valued assets classified under Level 3.

Concentration of credit risk

Financial instruments that potentially subject us to a concentration of credit risk are primarily cash, investment in debt securities and accounts receivable. All of our cash and investment in debt securities are maintained with financial institutions that management believes are creditworthy. By policy, we limit the concentration of credit risk by diversifying our investments among a variety of high credit-quality issuers. Due to the short-term nature of these investments, we believe we do not have a material exposure to credit risk arising from our investments.

Concentration of credit risk with respect to our accounts receivable is limited due to our small number of customers. Our accounts receivable consists mostly of outstanding invoices from our sale of TAVALISSE to our three specialty distributors. Accounts receivable may also include outstanding invoice or invoices from our collaboration partners with respect to the related sponsored research and license agreements, as well as outstanding invoice or invoices from the US Government with respect to the related government contract. As of December 31, 2021, 85% of our accounts receivable are outstanding invoices from our three specialty distributors, and the remaining 15% are outstanding invoices from the US Government and from other collaboration partners, Grifols, Kissei and Medison. As of December 31, 2020, 97% of our accounts receivable consisted of outstanding invoices from our specialty distributors, and the remaining 3% was related to outstanding invoices from our collaboration partners, Grifols and Medison.

See "Note 3 - Revenues" for summary of revenues from each of our customers who individually accounted for 10% or more of the total net product sales and revenues from collaborations.

Property and equipment

Property and equipment are stated at cost. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which range from three to seven years.

Research and development expenses

Research and development expenses include costs for scientific personnel, supplies, equipment, consultants, research sponsored by us, allocated facility costs, costs related to pre-clinical and clinical trials, including raw materials, and stock-based compensation expense. All such costs are charged to research and development expense as incurred and at the time raw materials are purchased.

We have various contracts with third parties related to our research and development activities. Costs that are incurred but not billed to us as of the end of the period are accrued. We make estimates of the amounts incurred in each period based on the information available to us and our knowledge of the nature of the contractual activities generating such costs. Clinical trial contract expenses are accrued based on units of activity. Expenses related to other research and development contracts, such as research contracts, toxicology study contracts and manufacturing contracts are estimated to be incurred generally on a straight-line basis over the duration of the contracts. Raw materials and study materials not related to our approved drug, purchased for us by third parties are expensed at the time of purchase.

Leases

We adopted ASU No. 2018-11*, Leases (Topic 842): Targeted Improvements* as of January 1, 2019. Pursuant to Topic 842, all of our leases outstanding on January 1, 2019 continued to be classified as operating leases. As a result of the adoption of Topic 842, we recognized $32.8 million in operating right-of-use lease asset and $33.2 million in lease liability, and derecognized $0.4 million of deferred rent in the balance sheet at adoption date. These were calculated using the present value of our remaining lease payments using an estimated incremental borrowing rate of 9%. There was no cumulative-effect adjustment on our accumulated deficit as of January 1, 2019. For our sublease agreement wherein we are the lessor, the same practical expedients apply to both lessor and lessee. Therefore, the sublease continues to be classified as an operating lease under Topic 842. Further, the adoption of Topic 842 did not have an impact on our sublease on the date of adoption since the expected sublease income is equal to the expected lease costs for the head leases over the remaining period of the lease term, and therefore, no impairment of the operating right-of-use asset was needed upon the adoption of Topic 842.

As of December 31, 2021, our leases continued to be classified as operating leases. Following the adoption of Topic 842 as discussed above, operating right-of-use lease asset and operating lease liability are presented on our balance sheet. Right-of-use lease assets represent our right to use the underlying asset for the lease term and the lease liability represents our commitment to make the lease payments arising from the lease. Right-of-use lease assets and lease liability are recognized at the commencement date based on the present value of remaining lease payments over the lease term. The operating right-of-use lease asset includes any lease payments made prior to commencement. The lease term may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Operating lease expense is recognized on a straight-line basis over the lease term, subject to any changes in the lease or expectations regarding the terms. Variable lease costs such as common area costs and property taxes are expensed as incurred. Leases with an initial term of 12 months or less are not recorded on the balance sheet.

For our sublease agreement wherein we are the lessor, sublease income will be recognized on a straight-line basis over the term of the sublease. The difference between the cash received, and the straight-line lease income recognized, if any, will be recorded within prepaid and other current assets in the balance sheet.

Income taxes

We use the asset and liability method to account for income taxes. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities from a change in tax rates is recognized in income in the period the change is enacted. A valuation allowance is established to reduce deferred tax assets to an amount whose realization is more likely than not.

Restructuring

Restructuring costs comprised of severance, other termination benefit costs, stock-based compensation expense for stock award and stock option modifications related to workforce reductions and accelerated depreciation. We recognize restructuring charges when the liability is probable, and the amount is estimable. Employee termination benefits are accrued at the date management has committed to a plan of termination and affected employees have been notified of their termination date and expected severance benefits.

Recent accounting pronouncements

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740) Simplifying the Accounting for Income Taxes*, which simplifies the accounting for income taxes by removing variety of exceptions within the framework of ASC 740. There were nine amendments in the ASU, such as the elimination of the incremental approach to intraperiod tax allocation, recognition of deferred tax liability for outside basis differences, changes to the accounting of hybrid tax regimes, amendments to the accounting of tax basis step-up in goodwill, clarification on separate financial statements of legal entities not subject to tax, guidance on the accounting for ownership changes in investments, and guidance on interim-period accounting for tax law changes and year-to-date loss limitations. The guidance is effective for fiscal years beginning after December 15, 2020 and for interim periods within those fiscal years. We adopted this new standard on January 1, 2020 with no material impact on our financial statements and disclosures.

In November 2021, the FASB issued ASU No. 2021-10, *Government Assistance (Topic 832) Disclosures by Business Entities about Government Assistance.* Current GAAP has no specific authoritative guidance on the accounting for, or the disclosure of, government assistance received by business entities. The amendments in this update improve financial reporting by requiring disclosures that increase the transparency of transactions with a government accounted for by applying a grant or contribution accounting model by analogy, including the types of transactions, the accounting for those transactions, and the effect of those transactions on an entity's financial statements. The amendments in this update require the following annual disclosures about transactions with a government that are accounted for by applying a grant or contribution accounting model by analogy, including: (1) information about the nature of the transactions and the related accounting policy used to account for the transactions; (2) the line items on the balance sheet and income statement that are affected by the transactions, and the amounts applicable to each financial statement line item; and (3) the significant terms and conditions of the transactions, including commitments and contingencies. The amendments in this update are effective for all entities within their scope for financial statements issued for annual periods beginning after December 15, 2021. Early application of the amendments is permitted. We adopted this update during the year ended December 31, 2021 and accounted the award we received from the US Department of Defense in accordance with this update. See "Note 4 – Sponsored Research and License Agreements and Government Contract" for further discussion.

2. NET LOSS PER SHARE

Basic net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock outstanding during the period and the number of additional shares of common stock that would have been outstanding if potentially dilutive securities had been issued. Potentially dilutive securities include stock options, restricted stock units and shares issuable under our Purchase Plan. The dilutive effect of these potentially dilutive securities is reflected in diluted earnings per share using the treasury stock method. Under the treasury stock method, an increase in the fair market value of our common stock can result in a greater dilutive effect from potentially dilutive securities.

The following table sets forth the computation of basic and diluted loss per share for the periods presented (in thousands except per share amounts):

	Year Ended December 31,		
	2021	2020	2020
EPS Numerator:			
Net loss	$ (17,914)	$ (29,744)	$ (66,894)
EPS Denominator—Basic and Diluted:			
Weighted-average common shares outstanding	170,492	168,754	167,400
Net loss per share, basic and diluted	$ (0.11)	$ (0.18)	$ (0.40)

The potential shares of common stock that were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive are as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Outstanding stock options	30,009	27,260	22,671
Restricted stock units	226	—	—
Total	30,235	27,260	22,671

3. REVENUES

Revenues disaggregated by category were as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Product sales:			
Gross product sales	$ 81,186	$ 76,470	$ 53,082
Discounts and allowances	(18,176)	(14,774)	(9,310)
Total product sales, net	63,010	61,696	43,772
Revenues from collaborations:			
License revenues	70,553	40,358	8,696
Development milestones	1,875	2,100	5,500
Research and development services and others	3,298	4,467	1,320
Total revenues from collaborations	75,726	46,925	15,516
Government contract	10,500	—	—
Total revenues	$ 149,236	$ 108,621	$ 59,288

Our net product sales include sale of TAVALISSE in the US, net of chargebacks, discounts and fees, government and other rebates and returns. The following tables summarize the activities in chargebacks, discounts and fees, government and other rebates and returns that were accounted for within other accrued liabilities, for each of the periods presented (in thousands):

	Chargebacks, Discounts and Fees	Government and Other Rebates	Returns	Total
Balance as of January 1, 2021	$ 2,461	$ 2,115	$ 1,489	$ 6,065
Provision related to current period sales	10,731	5,036	1,021	16,788
Credit or payments made during the period	(9,788)	(4,657)	(493)	(14,938)
Balance as of December 31, 2021	$ 3,404	$ 2,494	$ 2,017	$ 7,915

	Chargebacks, Discounts and Fees	Government and Other Rebates	Returns	Total
Balance as of January 1, 2020	$ 1,293	$ 1,801	$ 238	$ 3,332
Provision related to current period sales	8,149	4,231	950	13,330
Adjustment related to prior period sales	(75)	(490)	565	—
Credit or payments made during the period	(6,906)	(3,427)	(264)	(10,597)
Balance as of December 31, 2020	$ 2,461	$ 2,115	$ 1,489	$ 6,065

Of the $18.2 million discounts and allowances from gross product sales for the year ended December 31, 2021, $16.8 million was accounted for as additions to other accrued liabilities and $1.4 million as reductions in accounts receivable (as it relates to allowance for prompt pay discount) and prepaid and other current assets (as it relates to certain chargebacks and other fees that were prepaid) in the balance sheet.

Of the $14.8 million discounts and allowances from gross product sales for the year ended December 31, 2020, $13.3 million was accounted for as additions to other accrued liabilities and $1.5 million as reductions in accounts receivable (as it relates to allowance for prompt pay discount) and prepaid and other current assets (as it relates to certain chargebacks and other fees that were prepaid) in the balance sheet.

For detailed discussions of our revenues from collaboration and government contract, see “Note 4 – Sponsored Research and License Agreements and Government Contract” below.

The following table summarizes revenues from each of our customers who individually accounted for 10% or more (wherein * denotes less than 10%) of the total net product sales and revenues from collaborations:

	Year Ended December 31,		
	2021	2020	2019
Lilly	48%	—	—
McKesson Specialty Care Distribution Corporation	20%	23%	30%
ASD Healthcare and Oncology Supply	17%	30%	37%
Grifols	*	41%	*

4. SPONSORED RESEARCH AND LICENSE AGREEMENTS AND GOVERNMENT CONTRACT

Sponsored Research and License Agreements

We conduct research and development programs independently and in connection with our corporate collaborators. As of December 31, 2021, we are a party to collaboration agreements with Lilly to develop and commercialize R552, a RIPK1 inhibitor, for the treatment of non-central nervous system (non-CNS) diseases and collaboration aimed at developing additional RIPK1 inhibitors for the treatment of central nervous system (CNS) diseases; with Grifols to commercialize fostamatinib for human diseases in all indications, including chronic ITP and autoimmune hemolytic anemia (AIHA), in Europe and Turkey; with Kissei Pharmaceutical Co., Ltd. (Kissei) to develop and commercialize fostamatinib in Japan, China, Taiwan and the Republic of Korea; and with Medison Pharma Trading AG (Medison Canada) and Medison Pharma Ltd. (Medison Israel and, together with Medison Canada, Medison) to commercialize fostamatinib in all indications, including chronic ITP and AIHA, in Canada and Israel, respectively.

Further, we are also a party to collaboration agreements, but do not have ongoing performance obligations with BerGenBio for the development and commercialization of AXL inhibitors in oncology, and with Daiichi to pursue research related to MDM2 inhibitors, a novel class of drug targets called ligases. We have an agreement with AZ for the development and commercialization of R256, an inhaled JAK inhibitor. In December 2021, AZ provided a notice to terminate the agreement effective April 19, 2022. Our collaboration agreement with Aclaris related to the development and commercialization of JAK inhibitors for the treatment of alopecia areata and other dermatological conditions was terminated in April 2021.

Under the above existing agreements that we entered into in the ordinary course of business, we received or may be entitled to receive upfront cash payments, payments contingent upon specified events achieved by such partners and royalties on any net sales of products sold by such partners under the agreements. Total future contingent payments to us under all of above existing agreements, excluding terminated or terminating agreements, could exceed $1.3 billion if all potential product candidates achieved all of the payment triggering events under all of our current agreements (based on a single product candidate under each agreement). Of this amount, $279.5 million relates to the achievement of development events, $285.6 million relates to the achievement of regulatory events and $778.5 million relates to the achievement of certain commercial or launch events. This estimated future contingent amount does not include any estimated royalties that could be due to us if the partners successfully commercialize any of the licensed products. Future events that may trigger payments to us under the agreements are based solely on our partners' future efforts and achievements of specified development, regulatory and/or commercial events.

Global Exclusive License Agreement with Eli Lilly

On February 18, 2021, we entered into a global exclusive license agreement and strategic collaboration with Lilly (Lilly Agreement), which became effective on March 27, 2021, to develop and commercialize R552, a RIPK1 inhibitor, for the treatment of non-CNS diseases. In addition, the collaboration is aimed at developing additional RIPK1 inhibitors for the treatment of CNS diseases. Pursuant to the terms of the license agreement, we granted to Lilly exclusive rights to develop and commercialize R552 and related RIPK1 inhibitors in all indications worldwide. The agreement became effective in March 2021 upon clearance under the Hart-Scott-Rodino (HSR) Antitrust Improvements Act of 1976. The parties' collaboration is governed through a joint governance committee and appropriate subcommittees.

We are responsible for 20% of development costs for R552 in the US, Europe, and Japan, up to a specified cap. Lilly is responsible for funding the remainder of all development activities for R552 and other non-CNS disease development candidates. We have the right to opt- out of co-funding the R552 development activities in the US, Europe and Japan at two different specified times. If we exercise our first opt-out right (no later than September 30, 2023), under the Lilly Agreement, we are required to fund our share of the R552 development activities in the US, Europe, and Japan up to a maximum funding commitment of $65.0 million through April 1, 2024. If we decide not to exercise our opt-out rights, we will be required to share in global development costs of up to certain amounts at a specified cap, as provided for in the Lilly Agreement.

We are responsible for performing and funding initial discovery and identification of CNS disease development candidates. Following candidate selection, Lilly will be responsible for performing and funding all future development and commercialization of the CNS disease development candidates.

Under the terms of the license agreement, we were entitled to receive a non-refundable and non-creditable upfront cash payment amounting to $125.0 million, which we received in April 2021, and a potential for an additional $330.0 million in milestone payments upon the achievement of specified development and regulatory milestones by non-CNS disease products and $255.0 million in milestone payments upon the achievement of specified development and regulatory milestones by CNS disease products. We are also eligible to receive up to $100.0 million in sales milestone payments on a product-by-product basis for non-CNS disease products and up to $150.0 million in sales milestone payments on a product-by-product basis for CNS disease products. In addition, depending on the extent of our co-funding of R552 development activities, we would be entitled to receive tiered royalty payments on net sales of non-CNS disease products at percentages ranging from the mid-single digits to high-teens, subject to certain standard reductions and offsets. We would be entitled to receive tiered royalty payments on net sales of CNS disease products up to low-double digits, subject to certain standard reductions and offsets.

We accounted for this agreement under ASC 606 and identified the following distinct performance obligations at inception of the agreement: (a) granting of the license rights over the non-CNS penetrant intellectual property (IP), and (b) granting of the license rights over the CNS penetrant IP which will be delivered to Lilly upon completion of the additional research and development efforts specified in the agreement. We concluded each of these performance obligations is distinct. We based our assessment on the assumption that Lilly can benefit from each of the licenses on its own by developing and commercializing the underlying product using its own resources.

Under the Lilly Agreement, we are required to share 20% of the development costs for R552 in the US, Europe and Japan up to a specified cap. Given our rights to opt- out from the development of R552, we believe at the minimum, we have a commitment to fund the development costs up to $65.0 million as discussed above. We considered this commitment to fund the development costs as a significant financing component of the contract, which we accounted for as a reduction of the upfront fee to derive the transaction price. This financing component was recorded as a liability at its net present value of approximately $57.9 million using a 6.4% discount rate. Interest expense is being accreted on such liability over the expected commitment period. Interest expense accreted during the year ended December 31, 2021 was $2.8 million. As of December 31, 2021, the outstanding financing liability of $60.7 million to Lilly was included within other long-term liabilities, current portion, and other long-term liabilities in the balance sheet. As of December 31, 2021, Lilly billed us $2.1 million for our share of development costs under this agreement, which was subsequently paid in the first quarter of 2022.

We allocated the net transaction price of $67.1 million to each performance obligation based on our best estimate of its relative standalone selling price using the adjusted market assessment approach. We concluded that the license rights over the non-CNS penetrant IP represents functional IP that is not expected to change over time, and we have no ongoing or undelivered obligations relative to such IP that Lilly will benefit from the use of such IP on the delivery date. As such, the transaction price allocated to the non-CNS penetrant IP of $60.4 million was recognized as revenue in the year ended December 31, 2021 upon delivery of the non-CNS penetrant IP to Lilly in March 2021. For the delivery of license rights over the CNS penetrant IP, we are obligated to perform additional research and development efforts before Lilly can accept the license. The allocated transaction price to the CNS penetrant IP of $6.7 million is being recognized as revenue from the effective date of the Lilly Agreement through the eventual acceptance by Lilly using the input method. We recognized revenue for the year ended December 31, 2021 of $6.2 million relative to the delivery of CNS penetrant IP. As of December 31, 2021, the remaining deferred revenue amounted to $0.5 million.

