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, 2024

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	**94-3248524**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
611 Gateway Boulevard, Suite 900, South San Francisco, California	**94080**
(Address of principal executive offices)	(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. ☒

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

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

Indicate by 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, 2024, the last business day of the registrant's most recently completed second fiscal quarter, was $143.1 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 25, 2025, there were 17,862,958 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 2025 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission (SEC) 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," "would," "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: our business and scientific strategies; risks and uncertainties associated with the commercialization and marketing of our products in the United States (US) and outside the US; risks that the US Food and Drug Administration (FDA), European Medicines Agency (EMA), the Medicines and Healthcare Products Regulatory Agency (MHRA) or other regulatory authorities may make adverse decisions regarding our products; 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 obligations to entities party to commercial or licensing agreements with us and the timing of those obligations; our expectations with respect to regulatory submissions and approvals; our drug discovery technologies; our research and development expense; protection of our intellectual property and our intention to vigorously enforce our intellectual property rights; sufficiency of our cash and capital resources and the need for additional capital; our ability to successfully identify and acquire or in-license products or companies; our operations and legal risks; the effectiveness of our cybersecurity risk management process; and our acquisition of certain assets comprising rights to GAVRETO® (pralsetinib) in the US. 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 existing commercial products, TAVALISSE® (fostamatinib disodium hexahydrate), REZLIDHIA® (olutasidenib), and GAVRETO® (pralsetinib). To the extent that the commercial success of our products in the US and respective territories outside of the US is diminished or halted, our business, financial condition and results of operations may be adversely affected, and the price of our common stock may decline.
- We may not be able to successfully develop or commercialize our product candidates if problems arise in the clinical testing and/or approval process. There is a high risk that drug discovery and development efforts might not generate successful product candidates. If the results of our clinical trials do not meet the primary efficacy endpoints, or if the top-line data from the results of our clinical trials may not ultimately meet the requirements for an NDA approval by the FDA and other regulatory authorities, the commercial prospects of our business may be harmed, and our ability to generate product revenues may be delayed or eliminated.
- Our strategy to expand our hematology and oncology pipeline on our own, or through acquisitions or in-licensing of early or late-stage products or companies, or through partnerships with pharmaceutical and biotechnology companies, as well as academic institutions and government organizations, may not be successful.
- Even if we, or any of our collaborative partners, are able to continue to commercialize our products or any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, unfavorable health technology assessments (HTA), 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 our products and retain experienced commercial personnel, our business will be substantially harmed.
- We are subject to stringent and evolving healthcare regulatory, 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, audits, 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 our products, or of products with which we compete, our business may be harmed.
- Unforeseen safety issues could emerge with our products 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 third-party distribution facilities for the sale of our products and potential sale of any of our product candidates. If any or all of them become subject to adverse findings from inspections or face other difficulties to operate, then the distribution of our products may be interrupted or otherwise adversely affected.
- 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, MHRA 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 may be diminished, and the capital necessary to fund our operations will be increased. Additionally, approval of a drug under the accelerated drug approval program may be withdrawn or the labeled indication of the drug changed if trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug.

- 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 securing intellectual property rights and data exclusivity and other regulatory rights (such as orphan exclusivity, pediatric extensions and supplementary protection certificate) 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, partnering and commercialization activities.

- 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 developing and providing novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. We focus on products that address signaling pathways that are critical to disease mechanisms.

TAVALISSE (fostamatinib disodium hexahydrate) is our first product approved by the FDA. TAVALISSE is 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 and the United Kingdom (UK) (as TAVLESSE), and in Canada, Israel and Japan (as TAVALISSE) for the treatment of chronic ITP in adult patients.

REZLIDHIA (olutasidenib) is our second FDA-approved product. REZLIDHIA capsules are indicated for the treatment of adult patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test. We in-licensed REZLIDHIA from Forma Therapeutics, Inc., now Novo Nordisk (Forma), with exclusive, worldwide rights for its development, manufacturing and commercialization.