The remaining future variable consideration related to future milestone payments as discussed above were fully constrained because we cannot conclude that it is probable that a significant reversal of the amount of cumulative revenue recognized will not occur, given the inherent uncertainty of success with these future milestones. For sales-based milestones and royalties, we determined that the license is the predominant item to which the royalties or sales-based milestones relate. Accordingly, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Grifols License Agreement

In January 2019, we entered into an exclusive license agreement with Grifols to commercialize fostamatinib in all indications, including chronic ITP and AIHA, in Europe and Turkey. Under the agreement, we received an upfront payment of $30.0 million, with the potential for $297.5 million in total regulatory and commercial milestones. We will also receive stepped double-digit royalty payments based on tiered net sales which may reach 30% of net sales. In return, Grifols received exclusive rights to commercialize fostamatinib for human diseases, including chronic ITP, AIHA, and IgAN, in Europe and Turkey. Grifols also received an exclusive option to expand the territory under its exclusive and non-exclusive licenses to include the Middle East, North Africa and Russia (including Commonwealth of Independent States). In November 2020, Grifols exercised its option to include these territories as part of the licensed territories under the agreement. The agreement also required us to continue to conduct our long-term open-label extension study on patients with ITP through European Medicines Agency (EMA) approval of ITP in Europe or until the study ends as well as conduct the Phase 3 trial of fostamatinib in AIHA.

In December 2019, we entered into a Drug Product Purchase Agreement with Grifols wherein we agreed to supply and sell to Grifols at 30% mark up the drug product requested under an anticipated first and only purchase order until Grifols enters into a supply agreement directly with a third-party drug product manufacturer. In October 2020, we entered into a Commercial Supply Agreement with Grifols.

In January 2020, the European Commission granted a centralized Marketing Authorization (MA) for fostamatinib valid throughout the European Union (EU) and in the UK after the departure of the UK from the EU for the treatment of chronic immune thrombocytopenia in adult patients who are refractory to other treatments. With this approval, we received in February 2020 a $20.0 million non-refundable payment, comprised of a $17.5 million payment due upon Marketing Authorization Application (MAA) approval by the EMA of fostamatinib for the first indication and $2.5 million creditable advance royalty payment, based on the terms of our collaboration agreement with Grifols. The above milestone payment was allocated to the distinct performance obligations in the collaboration agreement with Grifols.

We accounted for this agreement under ASC 606 and identified the following distinct performance obligations at inception of the agreement: (a) granting of the license, (b) performance of research and regulatory services related to our ongoing long-term open-label extension study on patients with ITP, and (c) performance of research services related to our Phase 3 study in AIHA. In October 2020, we entered into a commercial supply agreement for the licensed territories. We concluded each of these performance obligations is distinct. We based our assessment on the following: (i) our assessment that Grifols can benefit from the license on its own by developing and commercializing the underlying product using its own resources, and (ii) the fact that the manufacturing services are not highly specialized in nature and can be performed by other vendors. Upon execution of our agreement with Grifols, we determined that the upfront fee of $5.0 million, which is the non-refundable portion of the $30.0 million upfront fee, represented the transaction price. In the first quarter of 2020, we revised the transaction price to include the $25.0 million of the upfront payment that is no longer refundable under our agreement and the $20.0 million payment received that is no longer constrained. We allocated the updated transaction price to the distinct performance obligations in our collaboration agreement based on our best estimate of the relative standalone selling price as follows: (a) for the license, we estimated the standalone selling price using the adjusted market assessment approach to estimate its standalone selling price in the licensed territories; (b) for the research and regulatory services, we estimated the standalone selling price using the cost plus expected margin approach. As a result of the adjusted transaction price, adjustments are recorded on a cumulative catch-up basis, and recorded as part of contract revenues from collaborations in the first quarter of 2020.

The remaining future variable consideration of $277.5 million related to future regulatory and commercial milestones were fully constrained due to the fact that it was probable that a significant reversal of cumulative revenue would occur, given the inherent uncertainty of success with these future milestones. We are recognizing revenues related the research and regulatory services throughout the term of the respective clinical programs using the input method. For sales-based milestones and royalties, we determined that the license is the predominant item to which the royalties or sales-based milestones relate. Accordingly, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

As of December 31, 2021 and 2020, the remaining deferred revenue was $0.7 million and $1.6 million, respectively, related to the performance of research services. During the year ended December 31, 2021, we recognized $0.9 million in revenue related to the research and development services. We also recognized $2.0 million in revenue for the delivery of drug supplies to Grifols for its commercialization. During the year ended December 31, 2020, we recognized $39.9 million in revenues related to the licensed rights in intellectual property and $3.8 million in revenues related to the research services performed. Additionally, we recognized $0.7 million in revenues for delivery of drug supply to Grifols for commercialization as well as $0.5 million related to Grifols' exercise of its option to include additional territories as discussed above. During the year ended December 31,2019, we recognized $4.7 million in revenues related to the license right and research and regulatory services performed.

Kissei License Agreement

In October 2018, we entered into an exclusive license and supply agreement with Kissei to develop and commercialize fostamatinib in all current and potential indications in Japan, China, Taiwan and the Republic of Korea. Kissei is responsible for performing and funding all development activities for fostamatinib in the above-mentioned territories. We received an upfront cash payment of $33.0 million, with the potential for up to an additional $147.0 million in development, regulatory and commercial milestone payments, and will receive mid- to upper twenty percent, tiered, escalated net sales-based payments for the supply of fostamatinib. Under the agreement, we granted Kissei the license rights to fostamatinib in the territories above and are obligated to supply Kissei with drug product for use in clinical trials and pre-commercialization activities. We are also responsible for the manufacture and supply of fostamatinib for all future development and commercialization activities under the agreement.

We accounted for this agreement under ASC 606 and identified the following distinct performance obligations at inception of the agreement: (a) granting of the license, (b) supply of fostamatinib for clinical use and (c) material right associated with discounted fostamatinib that are supplied for use other than clinical or commercial. In addition, we will provide commercial product supply if the product is approved in the licensed territory. We concluded that each of these performance obligations is distinct. We based our assessment on the following: (i) our assessment that Kissei can benefit from the license on its own by developing and commercializing the underlying product using its own resources and (ii) the fact that the manufacturing services are not highly specialized in nature and can be performed by other vendors. Moreover, we determined that the upfront fee of $33.0 million represented the transaction price and was allocated to the performance obligations based on our best estimate of the relative standalone selling price as follows: (a) for the license, we estimated the standalone selling price using the adjusted market assessment approach to estimate its standalone selling price in the licensed territories; (b) for the supply of fostamatinib and the material right associated with discounted fostamatinib, we estimated the standalone selling price using the cost plus expected margin approach. Variable consideration of $147.0 million related to future development and regulatory milestones was fully constrained because we cannot conclude that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur, given the inherent uncertainty of success with these future milestones. We will recognize revenues related to the supply of fostamatinib and material right upon delivery of fostamatinib to Kissei. For sales-based milestones and royalties, we determined that the license is the predominant item to which the royalties or sales-based milestones relate to. Accordingly, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

As of December 31, 2021 and 2020, the remaining deferred revenue was $1.4 million related to the material right associated with discounted fostamatinib supply. During the year ended December 31, 2021, we recognized $0.3 million revenue related to the supply of fostamatinib for clinical use. We did not recognize any revenues from our license agreement with Kissei during the year ended December 31, 2020. During the year ended December 31, 2019, we recognized $1.6 million revenue related to the supply of fostamatinib for clinical use and the material right associated with discounted fostamatinib.

Medison Commercial and License Agreements

In October 2019, we entered into two exclusive commercial and license agreements with Medison for the commercialization of fostamatinib for chronic ITP in Israel and in Canada, pursuant to which we received a $5.0 million upfront payment with respect to the agreement in Canada. We accounted for the agreement made with an upfront payment under ASC 606 and identified the following combined performance obligations at inception of the agreement: (a) granting of the license and (b) obtaining regulatory approval in Canada of fostamatinib in ITP. We determined that the non-refundable upfront fee of $5.0 million represented the transaction price. However, under the agreement, we have the option to buy back all rights to the product in Canada within six months from obtaining regulatory approval for the treatment of AIHA in Canada. The buyback option precludes us from transferring control of the license to Medison under ASC 606. We believe that the buyback provision, if exercised, will require us to repurchase the license at an amount equal to or more than the upfront $5.0 million. As such this arrangement is accounted for as a financing arrangement.

During the year ended December 31, 2021, we accrued interest amounting to $0.4 million related to this financing arrangement. No interest was accrued during the years ended December 31, 2020 and 2019. During the year ended December 31, 2021, we billed Medison $0.2 million related to the supply of fostamatinib for clinical use which was deferred and included the balance within the outstanding financing liability considering the buyback provision. As of December 31, 2021 and 2020, the outstanding financing liability of $5.6 million and $5.0 million, respectively, to Medison was included within other long-term liabilities in the balance sheet.

In August 2021, Medison Israel received the licenses for registrational approval from the Ministry of Health. Pursuant to the exclusive commercial and license agreement, this event triggered the first milestone that is the regulatory approval of the product in Israel for the first indication, for a non-refundable payment of $0.1 million. We recognized this amount as revenue during the year ended December 31, 2021.

Daiichi Collaboration Agreement

Pursuant to the Amended Collaboration Agreement dated April 20, 2005 with Daiichi, during the year ended December 31, 2021, we recognized $1.8 million of revenue related to the achievement of a certain milestone. During the year ended December 31, 2020, we also recognized $2.1 million related to the achievement of a certain milestone. All deliverables under the agreement had been previously delivered, and as such the above had been recognized as revenue in the corresponding periods such milestones were achieved.

Other license agreements

In February 2021, we entered into a non-exclusive license agreement with an unrelated third party whereby we granted such unrelated third-party rights to a certain patent. In consideration for the license rights granted, we received a one-time fee of $4.0 million. All the deliverables under the agreement had been delivered and the one-time fee was recognized as revenue during the year ended December 31, 2021.

Government Contract - US Department of Defense's JPEO-CBRND

In January 2021, we were awarded up to $16.5 million by the US Department of Defense to support our ongoing Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib for the treatment of hospitalized high-risk patients with COVID-19. The amount of award we will receive from the US Department of Defense is subject to submission of proper documentation as evidence of completion of certain clinical trial events or milestones as specified in the agreement, and approval by the US Department of Defense that such events or milestones have been met. We determined that this government award should be accounted for under IAS 2, *Accounting for Government Grants and Disclosure of Government Assistance,* which is outside of the scope of Topic 606, as the US Department of Defense is not receiving reciprocal value for their contributions. We record government contract revenue in the statement of operations in the period when it is probable that we will receive the award, which is when we comply with the conditions associated with the award and obtain approval from the US Department of Defense that such conditions have been met. During the year ended December 31, 2021, we recognized $10.5 million related to this grant, all of which had been invoiced and collected as of December 31, 2021. We expect to receive the remaining award of $6.0 million throughout the period we conduct our clinical trial, subject to us meeting certain clinical trial events or milestones and approval by the US Department of Defense as specified in the agreement.

5. STOCK-BASED COMPENSATION

Total stock-based compensation expense related to all of our stock-based awards was as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Selling, general and administrative	$ 7,337	$ 5,223	$ 6,453
Research and development	1,700	2,072	2,662
Restructuring charges	449	—	—
Total stock-based compensation expense	$ 9,486	$ 7,295	$ 9,115

In November 2021, we announced a reduction of workforce, primarily in the research organization. As a result, we entered in severance agreements with the affected employees, which provided, among others, extension of the date through which certain affected employees can exercise their vested options. As a result of these modifications, we recorded an incremental stock-based compensation expense of approximately $0.4 million for the year ended December 31, 2021. The incremental compensation expenses were computed based on the fair values of the modified awards on the modification date.

Equity Incentive Plans

On May 16, 2018, our stockholders approved the adoption of the Company's 2018 Equity Incentive Plan (2018 Plan). The 2018 Plan is the successor plan to the 2011 Equity Incentive Plan, the 2000 Equity Incentive Plan, and the 2000 Non-Employee Directors' Stock Option Plan. We have two active equity plans, our 2018 Plan and the Rigel's Inducement Plan, as amended (Inducement Plan, and together with 2018 Plan, the Equity Incentive Plans). The 2018 Plan provides for granting of stock awards to our officers, directors, all other employees and consultants. The Inducement Plan, which is a non-stockholder approved stock plan, is intended mainly to provide an inducement material by granting awards for certain individuals to enter into employment with us. Awards granted under our Equity Incentive Plans expire no later than 10 years from the date of grant. Awards may be granted with different vesting terms from time to time. To date, we granted stock options and restricted stock units (RSUs) under our Equity Incentive Plans.

In January 2021, our Board of Directors approved the 825,000 shares increase in available number of shares for future grant under our 2018 Plan, which became effective upon approval by our stockholders during the stockholders annual meeting in May 2021. In September 2021 and January 2022, our Board of Directors approved the increase of 469,000 shares and 610,000 shares, respectively, in common stock reserved for issuance under the Inducement Plan. As of December 31, 2021, a total of 41,739,675 shares and 1,752,333 shares are authorized for issuance under the 2018 Plan and Inducement Plan, respectively.

Stock Options and RSUs

The following table summarizes stock option and RSU activity, and shares available for grant under our Equity Incentive Plans for the periods presented:

		Stock Options			Restricted Stock Units	
	Shares Available For Grant	Number of Shares	Weighted Average Exercise Price	Weighted Intrinsic Value (in thousands)	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2020	14,218,190	27,260,463	$ 3.05		—	$ —
Authorized for grant	825,000					
Granted	(7,231,731)	6,997,981	$ 3.65		233,750	$ 3.67
Exercised	—	(1,353,426)	$ 2.49		—	$ —
Cancelled and forfeited	2,903,853	(2,896,353)	$ 3.95		(7,500)	$ 3.68
Outstanding as of December 31, 2021	10,715,312	30,008,665	$ 3.13	$ 6,812	226,250	$ 3.67
Vested and Expected to Vest as of December 31, 2021		28,017,415	$ 3.13	$ 6,611		
Exercisable as of December 31, 2021		19,647,126	3.23	$ 4,819		

Of the total stock options outstanding as of December 31, 2021 above, 1,991,250 shares outstanding are performance-based stock options wherein the achievement of the corresponding corporate-based milestones were not considered as probable. Accordingly, the related grant date fair value for these performance-based stock options of $4.0 million has not been recognized as stock-based compensation expense as of December 31, 2021.

During the year ended December 31, 2021, 2020 and 2019, stock options vested were 4,765,814 shares, 4,386,910 shares and 4,442,936 shares, respectively, with weighted-average exercise price of $2.67 per share, $2.41 per share, and $3.26 per share, respectively.

The aggregate intrinsic values of stock options outstanding, vested and expected to vest, and exercisable represents the difference between the exercise price of the underlying awards and the quoted price of our common stock for the options that were in-the-money as of December 31, 2021. During the year ended December 31, 2021, 2020 and 2019, aggregate intrinsic values of stock option exercises was approximately $2.1 million, $0.5 million and $0.01 million, respectively, representing the difference between the fair value of our common stock at the date of exercise and the exercise price paid.

During the year ended December 31, 2021, 2020 and 2019, we granted options to purchase 6,997,981 shares, 8,462,090 shares and 7,457,575 shares of common stock, respectively, with weighted-average grant date fair value of $2.34 per share, $1.42 per share and $1.27 per share, respectively.

The following table summarizes the weighted-average assumptions relating to stock options granted during the periods presented:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	1.0 %	1.2 %	2.4 %
Expected term (in years)	6.4	6.5	6.5
Dividend yield	0.0 %	0.0 %	0.0 %
Expected volatility	70.5 %	66.1 %	65.5 %

As of December 31, 2021, there were approximately $12.9 million of unrecognized stock-based compensation cost which is expected to be recognized over the remaining weighted-average period of 2.77 years, related to time-based stock options, performance-based stock options wherein achievement of the corresponding corporate-based milestones was considered as probable, and RSUs.

Details of our stock options by exercise price are as follows as of December 31, 2021:

	Options Outstanding			Options Exercisable	
Exercise Price	Number of Shares	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price
$1.75 - $2.00	4,530,317	6.86	$ 1.95	3,062,689	$ 1.95
$2.02 - $2.34	6,288,002	5.42	$ 2.21	4,821,308	$ 2.18
$2.37 - $2.64	4,256,738	7.63	$ 2.45	1,939,507	$ 2.45
$2.72 - $3.54	5,718,865	6.91	$ 3.29	2,746,933	$ 3.04
$3.55 - $3.85	4,209,804	5.83	$ 3.66	2,445,879	$ 3.65
$3.87 - $7.60	4,260,947	4.60	$ 4.81	3,886,818	$ 4.84
$8.02 - $8.85	743,992	0.07	$ 8.16	743,992	$ 8.16
$1.75 - $8.85	30,008,665	6.04	$ 3.13	19,647,126	$ 3.23

Employee Stock Purchase Plan

Our Purchase Plan permits eligible employees to purchase common stock at a discount through payroll deductions during defined offering periods. Under our Purchase Plan, for the year ended December 31, 2021, 2020 and 2019, we issued 932,018 shares, 567,391 shares and 747,691 shares of common stock, respectively, at an average price of $1.51 per share, $1.54 per share and $1.92 per share, respectively.

In January 2021, our Board of Directors approved the 5,500,000 shares increase in the maximum number of shares authorized for issuance under the Purchase Plan, which became effective upon approval by our stockholders during the annual stockholders meeting in May 2021. As of December 31, 2021, there were 4,584,484 shares reserved for future issuance under the Purchase Plan.

The fair value of awards granted under our Purchase Plan is estimated on the date of grant using the Black-Scholes option pricing model, which uses weighted-average assumptions. Our Purchase Plan provides for a twenty-four-month offering period comprised of four six-month purchase periods with a look-back option. A look-back option is a provision in our Purchase Plan under which eligible employees can purchase shares of our common stock at a price per share equal to the lesser of 85% of the fair market value on the first day of the offering period or 85% of the fair market value on the purchase date. Our Purchase Plan also includes a feature that provides for a new offering period to begin when the fair market value of our common stock on any purchase date during an offering period falls below the fair market value of our common stock on the first day of such offering period. This feature is called a "reset." Participants are automatically enrolled in the new offering period.

We had a "reset" on January 2, 2020 because the fair market value of our stock on December 31, 2019 was lower than the fair market value of our stock on January 1, 2019, the first day of the offering period. Following the "reset" in January 2020, January 1, 2020 was the new first day of the two-year offering period of our Purchase Plan. We applied modification accounting in accordance with the relevant accounting guidance. The total incremental fair value associated with this "reset" was approximately $0.8 million was recognized as expense from January 1, 2020 to December 31, 2021. In July 2020, we had another "reset" because the fair market value of our stock on June 30, 2020 was lower than the fair market value of our stock on January 1, 2020. Following the "reset" in July 2020, July 1, 2020 was the new start date of our two-year offering period of our Purchase Plan. We applied modification accounting in accordance with the relevant accounting guidance. The total incremental fair value associated with this "reset" was approximately $0.5 million and is being amortized to expenses from July 1, 2020 to June 30, 2022.

The table below summarizes the weighted-average assumptions related to our Purchase Plan for periods presented. Expected volatilities for our Purchase Plan are based on the two-year historical volatility of our stock. Expected term represents the weighted-average of the purchase periods within the offering period. The risk-free interest rate for periods within the expected term is based on US Treasury constant maturity rates.

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	*	1.0 %	2.7 %
Expected term (in years)	*	1.6	1.5
Dividend yield	*	0.0 %	0.0 %
Expected volatility	*	62.3 %	62.6 %

* Not a measurement period since the last two-year offering period started on January 1, 2020, and there was no reset in 2021.

The weighted average fair value of awards under our Purchase Plan at the measurement period during the year ended December 31, 2020 and 2019 was $0.87 per share and $1.07 per share, respectively. As of December 31, 2021, unrecognized stock-based compensation cost related to our Purchase Plan amounted to $0.1 million, which is expected to be recognized over the remaining weighted average period of 0.17 years.

6. INVENTORIES

The following table summarizes inventories, net as of the periods presented (in thousands):

	December 31,	
	2021	2020
Raw materials	$ 5,142	$ —
Work in process	162	1,189
Finished goods	1,312	449
Total	$ 6,616	$ 1,638

As of December 31, 2020, we have $4.0 million in advance payments to our manufacturer of our raw materials, which was included as part of Prepaid and Other Current Assets in our balance sheet. During the first quarter of 2021, the production of raw materials was completed, and ownership was transferred to us. Accordingly, such advance payments were reclassified to inventories as raw materials.

7. CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS

Cash, cash equivalents and short-term investments consisted of the following (in thousands):

	December 31,	
	2021	2020
Cash	$ 6,249	$ 1,988
Money market funds	6,842	19,487
U.S. treasury bills	35,366	10,034
Government-sponsored enterprise securities	14,678	4,920
Corporate bonds and commercial paper	61,832	20,898
	$ 124,967	$ 57,327
Reported as:		
Cash and cash equivalents	$ 18,890	$ 30,373
Short-term investments	106,077	26,954
	$ 124,967	$ 57,327

Cash equivalents and short-term investments include the following securities with gross unrealized gains and losses (in thousands):

December 31, 2021	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury bills	$ 35,416	$ —	$ (50)	$ 35,366
Government-sponsored enterprise securities	14,705	—	(27)	14,678
Corporate bonds and commercial paper	61,857	2	(27)	61,832
Total	$ 111,978	$ 2	$ (104)	$ 111,876

December 31, 2020	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury bills	$ 10,036	$ —	$ (2)	$ 10,034
Government-sponsored enterprise securities	4,920	—	—	4,920
Corporate bonds and commercial paper	20,900	—	(2)	20,898
Total	$ 35,856	$ —	$ (4)	$ 35,852

As of December 31, 2021 and 2020, our cash equivalents and short-term investments had a weighted-average time to maturity of approximately 196 days and 78 days, respectively. Our short-term investments are classified as available-for-sale securities. Accordingly, we have classified certain securities as short-term investments on our balance sheets as they are available for use in the current operations. As of December 31, 2021, we had no investments that had been in a continuous unrealized loss position for more than 12 months. As of December 31, 2021, a total of 39 individual securities had been in an unrealized loss position for 12 months or less, and the losses were determined to be temporary. The gross unrealized losses above were caused by interest rate increases. No significant facts or circumstances have arisen to indicate that there has been any significant deterioration in the creditworthiness of the issuers of the securities held by us. Based on our review of these securities, including the assessment of the duration and severity of the unrealized losses, there were no other-than-temporary impairments for these securities as of December 31, 2021.

The following table shows the fair value and gross unrealized losses of our investments in individual securities that are in an unrealized loss position, aggregated by investment category (in thousands):

December 31, 2021	Fair Value	Unrealized Losses
U.S. treasury bills	$ 35,366	$ (50)
Government-sponsored enterprise securities	14,678	(27)
Corporate bonds and commercial paper	37,993	(27)
Total	$ 88,037	$ (104)

8. FAIR VALUE

The table below summarizes the fair value of our cash equivalents and short-term investments measured at fair value on a recurring basis, and are categorized based upon the lowest level of significant input to the valuations (in thousands):

	Assets at Fair Value as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 6,842	$ —	$ —	$ 6,842
U.S. treasury bills	—	35,366	—	35,366
Government-sponsored enterprise securities	—	14,678	—	14,678
Corporate bonds and commercial paper	—	61,832	—	61,832
Total	$ 6,842	$ 111,876	$ —	$ 118,718

	Assets at Fair Value as of December 31, 2020			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 19,487	$ —	$ —	$ 19,487
U.S. treasury bills	—	10,034	—	10,034
Government-sponsored enterprise securities	—	4,920	—	4,920
Corporate bonds and commercial paper	—	20,898	—	20,898
Total	$ 19,487	$ 35,852	$ —	$ 55,339

9. OTHER BALANCE SHEET COMPONENTS

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

	December 31,	
	2021	2020
Laboratory equipment	$ 12,154	$ 11,957
Computer and software	1,783	1,783
Furniture and equipment	2,107	1,793
Fixed assets in progress	691	819
Total property and equipment	16,735	16,352
Less accumulated depreciation and amortization	(14,551)	(13,676)
Property and equipment, net	$ 2,184	$ 2,676

Total depreciation and amortization expense were $1.2 million, $0.7 million and $0.7 million for the year ended December 31, 2021, 2020 and 2019, respectively. Depreciation and amortization expense for the year ended December 31, 2021 include an impairment charge of $0.1 million. See “Note 14 – Restructuring Charges” for related discussions.

Other accrued liabilities consist of the following (in thousands):

	December 31,	
	2021	2020
Revenue reserves	$ 5,898	$ 4,577
Accrued expenses	3,580	3,661
Refund liability	2,017	1,488
Income tax payable	605	—
Accrued professional fees	204	1,017
Accrued interest payable	387	271
Total	$ 12,691	$ 11,014

Revenue reserves includes chargebacks, discounts, and fees, as well as government and other rebates. Refund liability relates to allowance for sales returns. See “Note 3 – Revenues” for related details.

10. DEBT

On September 27, 2019 (Closing Date), we entered into a Credit and Security Agreement (Credit Agreement) with MidCap Financial Trust (MidCap). The Credit Agreement provides for a $60.0 million term loan credit facility with the following tranches: (i) on the Closing Date, $10.0 million aggregate principal amount of term loans (Tranche 1), (ii) until December 31, 2020, an additional $10.0 million term loan facility at our option (Tranche 2), (iii) until March 31, 2021, an additional $20.0 million term loan facility subject to the satisfaction of certain conditions and at our option (Tranche 3) and (iv) until March 31, 2022, an additional $20.0 million term loan facility subject to the satisfaction of certain conditions and at our option (Tranche 4). The obligations under the Credit Agreement are secured by a perfected security interest in all of our assets except for intellectual property and certain other customary excluded property pursuant to the terms of the Credit Agreement.

At the Closing Date, $10.0 million was funded in an initial tranche. In March 2020, we signed a credit extension form for Tranche 2 amounting to $10.0 million, which we received in May 2020. In April 2021, we amended the Credit Agreement to extend the period through which Tranche 3 will be available through March 31, 2022, subject to the satisfaction of certain conditions and at our option. As of December 31, 2021, the facility gives us the ability to access an additional $40.0 million at our option, subject to the achievement of certain customary conditions. On February 11, 2022, we entered into Second Amendment to our Credit Agreement with Midcap. See “Note 15 – Subsequent Events” for further discussions.

The outstanding principal balance of the loan bears interest at an annual rate of one-month LIBOR (or a comparable applicable index rate determined pursuant to the Credit Agreement if the LIBOR is no longer available) plus 5.65%, subject to a LIBOR floor of 1.50% and is payable monthly in arrears. Commencing on October 1, 2019, the Credit Agreement provides that we initially make interest-only payments for 24 months followed by 36 months of amortization payments. The interest-only period can be extended to 36 months (first interest-only extension) and again to 48 months (second interest-only extension) upon the satisfaction of certain conditions set forth in the Credit Agreement. In June 2021, we satisfied the first interest-only extension conditions under the Credit Agreement which effectively extended the interest-only period to 36 months or through October 1, 2022. All unpaid principal and accrued interest are due and payable no later than September 1, 2024. A final payment fee of 2.5% of principal is due on the final payment of the term loan.

We may make voluntary prepayments, in whole or in part, subject to certain prepayment premiums and additional interest payments. The Credit Agreement also contains certain provisions, such as event of default and change in control provisions, which, if triggered, would require us to make mandatory prepayments on the term loan, which are subject to certain prepayment premiums and additional interest payments.

As of December 31, 2021 and 2020, the outstanding balance of the loan, net of unamortized debt discount, was $19.9 million and $19.8 million, respectively, and is presented under long-term liabilities. As of December 31, 2021, we deemed that it is probable that we will satisfy the second interest-only criteria. Accordingly, we classified our outstanding loan as long-term liabilities in the Balance Sheet. Debt issuance costs are recorded as a direct deduction from the term loan on the balance sheet and are being amortized ratably as interest expense over the term of the loan, using the effective interest method. As December 31, 2021 and 2020, the unamortized issuance costs and debt discounts amounted to $0.1 million and $0.2 million, respectively.

For the year ended December 31, 2021, 2020 and 2019, interest expense, including amortization of the debt discount and accretion of the final fees related to the Credit Agreement was $1.7 million, $1.4 million and $0.2 million, respectively. Accrued interest of $0.4 million was included within other accrued liabilities in the balance sheet as of December 31, 2021.

The following table presents the future minimum principal payments of the outstanding loan as of December 31, 2021 under the current interest-only period as discussed above (in thousands):

For year ending December 31,		
2022	$	2,500
2023		10,000
2024		7,500
Principal amount (Tranches 1 and 2)	$	20,000

The Credit Agreement contains certain covenants which, among others, require us to deliver financial reports at designated times of the year and maintain minimum net revenues and $10.0 million of cash upon the draw Tranche 3 or Tranche 4. As of December 31, 2021, we were not in violation of any covenants.

11. LEASES

We currently lease our research and office space under a noncancelable lease agreement with our landlord, Healthpeak Properties, Inc. (formerly known as HCP BTC, LLC), which was originally set to expire in 2018. The lease term provides for renewal option for up to two additional periods of five years each. In July 2017, we exercised our option to extend the term of our lease for another five years through January 2023 and modified the amount of monthly base rent during such renewal period.

In December 2014, we entered into a sublease agreement, which was amended in 2017, with an unrelated third party to occupy approximately 57,000 square feet of our research and office space. In February 2017, we entered into an amendment to the sublease agreement to increase the subleased research and office space for an additional 9,328 square feet under the same term of the sublease. Effective July 2017, the sublease agreement was amended primarily to extend the term of the sublease through January 2023 and modified the monthly base rent to equal the amount we will pay our landlord. Because the future sublease income under the extended sublease agreement is the same as the amount we will pay our landlord, we did not recognize any loss on sublease relative to this amendment. As of December 31, 2021, we expect to receive approximately $5.1 million in future sublease income (excluding our subtenant's share of facilities operating expenses) through January 2023.

As of December 31, 2021 and 2020, we had operating lease right-of-use asset of $9.7 million and $17.9 million, respectively, and lease liability of $10.7 million and $19.3 million, respectively, in the balance sheet. The weighted average remaining term of our lease as of December 31, 2021 was 1.08 years.

As of December 31, 2021, we received from our landlord leasehold improvement incentives amounting to $0.6 million related to leasehold improvements. We record these leasehold improvement incentives as a reduction to operating lease right-of-use asset and lease liability until the lease ends and the asset is transferred.

We recorded rent expense on a straight-line basis for our lease, net of sublease income. For our sublease arrangement which we classified as an operating lease, our loss on the sublease was comprised of the present value of our future payments to our landlord less the present value of our future rent payments expected from our subtenant over the term of the sublease.

The components of our operating lease expense for the periods presented were as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Fixed operating lease expense	$ 5,360	$ 5,360	$ 5,248
Variable operating lease expense	910	926	745
Total operating lease expense	$ 6,270	$ 6,286	$ 5,993

Supplemental information related to the Company's operating lease for the periods presented were as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Cash payments included in the measurement of operating lease liabilities	$ 10,082	$ 9,694	$ 9,321

We have the following operating sublease information for the periods presented (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Fixed sublease expense	$ 4,381	$ 4,381	$ 4,381
Variable sublease expense	917	962	829
Sublease income	(5,298)	(5,343)	(5,210)
Net	$ —	$ —	$ —

As of December 31, 2021, future minimum lease payments and obligations under our noncancelable operating lease, net of expected sublease receipts, were as follows (in thousands):

	Operating Lease	Sublease Receipts	Net
For year ending December 31,			
2022	$ 10,485	(4,716)	$ 5,769
2023	877	(394)	483
Total minimum payments required	$ 11,362	$ (5,110)	$ 6,252

Rent expense under our operating lease amounted to approximately $6.3 million, $6.3 million and $6.0 million for the years ended December 31, 2021, 2020 and 2019, respectively.

12. STOCKHOLDERS' EQUITY

Preferred Stock

We are authorized to issue 10,000,000 shares of preferred stock. As of December 31, 2021 and 2020, there were no issued and outstanding shares of preferred stock. Our board of directors is authorized to fix or alter the designation, powers, preferences and rights of the shares of each series of preferred shares, and the qualifications, limitations or restrictions of any wholly unissued shares, to establish from time to time the number of shares constituting any such series, and to increase or decrease the number of shares, if any.

Common Stock

Our Certificate of Incorporation as amended and restate in May 2018, authorizes us to issue 400,000,000 shares of common stock. Common stock issued and outstanding as of December 31, 2021 and 2020 were 171,602,226 shares and 169,316,782 shares, respectively.

Open Market Sale Agreement

In August 2020, we entered into an Open Market Sale Agreement with Jefferies LLC (Jefferies), as our sole sales agent pursuant to which we may sell from time to time, through Jefferies, shares of our common stock in sales deemed to be "at-the-market offerings" as defined in Rule 415 under the Securities Act, subject to conditions specified in the Open Market Sale Agreement, including maintaining an effective registration statement covering the sale of shares under the Open Market Sale Agreement. In April 2021, the registration statement registering the sale of shares under the Open Market Sale Agreement expired. From the time of implementation of the Open Market Sale Agreement through expiration of the registration statement, no sales of shares occurred. A new automatic shelf registration statement was filed on August 3, 2021 to register the sale of up to a maximum aggregate offering price of $100.0 million of shares of our common stock that may be issued and sold from time to time under the Open Market Sale Agreement. As of December 31, 2021, no shares had been sold under the Open Market Sale Agreement.

13. INCOME TAXES

For the year ended December 31, 2021, we recorded provision for income tax of $0.6 million. This provision for income tax was related to the state tax liability primarily due to revenue recognized for the Lilly Agreement. We do not expect to owe federal income taxes due to the sufficient net operating loss (NOL) carryforwards that were generated prior to the enactment of the Tax Cuts and Jobs Act (Tax Act), as well as significant research and development credit carryforwards. We continue to record a full valuation allowance on our deferred tax assets considering our cumulative losses in prior years and forecasted losses in the future. For the years ended December 31, 2020 and 2019, our loss before income taxes was from domestic operations and we did not record provision for income taxes other than minimum state taxes due to our net loss.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of our deferred tax assets are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets		
Net operating loss carryforwards	$ 229,364	$ 240,767
Orphan drug and research and development credits	66,616	64,252
Deferred compensation	8,819	7,760
Lease liabilities	2,564	4,399
Capitalized inventory	47	34
Deferred revenue	16,297	1,405
Other, net	1,626	1,765
Deferred tax liabilities		
Operating lease right-of-use asset	(2,335)	(4,084)
Others	(607)	(537)
Total net deferred tax assets	322,391	315,761
Less: valuation allowance	(322,391)	(315,761)
Deferred tax assets, net of allowance	$ —	$ —

The reconciliation of the statutory federal income tax rate to the effective tax rate was as follows:

	Year Ended December 31,		
	2021	2020	2019
Federal statutory tax rate	(21.0)%	(21.0)%	(21.0)%
State, Net of Federal Benefit	2.8 %	0.1 %	0.1 %
Valuation allowance	27.5 %	24.4 %	21.7 %
Stock compensation	5.6 %	4.7 %	2.8 %
Orphan drug and research and development credits	(14.0)%	(12.7)%	(5.1)%
Other, net	2.7 %	4.6 %	1.5 %
Effective tax rate	3.6 %	0.1 %	0.0 %

In general, under Section 382 of the Internal Revenue Code (Section 382), a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change net operating loss carryovers and tax credits to offset future taxable income. Our existing net operating loss carryforwards and tax credits are subject to limitations arising from ownership changes which occurred in previous periods. We finalized our analysis of potential ownership changes and concluded our Section 382 owner shift analysis during the year ended December 31, 2012. We have updated our net operating loss carryforwards to reflect the results of the Section 382 owner shift analysis as of December 31, 2021. We did not experience any significant changes in ownership in 2021, 2020, and 2019. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 and result in additional limitations.

As of December 31, 2021, we had net operating loss carryforwards for federal income tax purposes of approximately $973.6 million. Of the federal net operating loss carryforward, $839.3 million, which expire beginning in the year 2025 and the remaining net operating loss carryforwards can be carried forward indefinitely, subject to annual limitation of 80% of taxable income. We also had state net operating loss carryforwards of approximately $371.7 million, which expire beginning in the year 2028.

We have general business credits of approximately $50.7 million, which will expire beginning in 2023, if not utilized, and is comprised of research and development credits and orphan drug credits. We also have state research and development tax credits of approximately $30.7 million, which have no expiration date.

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by approximately $6.6 million, $4.1 million and $21.6 million for the year ended December 31, 2021, 2020 and 2019, respectively.

The following table summarizes the activity related to our gross unrecognized tax benefits (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Balance at the beginning of the year	$ 8,901	$ 8,358	$ 8,358
Increase related to current year tax positions	285	543	543
Balance at the end of the year	$ 9,186	$ 8,901	$ 8,358

During the years ended December 2021, 2020 and 2019, the amount of unrecognized tax benefits increased due to additional research and development and orphan drug credits generated during those years. The reversal of the uncertain tax benefits would not affect the Company's effective tax rate to the extent that we continue to maintain a full valuation allowance against our deferred tax assets.

We are subject to federal income tax and various state taxes. Because of net operating loss and research credit carryovers, substantially all of our tax years remain open to examination.

Our policy is to recognize interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense. We currently have no tax positions that would be subject to interest or penalties.