GAVRETO (pralsetinib) is our third FDA-approved product which we began commercializing in June 2024. GAVRETO is a once daily, small molecule, oral, kinase inhibitor of wild-type rearranged during transfection (RET) and oncogenic RET fusions. GAVRETO is approved by the FDA for the treatment of adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA-approved test. GAVRETO is also approved under accelerated approval based on overall response rate and duration response rate, for the treatment of adult and

pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). We acquired the rights to research, develop, manufacture and commercialize GAVRETO in the US from Blueprint Medicines Corporation (Blueprint) pursuant to an Asset Purchase Agreement entered in February 2024.

We continue to advance the development of R289, our dual interleukin receptor-associated kinases 1 and 4 (IRAK 1/4) inhibitor program, in an open-label, Phase 1b study to determine the tolerability and preliminary efficacy of the drug in patients with lower-risk myelodysplastic syndrome (MDS) who are relapsed, refractory or resistant to prior therapies.

We have strategic development collaborations with the University of Texas MD Anderson Cancer Center (MDACC) to expand our evaluation of olutasidenib in AML and other hematologic cancers with IDH1 mutations, and with Collaborative Network for Neuro-Oncology Clinical Trials (CONNECT) to conduct a Phase 2 clinical trial to evaluate olutasidenib in combination with temozolomide in patients with high-grade glioma (HGG) harboring an IDH1 mutation.

We have a receptor-interacting serine/threonine-protein kinase 1 (RIPK1) inhibitor program in clinical development with our partner Eli Lilly and Company (Lilly). We also have product candidates in clinical development with partners BerGenBio ASA (BerGenBio) and Daiichi Sankyo (Daiichi).

Business Updates

TAVALISSE in ITP

In 2024, we recognized $104.8 million of TAVALISSE net product sales, a 12% increase compared to $93.7 million in 2023. The increase was primarily due to increased quantities sold, as well as increased price per bottle, partially offset by higher revenue reserves driven by increased government and private payor rebates.

REZLIDHIA in R/R AML with mIDH1

In 2024, we recognized $23.0 million of REZLIDHIA net product sales, a 118% increase compared to $10.6 million in 2023. The increase was primarily due to increased quantities sold primarily driven by increased number of patients under therapy, partially offset by higher revenue reserves primarily due to increased government rebates.

GAVRETO (pralsetinib) in metastatic RET fusion-positive NSCLC and advanced thyroid cancers

In 2024, we recognized $17.1 million of GAVRETO net product sales. We began our commercialization of GAVRETO in June 2024. We distribute and market GAVRETO for approved indications in RET fusion-positive NSCLC and advanced thyroid cancers. We believe GAVRETO is highly synergistic with our current product portfolio, and we expect to continue to leverage our existing commercial infrastructure to ensure current and newly prescribed GAVRETO patients have continued access to this important treatment option. We acquired GAVRETO from Blueprint pursuant to an Asset Purchase Agreement entered into on February 22, 2024. Pursuant to the Asset Purchase Agreement, we purchased certain assets comprising the right to research, develop, manufacture and commercialize GAVRETO in the US. Under the terms of the agreement, we agreed to pay Blueprint a purchase price of $15.0 million, of which, $10.0 million was paid in July 2024 following our first commercial sale of GAVRETO at the end of June 2024, and an additional $5.0 million payable on the first anniversary of the closing date of the agreement, subject to certain conditions. Blueprint is also eligible to receive up to $97.5 million in future commercial milestone payments and up to $5.0 million in future regulatory milestone payments, in addition to tiered royalties ranging from 10% to 30%.

Simultaneously and in conjunction with entering into the Asset Purchase Agreement, we also entered into certain supporting agreements, including a customary transition agreement. We also agreed to purchase certain drug product inventories from Blueprint under a Material Transfer Agreement, and received such inventories amounting to approximately $6.5 million during the year ended December 31, 2024.