14. RESTRUCTURING CHARGES

In November 2021, we announced a reduction in our workforce primarily in the research organization. We recorded restructuring charges of $3.5 million in the statements of operations for the year ended December 31, 2021, comprised of $2.9 million cash severance, bonus and related employee benefits and taxes of affected employees, $0.4 million of stock-based compensation expense related to option modification and $0.1 million impairment of certain property and equipment which was recorded within depreciation expense As of December 31, 2021, we have approximately $2.2 million outstanding unpaid cash severance, bonus and related employee benefits and taxes included within accrued compensation in the balance sheet, which are expected to be paid in the first quarter of 2022.

15. SUBSEQUENT EVENTS

Second Amendment to Credit Facility with MidCap

On February 11, 2022, we entered into Second Amendment to our Credit Agreement with MidCap, among other things, amend the applicable funding conditions, applicable commitments and certain other terms relating to available credit facilities (Tranches 3 and 4), add additional term loan credit facility (Tranche 5), and revise certain terms related to the financial covenants. Following the amendment, the Credit Agreement gives us the ability to access the following available credit facilities: (i) on the closing date of the Second Amendment, $10.0 million term loan facility (Tranche 3), (ii) until August 31, 2022, an additional $10.0 million aggregate principal amount of term loan facility at our option (Tranche 4), and (iii) until March 31, 2023, an additional $20.00 million term aggregate principal amount of term loan facility subject to the satisfaction of applicable funding conditions which include minimum net revenue and compliance with financial covenants set forth in the Credit Agreement. At the Second Amendment effective date, $10.0 million was funded (Tranche 3).

SUPPLEMENTARY DATA

Schedule II - Valuation and Qualifying Accounts

All schedules are omitted because they are not applicable, or the required information is shown in the financial statements or notes thereto.

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

None.

Item 9A. Controls and Procedures

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Exchange Act. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Annual Report.

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 Rules 13a-15(f). Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on our evaluation under the framework in *Internal Control—Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2021.

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 attestation report which is set forth below in this Annual Report on Form 10-K.

Changes in Internal Controls over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the fourth quarter of 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

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

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Rigel Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Rigel Pharmaceuticals, 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, Rigel Pharmaceuticals, 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 balance sheets of the Company as of December 31, 2021 and 2020, the related statements of operations, comprehensive loss, stockholders' 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 March 1, 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 Annual 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 Francisco, California
March 1, 2022

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information regarding our directors, executive officers and corporate governance is incorporated by reference to the information set forth under the captions "Election of Directors" and "Management—Executive Officers" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2022. Such information is incorporated herein by reference.

Information regarding compliance with Section 16(a) of the Exchange Act is incorporated by reference to the information set forth under the caption "Delinquent Section 16(a) Reports" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information, if any, is incorporated herein by reference.

Item 11. Executive Compensation

Information regarding executive and director compensation is incorporated by reference to the information set forth under the captions "Compensation Discussion and Analysis," "Executive Compensation" and "Director Compensation" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Information regarding Compensation Committee interlocks and insider participation is incorporated by reference to the information set forth under the caption "Compensation Committee Interlocks and Insider Participation" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Information regarding our Compensation Committee's review and discussion of our Compensation Discussion and Analysis is incorporated by reference to the information set forth under the caption "Compensation Committee Report" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information is incorporated herein by reference.

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

Information regarding security ownership of certain beneficial owners and management and securities authorized for issuance under our equity compensation plans is incorporated by reference to the information set forth under the caption "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" and "Equity Compensation Plan Information" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information is incorporated herein by reference.

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

Information regarding certain relationships and related transactions and director independence is incorporated by reference to the information set forth under the captions "Transactions with Related Persons" and "Information Regarding the Board of Directors and Corporate Governance" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

Information regarding principal accounting fees and services is incorporated by reference to the information set forth under the caption "Ratification of Selection of Independent Registered Public Accounting Firm" in our Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021. Such information is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

1. Financial Statements—Index to Financial Statements in Part II, Item 8 of this Annual Report on Form 10-K.

2. See Exhibit Index at the end of this Annual Report, which is incorporated herein by reference. The Exhibits listed in the accompanying Exhibit Index are filed as part of this report.

EXHIBIT INDEX

3.1	Amended and Restated Certificate of Incorporation (filed as an exhibit to Rigel's Current Report on Form 8- K dated May 29, 2012, and incorporated herein by reference).
3.2	Amended and Restated Bylaws (filed as an exhibit to Rigel's Current Report on Form 8-K, dated February 2, 2007, and incorporated herein by reference).
3.3	Certificate of Amendment to the Amended and Restated Certificate of Incorporation (filed as an exhibit to Rigel's Current Report on Form 8-K, dated May 16, 2018, and incorporated herein by reference).
4.1	Description of Capital Stock (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2020 filed on February 27, 2020 and incorporated herein by reference).
4.2	Form of warrant to purchase shares of common stock (filed as an exhibit to Rigel's Registration Statement on Form S-1, as amended, and incorporated herein by reference).
4.3	Specimen Common Stock Certificate (filed as an exhibit to Rigel's Current Report on Form 8-K dated June 24, 2003, and incorporated herein by reference).
4.4	Warrant issued to HCP BTC, LLC for the purchase of shares of common stock (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2009 and incorporated herein by reference).
10.1+	Form of Stock Option Agreement pursuant to 2000 Equity Incentive Plan (filed as an exhibit to Rigel's Registration Statement on Form S-1, as amended, and incorporated herein by reference).
10.2	Build-to-Suit Lease between Rigel and Slough BTC, LLC, dated May 16, 2001 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2001 and incorporated herein by reference).
10.3 ^	Amendment to Build-to-Suit Lease between Rigel and Slough BTC, LLC, dated October 18, 2002 (filed as an exhibit to Rigel's Annual Report on Form 10-K, as amended, for the fiscal year ended December 31, 2002 and incorporated herein by reference).
10.4	Amendment No. Two to Build-to-Suit Lease between Rigel and Slough BTC, LLC, dated January 31, 2005 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2009 and incorporated herein by reference).
10.5	Amendment No. Three to Build-to-Suit Lease between Rigel and Slough BTC, LLC, dated January 31, 2005 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2009 and incorporated herein by reference).
10.6	Amendment No. Four to Build-to-Suit Lease between Rigel and HCP BTC, LLC, dated February 1, 2009 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2009 and incorporated herein by reference).
10.7 ^	Collaboration Agreement between Rigel and Daiichi Pharmaceutical Co., Ltd., dated August 1, 2002 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2002 and incorporated herein by reference).
10.8+ ^	Offer Letter from Rigel Pharmaceuticals, Inc. to Wolfgang Dummer, dated October 3, 2020 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2019 filed on February 27, 2020 and incorporated herein by reference).

10.9+	Form of Indemnity Agreement (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2007, as amended, and incorporated herein by reference).
10.10+	2000 Equity Incentive Plan, as amended (filed as an exhibit to Rigel's Registration Statement on Form S-8 filed on June 21, 2013 and incorporated herein by reference).
10.11+	2000 Non-Employee Directors' Stock Option Plan, as amended (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017 filed on August 21, 2017 and incorporated herein by reference).
10.12+	Amended and Restated Change of Control Severance Plan (filed as an exhibit to Rigel's Annual Report on Form 10-K for the fiscal year ended December 31, 2010 and incorporated herein by reference).
10.13+	2000 Employee Stock Purchase Plan, as amended (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 filed on August 3, 2021 and incorporated herein by reference).
10.14 ^	License and Collaboration Agreement between Rigel and AstraZeneca AB, dated February 15, 2010 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010 and incorporated herein by reference).
10.15+	2011 Equity Incentive Plan, as amended (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017 filed on August 21, 2017 and incorporated herein by reference).
10.16+	Form of Stock Option Agreement pursuant to 2011 Equity Incentive Plan (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2011 and incorporated herein by reference).
10.17+	Form of Stock Option Grant Notice, Option Agreement and Notice of Exercise under the Rigel Inducement Plan (filed as an exhibit to Rigel's Current Report on Form 8-K filed on October 11, 2016, and incorporated herein by reference).
10.18	Amendment No. Five to Build-to-Suit Lease between Rigel Pharmaceuticals, Inc. and HCP BTC, LLC, dated July 24, 2017 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed on March 6, 2018, and incorporated herein by reference).
10.19+	Executive Severance Plan (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2018 filed on May 1, 2018 and incorporated herein by reference).
10.20+	Executive Severance Plan (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020 filed on May 5, 2020 and incorporated herein by reference).
10.21+	2018 Equity Incentive Plan, as amended (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 filed on August 3, 2021 and incorporated herein by reference).
10.22+ ^	Offer Letter from Rigel Pharmaceuticals, Inc. to Dean Schorno, dated May 22, 2018 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 filed on August 8, 2018 and incorporated herein by reference).
10.23 ^	Collaboration and License Agreements with Kissei Pharmaceutical Co., Ltd. (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2018 filed on February 28, 2019 and incorporated herein by reference).

10.24 ^	Supply Agreements with Kissei Pharmaceutical Co., Ltd. (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2018 filed on February 28, 2019 and incorporated herein by reference).
10.25 ^	Credit and Security Agreement, dated as of September 27, 2019, among Rigel Pharmaceuticals, Inc. MidCap Financial Trust, as agent and lender, and the additional lenders from time to time party thereto (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 filed on November 5, 2019 and incorporated herein by reference).
10.26 ^	Exclusive Commercialization License Agreement with Grifols Worldwide Operations Limited (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 filed on May 7, 2019 and incorporated herein by reference).
10.27+	2020 Cash Incentive Plan (filed as an exhibit to Rigel's Current Report on Form 8-K filed on November 22, 2019, and incorporated herein by reference).
10.28+	2021 Cash Incentive Plan (filed as an exhibit to Rigel's Current Report on Form 8-K filed on February 3, 2021, and incorporated herein by reference).
10.29+ ^	Offer Letter from Rigel Pharmaceuticals, Inc. to David Santos, dated July 13, 2020 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 5, 2020, and incorporated herein by reference).
10.30 ^	License and Collaboration Agreement between Rigel and Eli Lilly and Company, dated February 28, 2021 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed on May 5, 2021, and incorporated herein by reference).
10.31#+	Rigel Pharmaceuticals, Inc. Inducement Plan, as amended.
10.32+#	Non-Employee Director Compensation Policy, as amended.
10.33+	2022 Cash Incentive Plan (filed as an exhibit to Rigel's Current Report on Form 8-K filed on January 28, 2022, and incorporated herein by reference).
10.34# ^	First Amendment to the Credit and Security Agreement with MidCap Financial Trust dated April 2, 2021.
10.35# ^	Second Amendment to the Credit and Security Agreement with MidCap Financial Trust, dated February11, 2022.
23.1#	Consent of Independent Registered Public Accounting Firm.
24.1#	Power of Attorney (included on signature page).
31.1#	Certification required by Rule 13a-14(a) or Rule 15d-14(a).
31.2#	Certification required by Rule 13a-14(a) or Rule 15d-14(a).
32.1*#	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. 1350).
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.LAB#	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE#	Inline XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF#	Inline XBRL Taxonomy Extension Definition Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

+ Indicates a management contract or compensatory plan or arrangement.

* The certification attached as Exhibit 32.1 accompanies this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the registrant for purposes of Section 18 of the Exchange Act.

^ Certain marked information has been omitted from this exhibit because it is both not material and is the type that the registrant treats as private and confidential.

Filed herewith.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of the Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on March 1, 2022.

RIGEL PHARMACEUTICALS, INC.

By: /s/ RAUL R. RODRIGUEZ
Raul R. Rodriguez
Chief Executive Officer
(Principal Executive Officer)

By: /s/ DEAN L. SCHORNO
Dean L. Schorno
Chief Financial Officer
(Principal Financial Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Raul R. Rodriguez and Dean L. Schorno, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place, and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all 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 connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or any of them or their or his substitute or substitutes, may lawfully 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/ RAUL R. RODRIGUEZ Raul R. Rodriguez	Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2022
/s/ DEAN L. SCHORNO Dean L. Schorno	Chief Financial Officer (Principal Financial Officer)	March 1, 2022
/s/ GARY A. LYONS Gary A. Lyons	Chairman of the Board	March 1, 2022
/s/ KAMIL ALI-JACKSON Kamil Ali-Jackson	Director	March 1, 2022
/s/ BRADFORD S. GOODWIN Bradford S. Goodwin	Director	March 1, 2022
/s/ ALISON L. HANNAH Alison L. Hannah	Director	March 1, 2022
/s/ KEITH A. KATKIN Keith A. Katkin	Director	March 1, 2022
/s/ BRIAN L. KOTZIN Brian L. Kotzin	Director	March 1, 2022
/s/ GREGG LAPOINTE Gregg Lapointe	Director	March 1, 2022

/s/ Walter H. Moos Walter H. Moos	Director	March 1, 2022
/s/ Jane Wasman Jane Wasman	Director	March 1, 2022

Exhibit 10.31

RIGEL PHARMACEUTICALS, INC.

INDUCEMENT PLAN

ADOPTED BY THE COMPENSATION COMMITTEE: OCTOBER 10, 2016

AMENDED BY THE COMPENSATION COMMITTEE: JANUARY 3, 2017

AMENDED BY THE COMPENSATION COMMITTEE: AUGUST 16, 2017

AMENDED BY THE COMPENSATION COMMITTEE: NOVEMBER 7, 2017

AMENDED BY THE COMPENSATION COMMITTEE: DECEMBER 23, 2017

AMENDED BY THE COMPENSATION COMMITTEE: JANUARY 24, 2018

AMENDED BY THE COMPENSATION COMMITTEE: AUGUST 19, 2020

AMENDED BY THE COMPENSATION COMMITTEE: SEPTEMBER 30, 2021

AMENDED BY THE COMPENSATION COMMITTEE: JANUARY 4, 2022

1. GENERAL.

(a) Eligible Stock Award Recipients. The only persons eligible to receive grants of Stock Awards under this Plan are individuals who satisfy the standards for inducement grants under NASDAQ Marketplace Rule 5635(c)(4) and the related guidance under NASDAQ IM 5635-1. A person who previously served as an Employee or Director will not be eligible to receive Stock Awards under the Plan, other than following a *bona fide* period of non-employment. Persons eligible to receive grants of Stock Awards under this Plan are referred to in this Plan as "***Eligible Employees***". These Stock Awards must be approved by either a majority of the Company's "***Independent Directors***" (as such term is defined in NASDAQ Listing Rule 5605(a)(2)) or the Company's compensation committee, provided such committee is comprised solely of Independent Directors (the "***Independent Compensation Committee***") in order to comply with the exemption from the stockholder approval requirement for "inducement grants" provided under Rule 5635(c)(4) of the NASDAQ Listing Rules. NASDAQ Marketplace Rule 5635(c)(4) and the related guidance under NASDAQ IM 5635-1 are referred to in this Plan as the "***Inducement Award Rules***".

(b) Available Awards. The Plan provides for the grant of Options and Restricted Stock Unit Awards. All Options will be Nonstatutory Stock Options. Awards intended to qualify as stockholder-approved performance based compensation for purposes of Section 162(m) of the Code may not be granted under this Plan.

(c) Purpose. This Plan, through the granting of Stock Awards, is intended to provide (i) an inducement material for certain individuals to enter into employment with the Company within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules, (ii) incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and (iii) a means by which Eligible Employees may be given an opportunity to benefit from increases in value of the Common Stock through the granting of Stock Awards.

2. ADMINISTRATION.

(a) Administration by Board. The Board will administer the Plan, provided, however, that Stock Awards may only be granted by either (i) a majority of the Company's Independent Directors or (ii) the Independent Compensation Committee. Subject to those constraints and the other constraints of the Inducement Award Rules, the Board may delegate some of its powers of administration of the Plan to a Committee, as provided in Section 2(c).

(b) Powers of Board. The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan and the Inducement Award Rules:

(i) To determine: (A) who will be granted Stock Awards; (B) when and how each Stock Award will be granted; (C) what type of Stock Award will be granted; (D) the provisions of each Stock Award (which need not be identical), including when a person will be permitted to exercise or otherwise receive cash or Common Stock under the Stock Award; (E) the number of shares of Common Stock subject to, or the cash value of, a Stock Award; and (F) the Fair Market Value applicable to a Stock Award; provided, however, that Stock Awards may only be granted by either (i) a majority of the Company's Independent Directors or (ii) the Independent Compensation Committee.

(ii) To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for administration of the Plan and Stock Awards. The Board, in the exercise of these powers, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement, in a manner and to the extent it will deem necessary or expedient to make the Plan or Stock Award fully effective.

(iii) To settle all controversies regarding the Plan and Stock Awards granted under it.

(iv) To accelerate, in whole or in part, the time at which a Stock Award may be exercised or vest (or at which cash or shares of Common Stock may be issued).

(v) To suspend or terminate the Plan at any time. Except as otherwise provided in the Plan or a Stock Award Agreement, suspension or termination of the Plan will not materially impair a Participant’s rights under his or her then-outstanding Stock Award without his or her written consent except as provided in subsection (viii) below.

(vi) To amend the Plan in any respect the Board deems necessary or advisable, including, without limitation, adopting amendments relating to nonqualified deferred compensation under Section 409A of the Code and/or making the Plan or Stock Awards granted under the Plan exempt from or compliant with the requirements for nonqualified deferred compensation under Section 409A of the Code, subject to the limitations, if any, of applicable law. If required by applicable law or listing requirements, and except as provided in Section 9(a) relating to Capitalization Adjustments, the Company will seek stockholder approval of any amendment of the Plan that (A) materially increases the number of shares of Common Stock available for issuance under the Plan, (B) materially expands the class of individuals eligible to receive Stock Awards under the Plan, (C) materially increases the benefits accruing to Participants under the Plan, (D) materially reduces the price at which shares of Common Stock may be issued or purchased under the Plan, (E) materially extends the term of the Plan, or (F) materially expands the types of Stock Awards available for issuance under the Plan. Except as otherwise provided in the Plan (including subsection (viii) below) or a Stock Award Agreement, no amendment of the Plan will materially impair a Participant’s rights under an outstanding Stock Award without the Participant’s written consent.

(vii) To submit any amendment to the Plan for stockholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Rule 16b-3 of Exchange Act or any successor rule.