R289, an Oral IRAK 1/4 Inhibitor for Lower-Risk MDS

We advanced the development of our dual IRAK 1/4 inhibitor program, following evaluation of single and multiple ascending doses of R289 in healthy subjects. The ongoing Phase 1b open-label, multicenter study evaluates the safety, tolerability and preliminary efficacy of R289 in patients with R/R lower-risk MDS. This Phase 1b study is expected to enroll approximately 86 patients (up to 36 patients in the dose escalation phase, up to 40 patients in the dose expansion phase, and 10 less heavily pre-treated patients in an exploratory cohort). The primary objective of the study is safety, with secondary and exploratory objectives to assess preliminary efficacy and characterize the pharmacokinetic and pharmacodynamic profile of R289. The safety and efficacy data from this Phase 1b study is intended to inform the recommended dose of R289 for further clinical evaluation in lower-risk MDS. Enrollment in the fifth dose level (500 mg / 250 mg split dose) is complete and the new sixth dose level (500 mg twice daily) is now open for enrollment. In December 2024, initial data from the dose escalation part of the Phase 1b study was presented at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition. In summary, R289 was generally well tolerated with preliminary signs of efficacy in a heavily pretreated lower-risk MDS patient population, the majority of whom were high transfusion burden (HTB) at baseline. Red blood cell (RBC)-transfusion independence (RBC-TI) ≥8 weeks was achieved by three patients (1 at 500 mg QD and 2 at 750 mg QD); two HTB patients achieved RBC-TI >24 weeks. The median duration of RBC-TI was 29 weeks (range 12.7-51.9 weeks). One HTB patient receiving 500 mg QD achieved a minor hematologic improvement-erythroid (HI-E) response, with a 64% reduction in RBC transfusions compared to baseline. The three patients that achieved RBC-TI had peak hemoglobin increases exceeding 2.0 g/dL compared to baseline.

R289 was granted Fast Track designation by the FDA for the treatment of patients with previously-treated transfusion dependent lower-risk MDS in November 2024. In January 2025, the FDA granted R289 orphan drug designation for the treatment of myelodysplastic syndromes.

Olutasidenib in AML, Other Hematologic Cancers and HGG

In December 2023, we entered into a Strategic Collaboration Agreement with the MDACC, a comprehensive cancer research, treatment, and prevention center. The collaboration will expand our evaluation of olutasidenib in AML and other hematologic cancers with IDH1 mutations. Under the Strategic Collaboration Agreement, we will jointly lead the clinical development efforts with MDACC to evaluate the potential of olutasidenib to treat newly diagnosed and R/R patients with AML, higher-risk MDS, and advanced myeloproliferative neoplasms, in combination with other agents. The collaboration will also support the evaluation of olutasidenib as monotherapy in patients with IDH1 mutated clonal cytopenia of undetermined significance (CCUS) and lower-risk MDS, as well as maintenance therapy following hematopoietic stem cell transplant. Under the Strategic Collaboration Agreement, we will provide MDACC the study materials and $15.0 million in time-based milestone payments as compensation for services to be provided for the studies, over the five-year collaboration term, unless terminated earlier as provided for in the agreement. Through December 31, 2024, we provided $2.0 million funding to MDACC. MDACC has now opened for enrollment the four studies outlined in the multi-year strategic development alliance.

In January 2024, we announced our collaboration with CONNECT, an international collaborative network of pediatric cancer centers, to conduct a Phase 2 clinical trial to evaluate olutasidenib in combination with temozolomide in patients with HGG harboring an IDH1 mutation (TarGet-D). Under the collaboration, CONNECT will include the olutasidenib treatment arm (TarGet-D) within CONNECT's TarGet study, a molecularly guided Phase 2 umbrella clinical trial for HGG. In our sponsored arm, adolescents and young adult patients (<39 years old) with newly-diagnosed IDH1-mutation positive HGG will receive maintenance therapy with olutasidenib in combination with temozolomide for the first year after radiotherapy, followed by olutasidenib monotherapy for the second year. Under the collaboration, we will provide CONNECT with funding up to $3.0 million and study material over the four-year collaboration. CONNECT recently opened for enrollment the TARGET-D study, a Phase 2 study evaluating olutasidenib in combination with temozolomide, followed by olutasidenib monotherapy, as maintenance therapy for newly diagnosed adolescent and young adult patients (ages 12 to 39 years) with HGG harboring an IDH1 mutation.