(viii) To approve forms of Stock Award Agreements for use under the Plan and to amend the terms of any one or more outstanding Stock Awards, including, but not limited to, amendments to provide terms more favorable to the Participant than previously provided in the Stock Award Agreement, subject to any specified limits in the Plan that are not subject to Board discretion. A Participant’s rights under any Stock Award will not be impaired by any such amendment unless the Company requests the consent of the affected Participant, and the Participant consents in writing. However, a Participant’s rights will not be deemed to have been impaired by any such amendment if the Board, in its sole discretion, determines that the amendment, taken as a whole, does not materially impair the Participant’s rights. In addition, subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Stock Awards without the affected Participant’s consent (A) to clarify the manner of exemption from, or to bring the Stock Award into compliance with, Section 409A of the Code, or (B) to comply with other applicable laws or listing requirements.

(ix) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and that are not in conflict with the provisions of the Plan and/or Stock Award Agreements.

(x) To adopt such procedures and sub-plans as are necessary or appropriate (A) to permit participation in the Plan by individuals who are foreign nationals or employed outside the United States or (B) allow Stock Awards to qualify for special tax treatment in a foreign jurisdiction; *provided* that Board approval will not be necessary for immaterial modifications to the Plan or any Stock Award Agreement that are required for compliance with the laws of the relevant foreign jurisdiction.

(c) Delegation to Committee.

(i) General. The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board will thereafter be to the Committee or subcommittee). Any delegation of administrative powers will be reflected in resolutions, not inconsistent with the provisions of the Plan, adopted from time to time by the Board or Committee (as applicable). The Committee may, at any time, abolish the subcommittee and/or revest in the Committee any powers delegated to the subcommittee. The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated.

(ii) Rule 16b-3 Compliance. The Committee may consist solely of two or more Non-Employee Directors, in accordance with Rule 16b-3 of the Exchange Act.

(d) Effect of Board's Decision. All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

(e) Cancellation and Re-Grant of Stock Awards. Neither the Board nor any Committee will have the authority to: (i) reduce the exercise, purchase or strike price of any outstanding Option, or (ii) cancel any outstanding Option that has an exercise price or strike price greater than the current Fair Market Value of the Common Stock in exchange for cash or other Stock Awards under the Plan, unless the stockholders of the Company have approved such an action within twelve (12) months prior to such an event.

3. Shares Subject to the Plan.

(a) Share Reserve.

(i) Subject to Section 9(a) relating to Capitalization Adjustments, the aggregate number of shares of Common Stock that may be issued pursuant to Stock Awards will not exceed 3,427,000 shares (the "***Share Reserve***").

(ii) Shares may be issued under the terms of this Plan in connection with a merger or acquisition as permitted by NASDAQ Listing Rule 5635(c), NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable rule, and such issuance will not reduce the number of shares available for issuance under the Plan.

(b) Reversion of Shares to the Share Reserve. If a Stock Award or any portion of a Stock Award (i) expires or otherwise terminates without all of the shares covered by the Stock Award having been issued or (ii) is settled in cash (*i.e.*, the Participant receives cash rather than stock), such expiration, termination or settlement will nevertheless reduce (or otherwise offset) the number of shares of Common Stock that are available for issuance under the Plan. If any shares of Common Stock issued under a Stock Award are forfeited back to or repurchased by the Company because of the failure to meet a contingency or condition required to vest such shares in the Participant, then the shares that are forfeited or repurchased will not revert to and again become available for issuance under the Plan.

Any shares reacquired by the Company in satisfaction of tax withholding obligations on a Stock Award or as consideration for the exercise or purchase price of a Stock Award will not again become available for issuance under the Plan.

(c) Source of Shares. The stock issuable under the Plan will be shares of authorized but unissued or reacquired Common Stock, including shares repurchased by the Company on the open market or otherwise.

4. ELIGIBILITY.

(a) Eligibility for Specific Stock Awards. Stock Awards may only be granted to persons who are Eligible Employees described in Section 1(a) of the Plan, where the Stock Award is an inducement material to the individual's entering into employment with the Company or an Affiliate within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules, *provided however*, that Stock Awards may not be granted to Eligible Employees who are providing Continuous Service only to any "parent" of the Company, as such term is defined in Rule 405 of the Securities Act, unless (i) the stock underlying such Stock Awards is treated as "service recipient stock" under Section 409A of the Code (for example, because the Stock Awards are granted pursuant to a corporate transaction such as a spin off transaction), or (ii) the Company, in consultation with its legal counsel, has determined that such Stock Awards are otherwise exempt from or comply with the distribution requirements of Section 409A of the Code.

(b) Approval Requirements. All Stock Awards must be granted either by a majority of the Company's independent directors or the Independent Compensation Committee.

5. PROVISIONS RELATING TO OPTIONS.

Each Option will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options will be Nonstatutory Stock Options. The provisions of separate Options need not be identical; *provided, however*, that each Option Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Option Agreement or otherwise) the substance of each of the following provisions:

(a) Term. No Option will be exercisable after the expiration of 10 years from the date of its grant or such shorter period specified in the Option Agreement.

(b) Exercise Price. The exercise or strike price of each Option will be not less than 100% of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Option may be granted with an exercise price lower than 100% of the Fair Market Value of the Common Stock subject to the Option if such Option is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A of the Code.

(c) Purchase Price for Options. The purchase price of Common Stock acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of the stock subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of shares of Common Stock;

(iv) by a "net exercise" arrangement pursuant to which the Company will reduce the number of shares of Common Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that the Company will accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole shares to be issued. Shares of Common Stock will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) shares issuable upon exercise are used to pay the exercise price pursuant to the "net exercise," (B) shares are delivered to the Participant as a result of such exercise, and (C) shares are withheld to satisfy tax withholding obligations; or

(v) in any other form of legal consideration that may be acceptable to the Board and specified in the applicable Option Agreement.

(d) Transferability of Options. The Board may, in its sole discretion, impose such limitations on the transferability of Options as the Board will determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options will apply:

(i) Restrictions on Transfer. An Option will not be transferable except by will or by the laws of descent and distribution (or pursuant to subsections (ii) and (iii) below), and will be exercisable during the lifetime of the Participant only by the Participant. The Board may permit transfer of the Option in a manner that is not prohibited by applicable tax and securities laws. Except as explicitly provided in the Plan, an Option may not be transferred for consideration.

(ii) Domestic Relations Orders. Subject to the approval of the Board or a duly authorized Officer, an Option may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument.

(iii) Beneficiary Designation. Subject to the approval of the Board or a duly authorized Officer, a Participant may, by delivering written notice to the Company, in a form approved by the Company (or the designated broker), designate a third party who, on the death of the Participant, will thereafter be entitled to exercise the Option and receive the Common Stock or other consideration resulting from such exercise. In the absence of such a designation, the executor or administrator of the Participant's estate will be entitled to exercise the Option and receive the Common Stock or other consideration resulting from such exercise. However, the Company may prohibit designation of a beneficiary at any time, including due to any conclusion by the Company that such designation would be inconsistent with the provisions of applicable laws.

(e) Vesting Generally. The total number of shares of Common Stock subject to an Option may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of performance goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary. The provisions of this Section 5(e) are subject to any Option provisions governing the minimum number of shares of Common Stock as to which an Option may be exercised.

(f) Termination of Continuous Service. Except as otherwise provided in the applicable Option Agreement or other agreement between the Participant and the Company, if a Participant's Continuous Service terminates (other than for Cause and other than upon the Participant's death or Disability), the Participant may exercise his or her Option (to the extent that the Participant was entitled to exercise such Option as of the date of termination of Continuous Service) within the period of time ending on the earlier of (i) the date which occurs 3 months following the termination of the Participant's Continuous Service, and (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option within the applicable time frame, the Option will terminate.

(g) Extension of Termination Date. Except as otherwise provided in the applicable Stock Award Agreement, if the exercise of an Option following the termination of the Participant's Continuous Service (other than for Cause and other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option will terminate on the earlier of (i) the expiration of a total period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements, and (ii) the expiration of the term of the Option as set forth in the applicable Option Agreement. In addition, unless otherwise provided in a Participant's Option Agreement, if the sale of any Common Stock received upon exercise of an Option following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option will terminate on the earlier of (i) the expiration of a period of days or months (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Common Stock received upon exercise of the Option would not be in violation of the Company's insider trading policy, or (ii) the expiration of the term of the Option as set forth in the applicable Option Agreement.

(h) Disability of Participant. Except as otherwise provided in the applicable Option Agreement or other agreement between the Participant and the Company, if a Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Option (to the extent that the Participant was entitled to exercise such Option as of the date of termination of Continuous Service), but only within such period of time ending on the earlier of (i) the date 12 months following such termination of Continuous Service and (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option within the applicable time frame, the Option will terminate.

(i) Death of Participant. Except as otherwise provided in the applicable Option Agreement or other agreement between the Participant and the Company, if (i) a Participant's Continuous Service terminates as a result of the Participant's death, or (ii) the Participant dies within the period (if any) specified in the Option Agreement for exercisability after the termination of the Participant's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Participant was entitled to exercise such Option as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated to exercise the Option upon the Participant's death, but only within the period ending on the earlier of (i) the date 18 months following the date of death, and (ii) the expiration of the term of such Option as set forth in the Option Agreement. If, after the Participant's death, the Option is not exercised within the applicable time frame, the Option will terminate.

(j) Termination for Cause. Except as explicitly provided otherwise in a Participant's Stock Award Agreement or other individual written agreement between the Company or any Affiliate and the Participant, if a Participant's Continuous Service is terminated for Cause, the Option will terminate upon the date on which the event giving rise to the termination for Cause first occurred, and the Participant will be prohibited from exercising his or her Option from and after the date on which the event giving rise to the termination for Cause first occurred (or, if required by applicable law, the date of termination of Continuous Service). If a Participant's Continuous Service is suspended pending an investigation of the existence of Cause, all of the Participant's rights under the Option will also be suspended during the investigation period, except to the extent prohibited by applicable law.

(k) Non-Exempt Employees. If an Option is granted to an Employee who is a non-exempt employee for purposes of the Fair Labor Standards Act of 1938, as amended, the Option will not be first exercisable for any shares of Common Stock until at least 6 months following the date of grant of the Option (although the Option may vest prior to such date). Consistent with the provisions of the Worker Economic Opportunity Act, (i) if such non-exempt Employee dies or suffers a Disability, (ii) upon a Corporate Transaction in which such Option is not assumed, continued, or substituted, or (iii) upon the non-exempt Employee's retirement (as such term may be defined in the non-exempt Employee's Option Agreement in another agreement between the non-exempt Employee and the Company, or, if no such definition, in accordance with the Company's then current employment policies and guidelines), the vested portion of any Options may be exercised earlier than 6 months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option will be exempt from his or her regular rate of pay. To the extent permitted and/or required for compliance with the Worker Economic Opportunity Act to ensure that any income derived by a non-

exempt Employee in connection with the exercise, vesting or issuance of any shares under any other Option will be exempt from such Employee's regular rate of pay, the provisions of this paragraph will apply to all Options and are hereby incorporated by reference into such Option Agreements.

6. Provisions Relating to Restricted Stock Unit Awards.

Each Restricted Stock Unit Award Agreement will be in such form and will contain such terms and conditions as the Board deems appropriate. The terms and conditions of Restricted Stock Unit Award Agreements may change from time to time, and the terms and conditions of separate Restricted Stock Unit Award Agreements need not be identical. Each Restricted Stock Unit Award Agreement will conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(a) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Common Stock subject to the Restricted Stock Unit Award. The consideration to be paid (if any) by the Participant for each share of Common Stock subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

(b) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(c) Payment. A Restricted Stock Unit Award may be settled by the delivery of shares of Common Stock, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement.

(d) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the shares of Common Stock (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(e) Dividend Equivalents. Dividend equivalents may be credited in respect of shares of Common Stock covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional shares of Common Stock covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any additional shares covered by the Restricted Stock Unit Award credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying Restricted Stock Unit Award Agreement to which they relate.

(f) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Restricted Stock Unit Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

7. Covenants of the Company.

(a) Availability of Shares. The Company will keep available at all times the number of shares of Common Stock reasonably required to satisfy then-outstanding Stock Awards.

(b) Securities Law Compliance. The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise of the Stock Awards; *provided, however,* that this undertaking will not require the Company to register under the Securities Act the Plan, any Stock Award or any Common Stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts and at a reasonable cost, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company will be relieved from any liability for

failure to issue and sell Common Stock upon exercise of such Stock Awards unless and until such authority is obtained. A Participant will not be eligible for the grant of a Stock Award or the subsequent issuance of cash or Common Stock pursuant to the Stock Award if such grant or issuance would be in violation of any applicable securities law.

(c) No Obligation to Notify or Minimize Taxes. The Company will have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising such Stock Award. Furthermore, the Company will have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a Stock Award or a possible period in which the Stock Award may not be exercised. The Company has no duty or obligation to minimize the tax consequences of a Stock Award to the holder of such Stock Award.

8. MISCELLANEOUS.

(a) Use of Proceeds from Sales of Common Stock. Proceeds from the sale of shares of Common Stock pursuant to Stock Awards will constitute general funds of the Company.

(b) Corporate Action Constituting Grant of Stock Awards. Corporate action constituting a grant by the Company of a Stock Award to any Participant will be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Stock Award is communicated to, or actually received or accepted by, the Participant. In the event that the corporate records (*e.g.*, Board consents, resolutions or minutes) documenting the corporate action constituting the grant contain terms (*e.g.*, exercise price, vesting schedule or number of shares) that are inconsistent with those in the Stock Award Agreement as a result of a clerical error in the papering of the Stock Award Agreement, the corporate records will control and the Participant will have no legally binding right to the incorrect term in the Stock Award Agreement.

(c) Stockholder Rights. No Participant will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to a Stock Award unless and until (i) such Participant has satisfied all requirements for exercise of, or the issuance of shares of Common Stock under, the Stock Award pursuant to its terms, and (ii) the issuance of the Common Stock subject to such Stock Award has been entered into the books and records of the Company.

(d) No Employment or Other Service Rights. Nothing in the Plan, any Stock Award Agreement or any other instrument executed thereunder or in connection with any Stock Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or will affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, including, but not limited to, Cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate, or (iii) the service of a Director pursuant to the bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(e) Change in Time Commitment. In the event a Participant's regular level of time commitment in the performance of his or her services for the Company and any Affiliates is reduced (for example, and without limitation, if the Participant is an Employee of the Company and the Employee has a change in status from a full-time Employee to a part-time Employee or takes an extended leave of absence) after the date of grant of any Stock Award to the Participant, the Board has the right in its sole discretion to (i) make a corresponding reduction in the number of shares or cash amount subject to any portion of such Stock Award that is scheduled to vest or become payable after the date of such change in time commitment, and (ii) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Stock Award. In the event of any such reduction, the Participant will have no right with respect to any portion of the Stock Award that is so reduced or extended.

(f) Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award, and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Common Stock subject to the Stock Award for the Participant's own account and not with any present

intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, will be inoperative if (i) the issuance of the shares upon the exercise of a Stock Award or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act, or (ii) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(g) Withholding Obligations. Unless prohibited by the terms of a Stock Award Agreement, the Company may, in its sole discretion, satisfy any U.S. federal, state, local, foreign or other tax withholding obligation relating to a Stock Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding shares of Common Stock from the shares of Common Stock issued or otherwise issuable to the Participant in connection with the Stock Award; *provided, however*, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such other amount as may be necessary to avoid classification of the Stock Award as a liability for financial accounting purposes); (iii) withholding cash from a Stock Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant, including proceeds from the sale of shares of Common Stock issued pursuant to a Stock Award; or (v) by such other method as may be set forth in the Stock Award Agreement.

(h) Electronic Delivery. Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically, filed publicly at www.sec.gov (or any successor website thereto), or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

(i) Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Common Stock or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Stock Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code (to the extent applicable to a Participant). Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company. The Board is authorized to make deferrals of Stock Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(j) Compliance with Section 409A. Unless otherwise expressly provided for in a Stock Award Agreement and the Plan will be interpreted to the greatest extent possible in a manner that makes the Plan and the Stock Awards granted hereunder exempt from Section 409A of the Code, and, to the extent not so exempt, in compliance with Section 409A of the Code. If the Board determines that any Stock Award granted hereunder is not exempt from and is therefore subject to Section 409A of the Code, the Stock Award Agreement evidencing such Stock Award will incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code, and to the extent a Stock Award Agreement is silent on terms necessary for compliance, such terms are hereby incorporated by reference into the Stock Award Agreement. Notwithstanding anything to the contrary in this Plan (and unless the Stock Award Agreement specifically provides otherwise), if the shares of Common Stock are publicly traded, and if a Participant holding a Stock Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code) will be issued or paid before the date that is six (6) months following the date of such Participant's "separation from service" or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six (6) month period elapses, with the balance paid thereafter on the original schedule.

(k) Clawback/Recovery. All Stock Awards granted under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required

by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board may impose such other clawback, recovery or recoupment provisions in a Stock Award Agreement as the Board determines necessary or appropriate, including, but not limited to, a reacquisition right in respect of previously acquired shares of Common Stock or other cash or property upon the occurrence of an event constituting Cause. No recovery of compensation under such a clawback policy will be an event giving rise to a right to resign for "good reason" or "constructive termination" (or similar term) under any agreement with the Company or an Affiliate.

9. Adjustments upon Changes in Common Stock; Other Corporate Events.

(a) Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a) and (ii) the class(es) and number of securities and price per share of stock subject to outstanding Stock Awards. The Board will make such adjustments, and its determination will be final, binding and conclusive.

(b) Dissolution or Liquidation. In the event of a dissolution or liquidation of the Company, then all outstanding Stock Awards shall terminate immediately prior to such event.

(c) Corporate Transaction. In the event of (i) a sale, lease or other disposition of all or substantially all of the securities or assets of the Company, (ii) a merger or consolidation in which the Company is not the surviving corporation or (iii) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise (a "***Corporate Transaction***"), then any surviving corporation or acquiring corporation may assume any Stock Awards outstanding under the Plan or may substitute similar stock awards (including an award to acquire the same consideration paid to the stockholders in such Corporate Transaction) for those outstanding under the Plan. In the event any surviving corporation or acquiring corporation does not assume such Stock Awards or substitute similar stock awards for those outstanding under the Plan, then with respect to Stock Awards held by Participants whose Continuous Service has not terminated, the vesting of such Stock Awards (and, if applicable, the time during which such Stock Awards may be exercised) shall be accelerated in full, and the Stock Awards shall terminate if not exercised (if applicable) at or prior to such event. With respect to any other Stock Awards outstanding under the Plan, such Stock Awards shall terminate if not exercised (if applicable) prior to such event.

10. Termination or Suspension of the Plan.

The Board may suspend or terminate the Plan at any time. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

11. Effective Date of Plan; Timing of First Grant or Exercise.

The Plan will come into existence on the Effective Date. No Stock Award may be granted prior to the Effective Date.

12. Choice of Law.

The laws of the State of Delaware will govern all questions concerning the construction, validity and interpretation of this Plan, without regard to that state's conflict of laws rules.

13. Definitions. As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "Affiliate" means, at the time of determination, any "parent" or "subsidiary" of the Company, as such terms are defined in Rule 405 of the Securities Act. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(b) "***Board***" means the Board of Directors of the Company.

(c) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Common Stock subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, stock split, reverse stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other similar equity restructuring transaction, as that term is used in Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company will not be treated as a Capitalization Adjustment.

(d) "***Cause***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company or any Affiliate defining such term and, in the absence of such agreement, such term means, with respect to a Participant, the occurrence of any of the following events: (i) such Participant's conviction of any felony or any crime involving moral turpitude or dishonesty, (ii) such Participant's participation in a fraud or act of dishonesty against the Company, (iii) such Participant's conduct that, based upon a good faith and reasonable factual investigation and determination by the Board, demonstrates the Participant's gross unfitness to serve, or (iv) such Participant's intentional, material violation of any contract between the Company and the Participant or any statutory duty that the Participant has to the Company that the Participant does not correct within 30 days after written notice to the Participant thereof. The determination as to whether a Participant is being terminated for Cause will be made in good faith by the Company and will be final and binding on the Participant. Any determination by the Company that the Continuous Service of a Participant was terminated with or without Cause for the purposes of outstanding Stock Awards held by such Participant will have no effect upon any determination of the rights or obligations of the Company, any Affiliate or such Participant for any other purpose.

(e) "***Code***" means the U.S. Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(f) "***Committee***" means a committee of one (1) or more Independent Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(g) "***Common Stock***" means the common stock of the Company.

(h) "***Company***" means Rigel Pharmaceuticals, Inc., a Delaware corporation.

(i) "***Consultant***" means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Director, or payment of a fee for such service, will not cause a Director to be considered a "Consultant" for purposes of the Plan. Notwithstanding the foregoing, a person is treated as a Consultant under this Plan only if a Form S-8 Registration Statement under the Securities Act is available to register either the offer or the sale of the Company's securities to such person.

(j) "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service. For example, a change in status from an Employee of the Company to a Consultant of an Affiliate or to a Director will not constitute an interruption of Continuous Service. If the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any leave of absence

approved by the Board or chief executive officer, including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. In addition, if required for exemption from or compliance with Section 409A of the Code, the determination of whether there has been a termination of Continuous Service will be made, and such term will be construed, in a manner that is consistent with the definition of "separation from service" as defined under Treasury Regulation Section 1.409A-1(h). A leave of absence will be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

(k) "***Director***" means a member of the Board. Directors are not eligible to receive Stock Awards under the Plan with respect to their service in such capacity.

(l) "***Disability***" means the permanent and total disability of a person within the meaning of Section 22(e)(3) of the Code.

(m) "***Effective Date***" means October 10, 2016.

(n) "***Employee***" means any person employed by the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such services, will not cause a Director to be considered an "Employee" for purposes of the Plan.

(o) "***Entity***" means a corporation, partnership, limited liability company or other entity.

(p) "***Exchange Act***" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(q) "***Fair Market Value***" means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on any established market, the Fair Market Value of a share of Common Stock will be, unless otherwise determined by the Board, the closing sales price for such stock as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the last market trading day prior to the date of determination, as reported in a source the Board deems reliable.

(ii) Unless otherwise provided by the Board, if there is no closing sales price for the Common Stock on the date of determination, then the Fair Market Value will be the closing selling price on the last preceding date for which such quotation exists.

(iii) In the absence of such markets for the Common Stock, the Fair Market Value will be determined by the Board in good faith and in a manner that complies with Section 409A of the Code.

(r) "Independent Director" has the meaning set forth in Section 1(a) above.

(s) "***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("***Regulation S-K***")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3 of the Exchange Act.

(t) "***Nonstatutory Stock Option***" means any option granted pursuant to Section 4(b) of the Plan that does not qualify as an "incentive stock option" within the meaning of Section 422 of the Code.

(u) "***Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

(v) "***Option***" means a Nonstatutory Stock Option to purchase shares of Common Stock granted pursuant to the Plan.

(w) "***Option Agreement***" means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an Option grant. Each Option Agreement will be subject to the terms and conditions of the Plan.

(x) "***Optionholder***" means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(y) "***Participant***" means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(z) "***Plan***" means this Rigel Pharmaceuticals, Inc. Inducement Plan, as it may be amended.

(aa) "***Restricted Stock Unit Award***" means a right to receive shares of Common Stock which is granted pursuant to the terms and conditions of Section 6(b).

(bb) "***Restricted Stock Unit Award Agreement***" means a written agreement between the Company and a holder of a Restricted Stock Unit Award evidencing the terms and conditions of a Restricted Stock Unit Award grant. Each Restricted Stock Unit Award Agreement will be subject to the terms and conditions of the Plan.

(cc) ***"Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(dd) "***Securities Act***" means the Securities Act of 1933, as amended.

(ee) ***"Stock Award"*** means any right to receive Common Stock granted under the Plan, including an Option or a Restricted Stock Unit Award.

(ff) "***Stock Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of a Stock Award grant. Each Stock Award Agreement will be subject to the terms and conditions of the Plan.

Exhibit 10.32

RIGEL PHARMACEUTICALS, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Each member of the Board of Directors (the "***Board***") of Rigel Pharmaceuticals, Inc. (the "***Company***") who is not also serving as an employee of the Company or any of its subsidiaries (each such member, an "***Eligible Director***") will receive the compensation described in this Non-Employee Director Compensation Policy (this "***Policy***"). An Eligible Director may decline all or any portion of his or her compensation by giving notice to the Company prior to the date cash is to be paid or equity awards are to be granted, as the case may be. This Policy may be amended at any time in the sole discretion of the Board, or by the Compensation Committee of the Board at the recommendation of the Board.

Annual Cash Compensation

The annual cash compensation amount set forth below is payable to Eligible Directors in equal quarterly installments, payable in arrears on the last day of each fiscal quarter in which the service occurred. If an Eligible Director joins the Board or a committee of the Board at a time other than effective as of the first day of a fiscal quarter, each annual retainer set forth below will be pro-rated based on days served in the applicable fiscal year, with the pro-rated amount paid for the first fiscal quarter in which the Eligible Director provides the service, and regular full quarterly payments to be paid thereafter. All annual cash fees are vested upon payment.

1. Annual Board Service Retainer:
   a. All Eligible Directors: $50,000
   b. Non-executive chairperson of the Board: $90,000 (inclusive of Annual Board Service Retainer)
2. Annual Committee Member Service Retainer:
   a. Member of the Audit Committee: $12,000
   b. Member of the Compensation Committee: $10,000
   c. Member of the Nominating and Corporate Governance Committee: $10,000
   d. Member of the Finance Committee: $5,000
   e. Member of the Scientific and Clinical Trial Advisory Committee: $10,000
3. Annual Committee Chair Service Retainer (inclusive of Committee Member Service Retainer):
   a. Chairperson of the Audit Committee: $22,000
   b. Chairperson of the Compensation Committee: $15,000
   c. Chairperson of the Nominating and Corporate Governance Committee: $15,000
   d. Chairperson of the Finance Committee: $10,000
   e. Chairperson of the Scientific and Clinical Trial Advisory Committee: $15,000

The Company will also reimburse each of the Eligible Directors for his or her travel expenses incurred in connection with his or her attendance at Board and committee meetings. Travel expenses include reasonable air and ground transportation, meals, and hotel. Eligible expenses incurred must be itemized and submitted for payment with receipts attached.

Equity Compensation

The equity compensation set forth below will be granted under the Company's 2018 Equity Incentive Plan (as amended, the "***Plan***"), subject to the approval of the Plan by the Company's stockholders. All stock options granted under this Policy will be non-statutory stock options, with an exercise price per share equal to 100% of the Fair Market Value (as defined in the Plan) of the underlying common stock on the date of grant, and a term of 10 years from the date of grant (subject to earlier termination in connection with a termination of service as provided in the Plan).

1. Initial Grant: Without any further action of the Board, each person who is elected or appointed for the first time to be a Non-Employee Director automatically shall, upon the date of his or her initial election or

appointment to be a Non-Employee Director by the Board or stockholders of the Company, be granted an Initial Grant as an Option to purchase one-hundred and twenty thousand (120,000) shares of Common Stock on the terms and conditions set forth herein. Each Stock Award that is an option to purchase granted as an Initial Grant shall vest in accordance with the schedule set forth below that results in a shorter period of full vesting: (i) 1/36th of the shares of Common Stock subject to the Initial Grant shall vest each month after the date of grant over a period of three (3) years; or (ii) the Initial Grant shall vest in equal monthly installments after the date of grant over a period commencing on the date that the Non-Employee Director is appointed for the first time to be a Non-Employee Director by the Board and ending on the date of the Annual Meeting at which the Non-Employee Director is first scheduled to be considered for election to be a Non-Employee Director by the stockholders of the Company.

2. Annual Grant: Without any further action of the Board, a Non-Employee Director shall be granted an Annual Grant as follows: On the day following each Annual Meeting commencing with the Annual Meeting in 2021, each person who is then a Non-Employee Director automatically shall be granted an Annual Grant as (i) an Option to purchase thirty thousand (30,000) shares of Common Stock and (ii) twenty-five thousand (25,000) Restricted Stock Unit Awards. If the person has not been serving as a Non-Employee Director for the entire period since the preceding Annual Meeting, then the number of shares subject to the Annual Grant shall be reduced pro rata for each full quarter prior to the date of grant during which such person did not serve as a Non-Employee Director. Each Annual Grant shall vest such that 1/12th of the shares of Common Stock subject to such Annual Grant shall vest each month after the date of grant over a period of one (1) year and the Restricted Stock Unit Awards shall vest on the date prior to the Company's next Annual Meeting.

Compensation Limits Set in Equity Plan

If, with respect to an Annual Period (as defined in the Plan), the aggregate value of all compensation granted or paid, as applicable, to any individual for service as a Non-Employee Director exceeds the applicable limit on compensation paid to Non-Employee Directors contained in the Plan, then the compensation paid to such individual under this Policy shall be reduced in accordance with an independent compensation advisor.

Approved by the Compensation Committee of the Board of Directors: November 8, 2021
Ratified by the Board of Directors: November 10, 2021
Effective: November 8, 2021

Exhibit 10.34

[***] = CERTAIN MARKED INFORMATION HAS BEEN OMITTED FROM THIS EXHIBIT BECAUSE IT IS BOTH NOT MATERIAL AND IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

AMENDMENT NO. 1 TO CREDIT AND SECURITY AGREEMENT

This AMENDMENT NO. 1 TO CREDIT AND SECURITY AGREEMENT (this "**Agreement**") is made as of this 29th day of March, 2021, by and among **RIGEL PHARMACEUTICALS, INC.**, a Delaware corporation **("Rigel")**, as a Borrower, **MIDCAP FINANCIAL TRUST**, as Agent (in such capacity, together with its successors and assigns, "**Agent**") and the financial institutions or other entities from time to time parties to the Credit Agreement referenced below, each as a Lender.

RECITALS

A. Agent, Lenders and Borrower have entered into that certain Credit and Security Agreement, dated as of September 27, 2019 (as amended, supplemented or otherwise modified from time to time prior to the date hereof, the "**Existing Credit Agreement**" and, as the same is amended hereby and as it may be further amended, modified, supplemented and restated from time to time, the "**Credit Agreement**"), pursuant to which the Lenders have agreed to make certain advances of money and to extend certain financial accommodations to Borrower in the amounts and manner set forth in the Credit Agreement.

B. Borrower has requested, and Agent and Lenders have agreed, on and subject to the terms and conditions set forth in this Agreement and the other Financing Documents, to among other things (a) amend certain Applicable Funding Conditions, conditions precedent and other terms relating to Credit Facility #3, (b) amend the amortization schedule relating to Credit Facility #3, and (c) amend certain other provisions of the Existing Credit Agreement related to the foregoing.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing, the terms and conditions set forth in this Agreement, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Agent, Lenders and Borrower hereby agree as follows:

1. **Recitals.** This Agreement shall constitute a Financing Document and the Recitals and each reference to the Credit Agreement, unless otherwise expressly noted, will be deemed to reference the Credit Agreement as amended hereby. Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Credit Agreement (including those capitalized terms used in the Recitals hereto).

2. **Amendments to Existing Credit Agreement.** Subject to the terms and conditions of this Agreement, including, without limitation, the conditions to effectiveness set forth in Section 4 below, the Existing Credit Agreement is hereby amended as follows:

(a) The Credit Facility #3 Schedule attached to the Existing Credit Agreement is hereby deleted and replaced in its entirety with Schedule 1 to this Agreement; and

(b) The "Amortization Schedule (For Each Credit Facility)" in the Existing Credit Agreement is hereby deleted and replaced in its entirety with Schedule 2 to this Agreement.

3. **Representations and Warranties; Reaffirmation of Security Interest**. Borrower hereby (a) confirms that all of the representations and warranties set forth in the Credit Agreement are true and correct in all material respects (without duplication of any materiality qualifier in the text of such representation or warranty) with respect to Borrower as of the date hereof except to the extent that any such representation or warranty relates to a specific date in which case such representation or warranty shall be true and correct as of such earlier date, and (b) covenants to perform its respective obligations under the Credit Agreement. Borrower confirms and agrees that all

security interests and Liens granted to Agent continue in full force and effect, and all Collateral remains free and clear of any Liens, other than Permitted Liens. Nothing herein is intended to impair or limit the validity, priority or extent of Agent's security interests in and Liens on the Collateral. Borrower acknowledges and agrees that the Credit Agreement, the other Financing Documents and this Agreement constitute the legal, valid and binding obligation of Borrower, and are enforceable against Borrower in accordance with its terms, except as the enforceability thereof may be limited by bankruptcy, insolvency or other similar laws relating to the enforcement of creditors' rights generally and by general equitable principles.

4. **Conditions to Effectiveness**. This Agreement shall become effective as of the date on which each of the following conditions has been satisfied, as determined by Agent in its sole discretion:

(a) Agent shall have received (including by way of facsimile or other electronic transmission) a duly authorized, executed and delivered counterpart of the signature page to this Amendment from Borrower, Agent and the Lenders;

(b) all representations and warranties of Borrower contained herein shall be true and correct in all material respects (without duplication of any materiality qualifier in the text of such representation or warranty) as of the date hereof except to the extent that any such representation or warranty relates to a specific date in which case such representation or warranty shall be true and correct as of such earlier date (and such parties' delivery of their respective signatures hereto shall be deemed to be its certification thereof);

(c) prior to and after giving effect to the agreements set forth herein, no Default or Event of Default shall exist under any of the Financing Documents; and

(d) Agent shall have received such other documents, certificates, and information as Agent may reasonably request in connection with this Agreement.

5. **Release.** In consideration of the agreements of Agent and Lenders contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Borrower, voluntarily, knowingly, unconditionally and irrevocably, with specific and express intent, for and on behalf of itself and all of its respective parents, subsidiaries, affiliates, members, managers, predecessors, successors, and assigns, and each of its respective current and former directors, officers, shareholders, agents, and employees, and each of its respective predecessors, successors, heirs, and assigns (individually and collectively, the "Releasing Parties") does hereby fully and completely release, acquit and forever discharge each of Agent, Lenders, and each their respective parents, subsidiaries, affiliates, members, managers, shareholders, directors, officers and employees, and each of their respective predecessors, successors, heirs, and assigns (individually and collectively, the "Released Parties"), of and from any and all actions, causes of action, suits, debts, disputes, damages, claims, obligations, liabilities, costs, expenses and demands of any kind whatsoever, at law or in equity, whether matured or unmatured, liquidated or unliquidated, vested or contingent, choate or inchoate, known or unknown that the Releasing Parties (or any of them) has against the Released Parties or any of them (whether directly or indirectly), based in whole or in part on facts, whether or not now known, existing on or before the date hereof, that relate to, arise out of or otherwise are in connection with: (i) any or all of the Financing Documents or transactions contemplated thereby or any actions or omissions in connection therewith or (ii) any aspect of the dealings or relationships between or among Borrower, on the one hand, and any or all of the Released Parties, on the other hand, relating to any or all of the documents, transactions, actions or omissions referenced in clause (i) hereof, in each case, based in whole or in part on facts, whether or not now known, existing before the First Amendment Effective Date. Borrower acknowledges that the foregoing release is a material inducement to Agent's and each Lender's decision to enter into this Agreement and agree to the modifications contemplated hereunder, and has been relied upon by Agent and Lenders in connection therewith.

6. **No Waiver or Novation**. The execution, delivery and effectiveness of this Agreement shall not, except as expressly provided in this Agreement, operate as a waiver of any right, power or remedy of Agent, nor constitute a waiver of any provision of the Credit Agreement, the Financing Documents or any other documents, instruments and agreements executed or delivered in connection with any of the foregoing. Nothing herein is intended or shall be construed as a waiver of any existing Defaults or Events of Default under the Credit Agreement or the other Financing Documents or any of Agent's rights and remedies in respect of such Defaults or Events of Default. This

Agreement (together with any other document executed in connection herewith) is not intended to be, nor shall it be construed as, a novation of the Credit Agreement.

7. **Affirmation**. Except as specifically amended pursuant to the terms hereof, Borrower hereby acknowledges and agrees that the Credit Agreement and all other Financing Documents (and all covenants, terms, conditions and agreements therein) shall remain in full force and effect, and are hereby ratified and confirmed in all respects by Borrower. Borrower covenants and agrees to comply with all of the terms, covenants and conditions of the Credit Agreement and the Financing Documents, notwithstanding any prior course of conduct, waivers, releases or other actions or inactions on Agent's or any Lender's part which might otherwise constitute or be construed as a waiver of or amendment to such terms, covenants and conditions.

8. Miscellaneous**.**

(a) Reference to the Effect on the Credit Agreement. Upon the effectiveness of this Agreement, each reference in the Credit Agreement to "this Agreement," "hereunder," "hereof," "herein," or words of similar import shall mean and be a reference to the Credit Agreement, as amended by this Agreement. Except as specifically amended above, the Credit Agreement, and all other Financing Documents (and all covenants, terms, conditions and agreements therein), shall remain in full force and effect, and are hereby ratified and confirmed in all respects by Borrower.

(b) GOVERNING LAW. THIS AGREEMENT AND ALL DISPUTES AND OTHER MATTERS RELATING HERETO OR THERETO OR ARISING THEREFROM (WHETHER SOUNDING IN CONTRACT LAW, TORT LAW OR OTHERWISE), SHALL BE GOVERNED BY, AND SHALL BE CONSTRUED AND ENFORCED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK, WITHOUT REGARD TO CONFLICTS OF LAWS PRINCIPLES (OTHER THAN SECTION 5-1401 OF THE GENERAL OBLIGATIONS LAW).

(c) WAIVER OF JURY TRIAL. BORROWER, AGENT AND THE LENDERS PARTY HERETO HEREBY IRREVOCABLY WAIVES ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL ACTION OR PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY AND AGREES THAT ANY SUCH ACTION OR PROCEEDING SHALL BE TRIED BEFORE A COURT AND NOT BEFORE A JURY. BORROWER, AGENT AND EACH LENDER ACKNOWLEDGES THAT THIS WAIVER IS A MATERIAL INDUCEMENT TO ENTER INTO A BUSINESS RELATIONSHIP, THAT EACH HAS RELIED ON THE WAIVER IN ENTERING INTO THIS AGREEMENT, AND THAT EACH WILL CONTINUE TO RELY ON THIS WAIVER IN THEIR RELATED FUTURE DEALINGS. BORROWER, AGENT AND EACH LENDER WARRANTS AND REPRESENTS THAT IT HAS HAD THE OPPORTUNITY OF REVIEWING THIS JURY WAIVER WITH LEGAL COUNSEL, AND THAT IT KNOWINGLY AND VOLUNTARILY WAIVES ITS JURY TRIAL RIGHTS.

(d) Incorporation of Credit Agreement Provisions. The provisions contained in Article 12 (Choice of law; venue and jury trial waiver; California waivers) and Section 13.2 (Indemnification) of the Credit Agreement are incorporated herein by reference to the same extent as if reproduced herein in their entirety.

(e) Headings. Section headings in this Agreement are included for convenience of reference only and shall not constitute a part of this Agreement for any other purpose.

(f) Counterparts. This Agreement may be signed in any number of counterparts, each of which shall be deemed an original and all of which when taken together shall constitute one and the same instrument. The words "execution," "signed," "signature," and words of like import in this Amendment shall be deemed to include electronic signatures or electronic records, each of which shall be of the same legal effect, validity or enforceability as a manually executed signature or the use of a paper-based recordkeeping system, as the case may be, to the extent and as provided for in any applicable law, including the Federal Electronic Signatures in Global and National Commerce Act, the New York State Electronic Signatures and Records Act, or any other similar state laws based on the Uniform Electronic Transactions Act. Delivery of an executed counterpart of this Agreement by facsimile or by

electronic mail delivery of an electronic version (e.g., .pdf or .tif file) of an executed signature page shall be effective as delivery of an original executed counterpart hereof and shall bind the parties hereto.

(g) Entire Agreement. This Agreement constitutes the entire agreement and understanding among the parties hereto and supersedes any and all prior agreements and understandings, oral or written, relating to the subject matter hereof.

(h) Severability. In case any provision of or obligation under this Agreement shall be invalid, illegal or unenforceable in any applicable jurisdiction, the validity, legality and enforceability of the remaining provisions or obligations, or of such provision or obligation in any other jurisdiction, shall not in any way be affected or impaired thereby.

(i) Successors/Assigns. This Agreement shall bind, and the rights hereunder shall inure to, the respective successors and assigns of the parties hereto, subject to the provisions of the Credit Agreement and the other Financing Documents.

[SIGNATURES APPEAR ON FOLLOWING PAGES]

IN WITNESS WHEREOF, intending to be legally bound, the undersigned have executed this Agreement as of the day and year first hereinabove set forth.

AGENT:

MIDCAP FINANCIAL TRUST,

By: Apollo Capital Management, L.P.,
its investment manager

By: Apollo Capital Management GP, LLC,
its general partner

By: /s/ Maurice Amsellem
Name: Maurice Amsellem
Title: Authorized Signatory

LENDERS:

MIDCAP FINANCIAL TRUST,

By: Apollo Capital Management, L.P.,
its investment manager

By: Apollo Capital Management GP, LLC,
its general partner

By: /s/ Maurice Amsellem
Name: Maurice Amsellem
Title: Authorized Signatory

LENDERS:

ELM 2020-3 TRUST

By: MidCap Financial Services Capital Management, LLC, as Servicer

By: /s/ John O'Dea
Name: John O'Dea
Title: Authorized Signatory

ELM 2020-4 TRUST

By: MidCap Financial Services Capital Management, LLC, as Servicer

By: /s/ John O'Dea
Name: John O'Dea
Title: Authorized Signatory

LENDERS:

APOLLO INVESTMENT CORPORATION

By: Apollo Investment Management, L.P., as Advisor

By: ACC Management, LLC, as its General Partner

By: /s/ Joseph D. Glatt
Name: Joseph D. Glatt
Title: Vice President

BORROWER: **RIGEL PHARMACEUTICALS, INC.**

By: /s/ Dean Schorno
Name: Dean Schorno
Title: Executive Vice President and Chief Financial Officer

Schedule 1

Credit Facility #3:

Credit Facility and Type: Term, Tranche 3

Lenders for and their respective Applicable Commitments to this Credit Facility:

Lender	**Applicable Commitment**
Midcap Financial Trust	Fourteen Million Dollars ($14,000,000)
Apollo Investment Corporation	Six Million Dollars ($6,000,000)
Total:	**Twenty Million Dollars ($20,000,000)**

The following defined terms apply to this Credit Facility:

Applicable Funding Conditions: means the following:

(a) [***]; and

(b) Borrower is in compliance with all terms of the Financing Documents, including compliance with the financial covenant set forth in Sections 9.1 and 9.2, as of the most recent Testing Date.

Applicable Interest Period: means the one-month period starting on the first (1st) day of each month and ending on the last day of such month; *provided, however*, that the first (1st) Applicable Interest Period for each Credit Extension under this Credit Facility shall commence on the date that the applicable Credit Extension is made and end on the last day of such month.

Applicable Floor: means one and one half percent (1.50%) per annum for the Applicable Libor Rate.

Applicable Margin: a rate of interest equal to five and sixty-five one-hundredths percent (5.65%) per annum.

Applicable Prepayment Fee: means the following amount, calculated as of the date (the "**Accrual Date**") that the Applicable Prepayment Fee becomes payable in the case of prepayments required under the Financing Documents or the date any voluntary prepayment is made: (a) for an Accrual Date on or after the Closing Date through and including the date which is twelve (12) months after the Closing Date, two and one half percent (2.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); (b) for an Accrual Date after the date which is twelve (12) months after the Closing Date through and including the date which is twenty-four (24) months after the Closing Date, one and one half percent (1.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); and (c) for an Accrual Date after the date which is twenty-four (24) months after the Closing Date through and including the date immediately preceding the Maturity Date, one percent (1.0%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater).

Commitment Commencement Date: The satisfaction of the Applicable Funding Conditions for this Credit Facility.

Commitment Termination Date: the earliest to occur of (a) March 31, 2022, (b) the date on which any Credit Extensions are made by the Lenders in respect of Credit Facility #4, and (c) the delivery of a written notice by Agent to Borrower terminating the Applicable Commitments following an Event of Default that has not been waived or cured at the time such notice is delivered.

Minimum Credit Extension Amount: $20,000,000.00

Schedule 2

AMORTIZATION SCHEDULE (FOR EACH CREDIT FACILITY)

Credit Facility #1
Commencing on October 1, 2021 (the "**Initial Amortization Start Date**") and continuing on the first day of each calendar month thereafter, an amount equal to the aggregate principal amount advanced under Credit Facility #1 *divided by* thirty-six (36); *provided* if Borrower provides evidence satisfactory to Agent that the applicable IO Extension Conditions (as defined below) have been satisfied at least ten (10) Business Days prior to the Initial Amortization Start Date, then the Initial Amortization Start Date shall be extended such that principal payments shall commence on the applicable Extended Amortization Start Date and shall be in an amount equal to the aggregate principal amount advanced under Credit Facility #1 *divided by* the number of full calendar months remaining (including the month in which the first amortization payment is made) before the occurrence of the Maturity Date.

Credit Facility #2:
Commencing on the Initial Amortization Start Date and continuing on the first day of each calendar month thereafter, an amount equal to the aggregate principal amount advanced under Credit Facility #2 *divided by* thirty-six (36); *provided* if Borrower provides evidence satisfactory to Agent that the applicable IO Extension Conditions (as defined below) have been satisfied at least ten (10) Business Days prior to the applicable Initial Amortization Start Date, then the Initial Amortization Start Date shall be extended such that principal payments shall commence on the Extended Amortization Start Date and shall be in an amount equal to the aggregate principal amount advanced under Credit Facility #2 *divided by* the number of full calendar months remaining (including the month in which the first amortization payment is made) before the occurrence of the Maturity Date.

Credit Facility #3:
Commencing on the latest to occur of (a) the Initial Amortization Start Date, (b) the first day of the first full calendar month immediately following such Credit Extension, and (c) the applicable Extended Amortization Start Date (if any), and, in each case, continuing on the first day of each calendar month thereafter, an amount equal the outstanding Credit Extension in respect of Credit Facility #3 divided by the number of full calendar months remaining (including such first full calendar month) before the occurrence of the Maturity Date.

Credit Facility #4:
Commencing on the latest to occur of (a) the Initial Amortization Start Date, (b) the first day of the first full calendar month immediately following such Credit Extension, and (c) the applicable Extended Amortization Start Date (if any), and, in each case, continuing on the first day of each calendar month thereafter, an amount equal the outstanding Credit Extension in respect of Credit Facility #4 divided by the number of full calendar months remaining (including such first full calendar month) before the occurrence of the Maturity Date.

Notwithstanding anything to the contrary contained in the foregoing, the entire remaining outstanding principal balance under all Credit Extensions shall mature and be due and payable upon the Maturity Date.

For purposes hereof of this Amortization Schedule, the following terms shall have the following meanings:

"**IO Extension Conditions**" means [***].

"**Extended Amortization Start Date**" means the earlier to occur of (a) if Borrower has satisfied the First IO Extension Conditions but fails to satisfy the Second IO Extension Conditions, October 1, 2022, or (b) if Borrower has satisfied both the First IO Extension Conditions and the Second IO Extension Conditions, October 1, 2023.

Exhibit 10.35

[***] = CERTAIN MARKED INFORMATION HAS BEEN OMITTED FROM THIS EXHIBIT BECAUSE IT IS BOTH NOT MATERIAL AND IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

AMENDMENT NO. 2 TO CREDIT AND SECURITY AGREEMENT

This AMENDMENT NO. 2 TO CREDIT AND SECURITY AGREEMENT (this "**Agreement**") is made as of this 11th day of February, 2022, by and among **RIGEL PHARMACEUTICALS, INC.**, a Delaware corporation ("**Rigel**"), as a Borrower, **MIDCAP FINANCIAL TRUST**, as Agent (in such capacity, together with its successors and assigns, "**Agent**") and the financial institutions or other entities from time to time parties to the Credit Agreement referenced below, each as a Lender.

RECITALS

A. Agent, Lenders and Borrower have entered into that certain Credit and Security Agreement, dated as of September 27, 2019 (as amended by that certain Amendment No. 1 to Credit and Security, dated as of April 2, 2021 and as further amended, supplemented or otherwise modified from time to time prior to the date hereof, the "**Existing Credit Agreement**" and, as the same is amended hereby and as it may be further amended, modified, supplemented and restated from time to time, the "**Credit Agreement**"), pursuant to which the Lenders have agreed to make certain advances of money and to extend certain financial accommodations to Borrower in the amounts and manner set forth in the Credit Agreement.

B. Borrower has requested, and Agent and Lenders have agreed, on and subject to the terms and conditions set forth in this Agreement and the other Financing Documents, to among other things (a) amend the Applicable Funding Conditions, Applicable Commitments and certain other terms relating to Credit Facility #3, (b) amend the Applicable Funding Conditions, Applicable Commitments and certain other terms relating to Credit Facility #4, (c) add an additional term loan facility as Credit Facility #5, (d) revise certain terms related to the financial covenants and (e) amend certain other provisions of the Existing Credit Agreement related to the foregoing.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing, the terms and conditions set forth in this Agreement, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Agent, Lenders and Borrower hereby agree as follows:

1. **Recitals.** This Agreement shall constitute a Financing Document and the Recitals and each reference to the Credit Agreement, unless otherwise expressly noted, will be deemed to reference the Credit Agreement as amended hereby. Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Credit Agreement (including those capitalized terms used in the Recitals hereto).

2. **Amendments to Existing Credit Agreement.** Subject to the terms and conditions of this Agreement, including, without limitation, the conditions to effectiveness set forth in Section 4 below, the Existing Credit Agreement is hereby amended as follows:

   (a) Section 2.3(a) of the Existing Credit Agreement is hereby deleted and replaced in its entirety with the following:

   "(a) Nature of Credit Facility; Credit Extension Requests. Credit Extensions in respect of a Credit Facility may be requested by Borrower to be made by the applicable Lenders on any Business Day during the Draw Period for such Credit Facility, but no Credit Extensions in respect of a Credit Facility shall be made before the applicable Commitment Commencement Date or after the applicable Commitment Termination Date. For any Credit Extension requested under a Credit Facility (other than a Credit Extension on the Closing Date and the Credit Extensions on the Second

Amendment Effective Date), Agent must receive the completed Credit Extension Form by 12:00 noon (New York time) ten (10) Business Days prior to the date the Credit Extension is to be funded (other than the Credit Extension made on the Closing Date). To the extent any Credit Facility proceeds are repaid for any reason, whether voluntarily or involuntarily (including repayments from insurance or condemnation proceeds), Agent and the Lenders shall have no obligation to re-advance such sums to Borrower."

(b) Subclause (a)(iv) of Section 6.7 of the Existing Credit Agreement is hereby deleted and replaced in its entirety with the following:

"(iv) At any time after the earlier of (i) the Lenders have made Credit Extensions on or after August 31, 2022 in respect of Credit Facility #4 and (ii) the Lenders have made Credit Extensions in respect of Credit Facility #5, Borrower shall immediately (but in any event within three (3) Business Days) notify Agent if Borrower Unrestricted Cash has fallen below the Minimum Cash Threshold."

(c) Section 9.2 of the Existing Credit Agreement is hereby deleted and replaced in its entirety with the following:

"9.2 [***]."

(d) The definition of "Restricted Foreign Subsidiary" in Section 15 of the Existing Credit Agreement is hereby amended by:

(i) renumbering the existing clause (c) as clause (e) ; and

(ii) adding the following new clauses (c) and (d) in the appropriate alphabetical order therein:

"(c) Rigel Pharmaceuticals LTDA,"

"(d) Rigel Pharmaceuticals, S. de R.L. de C.V., and"

(e) [***]

(f) Section 15 of the Existing Credit Agreement is hereby amended by adding the following new defined terms in the appropriate alphabetical order therein:

""**Second Amendment**" means that certain Amendment No. 2 to Credit and Security Agreement dated February 11, 2022, among Borrower, Agent and Lenders party thereto."

""**Second Amendment Effective Date**" means February 11, 2022."

(g) The Credit Facility #3 Schedule attached to the Existing Credit Agreement is hereby deleted and replaced in its entirety with Schedule 1 to this Agreement.

(h) The Credit Facility #4 Schedule attached to the Existing Credit Agreement is hereby deleted and replaced in its entirety with Schedule 2 to this Agreement.

(i) Schedule 3 to this Agreement is hereby added to the Existing Credit Agreement immediately following Credit Facility #4 Schedule

(j) The Amortization Schedule attached to the Existing Credit Agreement is hereby deleted and replaced in its entirety with Schedule 4 to this Agreement.

(k) The following agreement shall hereby be deemed added to the list of Scheduled Material Agreements on the Disclosure Schedule:

"License and Collaboration Agreement, dated February 18, 2021, between Rigel Pharmaceuticals, Inc. and Eli Lilly and Company;"

3. **Representations and Warranties; Reaffirmation of Security Interest**. Borrower hereby (a) confirms that all of the representations and warranties set forth in the Credit Agreement are true and correct in all material respects (without duplication of any materiality qualifier in the text of such representation or warranty) with respect to Borrower as of the date hereof except to the extent that any such representation or warranty relates to a specific date in which case such representation or warranty shall be true and correct as of such earlier date, and (b) covenants to perform its respective obligations under the Credit Agreement. Each Borrower confirms and agrees that all security interests and Liens granted to Agent continue in full force and effect, and all Collateral remains free and clear of any Liens, other than Permitted Liens. Nothing herein is intended to impair or limit the validity, priority or extent of Agent's security interests in and Liens on the Collateral. Borrower acknowledges and agrees that the Credit Agreement, the other Financing Documents and this Agreement constitute the legal, valid and binding obligation of Borrower, and are enforceable against Borrower in accordance with its terms, except as the enforceability thereof may be limited by bankruptcy, insolvency or other similar laws relating to the enforcement of creditors' rights generally and by general equitable principles.

4. **Conditions to Effectiveness**. This Agreement shall become effective as of the date on which each of the following conditions has been satisfied, as determined by Agent in its sole discretion:

(a) Agent shall have received (including by way of facsimile or other electronic transmission) a duly authorized, executed and delivered counterpart of the signature page to this Amendment from Borrower, Agent and the Lenders;

a. Agent shall have received (including by way of facsimile or other electronic transmission) a duly authorized, executed and delivered counterpart of the signature page to the Amended and Restated Fee Letter from Borrower and Agent;

b. Agent shall have received a duly authorized, executed and delivered secretary's certificate from Borrower certifying as to (i) the names and signatures of each officer of Borrower authorized to execute and deliver this Agreement and all documents executed in connection therewith, (ii) the organizational documents of Borrower attached to such certificate are complete and correct copies of such organizational documents as in effect on the date of such certification, (iii) the resolutions of Borrower's board of directors or other appropriate governing body approving and authorizing the execution, delivery and performance of this Agreement and the other documents executed in connection therewith, and (iv) certificates attesting to the good standing of Borrower in each applicable jurisdiction;

c. Agent shall have received a duly authorized, executed and delivered Perfection Certificate dated as of the date hereof;

d. Agent shall have received, with respect to Borrower, (i) current UCC searches from the Secretary of State of its jurisdiction of organization; and (ii) judgment, pending litigation, federal tax lien, personal property tax lien, and corporate and partnership tax lien searches, in each applicable jurisdiction, in each case, with results reasonably acceptable to the Agent;

(b) all representations and warranties of Borrower contained herein shall be true and correct in all material respects (without duplication of any materiality qualifier in the text of such representation or warranty) as of the date hereof except to the extent that any such representation or warranty relates to a specific date in which case such representation or warranty shall be true and correct as of such earlier date (and such parties' delivery of their respective signatures hereto shall be deemed to be its certification thereof);

(c) prior to and after giving effect to the agreements set forth herein, no Default or Event of Default shall exist under any of the Financing Documents; and

(d) Agent shall have received such other documents, certificates, and information as Agent may reasonably request in connection with this Agreement.

5. **Release**. In consideration of the agreements of Agent and Lenders contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Borrower, voluntarily, knowingly, unconditionally and irrevocably, with specific and express intent, for and on behalf of itself and all of its respective parents, subsidiaries, affiliates, members, managers, predecessors, successors, and assigns, and each of its respective current and former directors, officers, shareholders, agents, and employees, and each of its respective predecessors, successors, heirs, and assigns (individually and collectively, the "Releasing Parties") does hereby fully and completely release, acquit and forever discharge each of Agent, Lenders, and each their respective parents, subsidiaries, affiliates, members, managers, shareholders, directors, officers and employees, and each of their respective predecessors, successors, heirs, and assigns (individually and collectively, the "Released Parties"), of and from any and all actions, causes of action, suits, debts, disputes, damages, claims, obligations, liabilities, costs, expenses and demands of any kind whatsoever, at law or in equity, whether matured or unmatured, liquidated or unliquidated, vested or contingent, choate or inchoate, known or unknown that the Releasing Parties (or any of them) has against the Released Parties or any of them (whether directly or indirectly), based in whole or in part on facts, whether or not now known, existing on or before the date hereof, that relate to, arise out of or otherwise are in connection with: (i) any or all of the Financing Documents or transactions contemplated thereby or any actions or omissions in connection therewith or (ii) any aspect of the dealings or relationships between or among any Borrower, on the one hand, and any or all of the Released Parties, on the other hand, relating to any or all of the documents, transactions, actions or omissions referenced in clause (i) hereof, in each case, based in whole or in part on facts, whether or not now known, existing before the date hereof. Borrower acknowledges that the foregoing release is a material inducement to Agent's and each Lender's decision to enter into this Agreement and agree to the modifications contemplated hereunder, and has been relied upon by Agent and Lenders in connection therewith.

6. **No Waiver or Novation**. The execution, delivery and effectiveness of this Agreement shall not, except as expressly provided in this Agreement, operate as a waiver of any right, power or remedy of Agent, nor constitute a waiver of any provision of the Credit Agreement, the Financing Documents or any other documents, instruments and agreements executed or delivered in connection with any of the foregoing. Nothing herein is intended or shall be construed as a waiver of any existing Defaults or Events of Default under the Credit Agreement or the other Financing Documents or any of Agent's rights and remedies in respect of such Defaults or Events of Default. This Agreement (together with any other document executed in connection herewith) is not intended to be, nor shall it be construed as, a novation of the Credit Agreement.

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(h) Severability. In case any provision of or obligation under this Agreement shall be invalid, illegal or unenforceable in any applicable jurisdiction, the validity, legality and enforceability of the remaining provisions or obligations, or of such provision or obligation in any other jurisdiction, shall not in any way be affected or impaired thereby.

(i) .Successors/Assigns. This Agreement shall bind, and the rights hereunder shall inure to, the respective successors and assigns of the parties hereto, subject to the provisions of the Credit Agreement and the other Financing Documents.

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By: Apollo Capital Management, L.P.,
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By: Apollo Capital Management GP, LLC,
its general partner

By: /s/ Maurice Amsellem
Name: Maurice Amsellem
Title: Authorized Signatory

LENDERS:

MIDCAP FINANCIAL TRUST,

By: Apollo Capital Management, L.P.,
its investment manager

By: Apollo Capital Management GP, LLC,
its general partner

By: /s/ Maurice Amsellem
Name: Maurice Amsellem
Title: Authorized Signatory

LENDERS:

ELM 2020-3 TRUST

By: MidCap Financial Services Capital Management, LLC, as Servicer

By: /s/ John O'Dea
Name: John O'Dea
Title: Authorized Signatory

ELM 2020-4 TRUST

By: MidCap Financial Services Capital Management, LLC, as Servicer

By: /s/ John O'Dea
Name: John O'Dea
Title: Authorized Signatory

LENDERS:

APOLLO INVESTMENT CORPORATION

By: Apollo Investment Management, L.P., as Advisor

By: ACC Management, LLC, as its General Partner

By: /s/ Joseph D. Glatt
Name: Joseph D. Glatt
Title: Vice President

BORROWER: **RIGEL PHARMACEUTICALS, INC.**

By: /s/ Dean Schorno
Name: Dean Schorno
Title: EVP, CFO

Schedule 1

Credit Facility #3:

Credit Facility and Type: Term, Tranche 3

Lenders for and their respective Applicable Commitments to this Credit Facility:

Lender	**Applicable Commitment**
MidCap Financial Trust	Seven Million Dollars ($7,000,000)
Apollo Investment Corporation	Three Million Dollars ($3,000,000)
Total:	**Ten Million Dollars ($10,000,000)**

The following defined terms apply to this Credit Facility:

Applicable Funding Conditions: N/A.

Applicable Interest Period: means the one-month period starting on the first (1st) day of each month and ending on the last day of such month; *provided, however*, that the first (1st) Applicable Interest Period for each Credit Extension under this Credit Facility shall commence on the date that the applicable Credit Extension is made and end on the last day of such month.

Applicable Floor: means one and one half percent (1.50%) per annum for the Applicable Libor Rate.

Applicable Margin: a rate of interest equal to five and sixty-five one-hundredths percent (5.65%) per annum.

Applicable Prepayment Fee: means the following amount, calculated as of the date (the "**Accrual Date**") that the Applicable Prepayment Fee becomes payable in the case of prepayments required under the Financing Documents or the date any voluntary prepayment is made: (a) for an Accrual Date on or after the Closing Date through and including the date which is twelve (12) months after the Closing Date, two and one half percent (2.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); (b) for an Accrual Date after the date which is twelve (12) months after the Closing Date through and including the date which is twenty-four (24) months after the Closing Date, one and one half percent (1.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); and (c) for an Accrual Date after the date which is twenty-four (24) months after the Closing Date through and including the date immediately preceding the Maturity Date, one percent (1.0%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater).

Commitment Commencement Date: the Second Amendment Effective Date.

Commitment Termination Date: the close of business on the Business Day following the Second Amendment Effective Date.

Minimum Credit Extension Amount: $10,000,000.00

Schedule 2

Credit Facility #4:

Credit Facility and Type: Term, Tranche 4

Lenders for and their respective Applicable Commitments to this Credit Facility:

Lender	**Applicable Commitment**
MidCap Financial Trust	Seven Million Dollars ($7,000,000)
Apollo Investment Corporation	Three Million Dollars ($3,000,000)
Total:	**Ten Million Dollars ($10,000,000)**

The following defined terms apply to this Credit Facility:

Applicable Funding Conditions: means:

(a) if the date on which the Credit Extensions under this Credit Facility #4 are to be made is prior to August 31, 2022, then the Applicable Funding Conditions are: N/A; or

(b) if the date on which the Credit Extensions under this Credit Facility #4 are to be made is on or after August 31, 2022, then the Applicable Funding Conditions are the following:

(i) [***]; and

(i) Borrower is in compliance with all terms of the Financing Documents, including compliance with the financial covenant set forth in Sections 9.1 and 9.2, as of the most recent Testing Date occurring prior to the date on which the Credit Extensions under this Credit Facility #4 are to be made.

Applicable Interest Period: means the one-month period starting on the first (1st) day of each month and ending on the last day of such month; *provided, however*, that the first (1st) Applicable Interest Period for each Credit Extension under this Credit Facility shall commence on the date that the applicable Credit Extension is made and end on the last day of such month.

Applicable Floor: means one and one half percent (1.50%) per annum for the Applicable Libor Rate.

Applicable Margin: a rate of interest equal to five and sixty-five one-hundredths percent (5.65%) per annum.

Applicable Prepayment Fee: means the following amount, calculated as of the date (the "**Accrual Date**") that the Applicable Prepayment Fee becomes payable in the case of prepayments required under the Financing Documents or the date any voluntary prepayment is made: (a) for an Accrual Date on or after the Closing Date through and including the date which is twelve (12) months after the Closing Date, two and one half percent (2.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); (b) for an Accrual Date after the date which is twelve (12) months after the Closing Date through and including the date which is twenty-four (24) months after the Closing Date, one and one half percent (1.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); and (c) for an Accrual Date after the date which is twenty-four (24) months after the Closing Date through and including the date immediately preceding the Maturity Date, one percent (1.0%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater).

Commitment Commencement Date: the Second Amendment Effective Date.

Commitment Termination Date: the earliest to occur of (a) March 31, 2023, (b) the date on which any Credit Extensions are made by the Lenders in respect of Credit Facility #5, and (c) the delivery of a written notice by Agent to Borrower terminating the Applicable Commitments following an Event of Default that has not been waived or cured at the time such notice is delivered.

Minimum Credit Extension Amount: $10,000,000.00

Schedule 3

Credit Facility #5:

Credit Facility and Type: Term, Tranche 5

Lenders for and their respective Applicable Commitments to this Credit Facility:

Lender	**Applicable Commitment**
MidCap Financial Trust	Fourteen Million Dollars ($14,000,000)
Apollo Investment Corporation	Six Million Dollars ($6,000,000)
Total:	**Twenty Million Dollars ($20,000,000)**

The following defined terms apply to this Credit Facility:

Applicable Funding Conditions: means the following:

(a) [***]; and

(3) Borrower is in compliance with all terms of the Financing Documents, including compliance with the financial covenant set forth in Sections 9.1 and 9.2, as of the most recent Testing Date occurring prior to the date on which the Credit Extensions under this Credit Facility #5 are to be made.

Applicable Interest Period: means the one-month period starting on the first (1st) day of each month and ending on the last day of such month; *provided, however*, that the first (1st) Applicable Interest Period for each Credit Extension under this Credit Facility shall commence on the date that the applicable Credit Extension is made and end on the last day of such month.

Applicable Floor: means one and one half percent (1.50%) per annum for the Applicable Libor Rate.

Applicable Margin: a rate of interest equal to five and sixty-five one-hundredths percent (5.65%) per annum.

Applicable Prepayment Fee: means the following amount, calculated as of the date (the "**Accrual Date**") that the Applicable Prepayment Fee becomes payable in the case of prepayments required under the Financing Documents or the date any voluntary prepayment is made: (a) for an Accrual Date on or after the Closing Date through and including the date which is twelve (12) months after the Closing Date, two and one half percent (2.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); (b) for an Accrual Date after the date which is twelve (12) months after the Closing Date through and including the date which is twenty-four (24) months after the Closing Date, one and one half percent (1.5%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater); and (c) for an Accrual Date after the date which is twenty-four (24) months after the Closing Date through and including the date immediately preceding the Maturity Date, one percent (1.0%) multiplied by the amount of the outstanding principal of the Credit Extension prepaid or required to be prepaid (whichever is greater).

Commitment Commencement Date: The satisfaction of the Applicable Funding Conditions for this Credit Facility.

Commitment Termination Date: the earliest to occur of (a) March 31, 2023, and (b) the delivery of a written notice by Agent to Borrower terminating the Applicable Commitments following an Event of Default that has not been waived or cured at the time such notice is delivered.

Minimum Credit Extension Amount: $20,000,000.00

Schedule 4

AMORTIZATION SCHEDULE (FOR EACH CREDIT FACILITY)

Credit Facility #1
Commencing on October 1, 2021 (the "**Initial Amortization Start Date**") and continuing on the first day of each calendar month thereafter, an amount equal to the aggregate principal amount advanced under Credit Facility #1 *divided by* thirty-six (36); *provided* if Borrower provides evidence satisfactory to Agent that the applicable IO Extension Conditions (as defined below) have been satisfied at least ten (10) Business Days prior to the Initial Amortization Start Date, then the Initial Amortization Start Date shall be extended such that principal payments shall commence on the applicable Extended Amortization Start Date and shall be in an amount equal to the aggregate principal amount advanced under Credit Facility #1 *divided by* the number of full calendar months remaining (including the month in which the first amortization payment is made) before the occurrence of the Maturity Date.

Credit Facility #2:
Commencing on the Initial Amortization Start Date and continuing on the first day of each calendar month thereafter, an amount equal to the aggregate principal amount advanced under Credit Facility #2 *divided by* thirty-six (36); *provided* if Borrower provides evidence satisfactory to Agent that the applicable IO Extension Conditions (as defined below) have been satisfied at least ten (10) Business Days prior to the applicable Initial Amortization Start Date, then the Initial Amortization Start Date shall be extended such that principal payments shall commence on the Extended Amortization Start Date and shall be in an amount equal to the aggregate principal amount advanced under Credit Facility #2 *divided by* the number of full calendar months remaining (including the month in which the first amortization payment is made) before the occurrence of the Maturity Date.

Credit Facility #3:
Commencing on the latest to occur of (a) the first day of the first full calendar month immediately following such Credit Extension, and (b) the applicable Extended Amortization Start Date (if any), and, in each case, continuing on the first day of each calendar month thereafter, Borrowers shall make principal payments in an amount equal the outstanding Credit Extension in respect of Credit Facility #3 divided by the number of full calendar months remaining (including such first full calendar month) before the occurrence of the Maturity Date.

Credit Facility #4:
Commencing on the latest to occur of (a) the first day of the first full calendar month immediately following such Credit Extension, and (b) the applicable Extended Amortization Start Date (if any), and, in each case, continuing on the first day of each calendar month thereafter, Borrowers shall make principal payments in an amount equal the outstanding Credit Extension in respect of Credit Facility #4 divided by the number of full calendar months remaining (including such first full calendar month) before the occurrence of the Maturity Date.

Credit Facility #5:
Commencing on the latest to occur of (a) the first day of the first full calendar month immediately following such Credit Extension, and (b) the applicable Extended Amortization Start Date (if any), and, in each case, continuing on the first day of each calendar month thereafter, Borrowers shall make principal payments in an amount equal the outstanding Credit Extension in respect of Credit Facility #5 divided by the number of full calendar months remaining (including such first full calendar month) before the occurrence of the Maturity Date.

Notwithstanding anything to the contrary contained in the foregoing, the entire remaining outstanding principal balance under all Credit Extensions shall mature and be due and payable upon the Maturity Date.

For purposes hereof of this Amortization Schedule, the following terms shall have the following meanings:

"**IO Extension Conditions**" means [***].

"**Extended Amortization Start Date**" means the earlier to occur of (a) if Borrower has satisfied the First IO Extension Conditions but fails to satisfy the Second IO Extension Conditions, October 1, 2022, or (b) if Borrower has satisfied both the First IO Extension Conditions and the Second IO Extension Conditions, October 1, 2023.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-8 Nos. 333-51184, 333-106532, 333-125895 and 333-148132) pertaining to the 2000 Equity Incentive Plan, the 2000 Employee Stock Purchase Plan and the 2000 Non-Employee Directors' Stock Option Plan of Rigel Pharmaceuticals, Inc.,

(2) Registration Statements (Form S-8 Nos. 333-155031 and 333-168495) pertaining to the 2000 Equity Incentive Plan and the 2000 Non-Employee Directors' Stock Option Plan of Rigel Pharmaceuticals, Inc.,

(3) Registration Statement (Form S-8 No. 333-134622) pertaining to the 2000 Equity Incentive Plan and 2000 Employee Stock Purchase Plan of Rigel Pharmaceuticals, Inc.,

(4) Registration Statement (Form S-8 No. 333-72492) pertaining to the 2001 Non-Officer Equity Incentive Plan of Rigel Pharmaceuticals, Inc.,

(5) Registration Statements (Form S-8 Nos. 333-107062, 333-139516 and 333-196535) pertaining to the 2000 Employee Stock Purchase Plan of Rigel Pharmaceuticals, Inc.,

(6) Registration Statement (Form S-8 No. 333-111782) pertaining to the 2000 Equity Incentive Plan of Rigel Pharmaceuticals, Inc.,

(7) Registration Statements (Form S-8 Nos. 333-175977 and 333-189523) pertaining to the 2011 Equity Incentive Plan, the 2000 Equity Incentive Plan and the 2000 Non-Employee Directors' Stock Option Plan of Rigel Pharmaceuticals, Inc.,

(8) Registration Statement (Form S-8 Nos. 333-212878 and 333-183130) pertaining to the 2011 Equity Incentive Plan of Rigel Pharmaceuticals, Inc.,

(10) Registration Statements (Form S-8 Nos. 333-214370, 333-216516 and 333-221400) pertaining to the Rigel Pharmaceuticals, Inc. Inducement Plan,

(11) Registration Statement (Form S-8 No. 333-219610) pertaining to the 2000 Non-Employee Directors' Stock Option Plan and the 2011 Equity Incentive Plan of Rigel Pharmaceuticals, Inc.,

(12) Registration Statement (Form S-8 No. 333-226700) pertaining to the 2018 Equity Incentive Plan and the Inducement Plan of Rigel Pharmaceuticals, Inc.,

(13) Registration Statements (Form S-8 Nos. 333-233064 and 333-240371) pertaining to the 2018 Equity Incentive Plan of Rigel Pharmaceuticals, Inc.,

(14) Registration Statements (Form S-8 No. 333- 257226) pertaining to the 2018 Equity Incentive Plan and the 2000 Employee Stock Purchase Plan of Rigel Pharmaceuticals, Inc., and

(15) Registration Statement (Form S-3 No. 333- 258426) of Rigel Pharmaceuticals, Inc. and in the related Prospectuses,

of our reports dated March 1, 2022, with respect to the financial statements of Rigel Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Rigel Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Rigel Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

San Francisco, California

March 1, 2022

Exhibit 31.1

CERTIFICATION

I, Raul R. Rodriguez, certify that:

1. I have reviewed this Annual Report on Form 10-K of Rigel Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

/s/ Raul R. Rodriguez

Raul R. Rodriguez
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Dean L. Schorno, certify that:

1. I have reviewed this Annual Report on Form 10-K of Rigel Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

/s/ Dean L. Schorno

Dean L. Schorno

Executive Vice President and Chief Financial Officer

Exhibit 32.1

CERTIFICATIONS OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Raul R. Rodriguez, Chief Executive Officer of Rigel Pharmaceuticals, Inc. (the "Company"), and Dean L. Schorno, Executive Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2021, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of March 1, 2022.

/s/ Raul R. Rodriguez	/s/ Dean L. Schorno
Raul R. Rodriguez	Dean L. Schorno
Chief Executive Officer	*Executive Vice President and Chief Financial Officer*

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Rigel Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10- K), irrespective of any general incorporation language contained in such filing.