Incrementally, we plan on initiating a Phase 2 clinical study in recurrent glioma. This, in combination with our strategic collaborations with MD Anderson and CONNECT, are aimed to expand our olutasidenib pipeline development programs.

Collaboration and License Agreement with Kissei

In September 2024, we announced the expansion of our relationship with Kissei, granting exclusive rights to develop and commercialize olutasidenib in all human diseases in Japan, Korea and Taiwan, pursuant to a collaboration and license agreement. Under the terms of the agreement, we received a one-time, non-creditable upfront cash payment of $10.0 million from Kissei, with the potential for up to an additional $152.5 million in development, regulatory and commercial milestone payments, and will receive mid twenty to lower thirty percent, tiered, escalated net sales-based payments for the supply of olutasidenib, subject to certain customary reductions and offsets. Pursuant to the agreement, Kissei is responsible for companion diagnostic development in Japan, for which we will share fifty percent of the costs incurred by Kissei, up to $3.0 million, which are creditable against future milestones and transfer price payments owed to us. We remain responsible for the manufacture and supply of olutasidenib for all development and commercialization activities under the agreement. Pursuant to the concurrently executed supply agreement, we will supply Kissei with bulk drug product for use under the collaboration and license agreement.

We in-licensed olutasidenib from Forma with exclusive, worldwide rights for its development, manufacturing and commercialization. Under the agreement with Forma, Forma is entitled to a certain portion of sublicensing revenue, which include, but are not limited to, upfront payments, milestone payments and royalties, that we receive from a third party sublicensee. Following the collaboration and license agreement with Kissei, we paid Forma a portion of the sublicensing revenue fee amounting to $2.3 million following our receipt of the upfront cash payment from Kissei.

Commercial License Agreement with Dr. Reddy's

In November 2024, we entered into a commercial license agreement with Dr. Reddy's Laboratories (Dr. Reddy's) to grant Dr. Reddy's an exclusive license to develop and commercialize olutasidenib in Dr. Reddy's territory which includes Latin America, South Africa, India, Australia, New Zealand, and certain countries in the Commonwealth of Independent States (CIS), Southeast Asia region and North Africa. Pursuant to the commercial license agreement, we were entitled to receive a $4.0 million one-time, non-refundable and non-creditable upfront payment, which amount, net of applicable foreign withholding taxes was received in February 2025. In addition, we are also entitled to a potential for up to an additional $36.0 million in regulatory and sales-based commercial milestone payments, and will receive high teens- to thirty percent, tiered, escalated net-sales based royalty payments for products sold in Dr. Reddy's territory, subject to certain standard reductions and offsets. Dr. Reddy's is responsible for performing and funding all development activities necessary to obtain regulatory approval and commercialize olutasidenib in the Dr. Reddy's territory. We are responsible for the exclusive manufacture and supply of olutasidenib for all future development and commercialization activities under the agreement.

As discussed above, Forma is entitled to a certain portion of sublicensing revenue from olutasidenib. Following the commercial license agreement with Dr. Reddy's, Forma is entitled to a portion of the sublicensing revenue from Dr. Reddy's, including $0.9 million upon our receipt of the upfront cash payment, net of applicable foreign withholding taxes, from Dr. Reddy's.

Global Strategic Partnership with Lilly

Lilly is continuing to advance ocadusertib (previously R552), an investigational, potent and selective RIPK1 inhibitor. Lilly has initiated the Phase 2a trial studying ocadusertib in adult patients with moderately to severely active rheumatoid arthritis. The Phase 2a enrollment of approximately 100 patients is ongoing, with preliminary analysis of the Phase 2a results anticipated in the first half of 2025. RIPK1 is implicated in a broad range of key inflammatory cellular processes and plays a key role in tumor necrosis factor 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.

Under the Lilly Agreement, we are responsible for 20% of the development costs for ocadusertib in the US, Europe and Japan, up to a specified cap, and Lilly is responsible for funding the remainder of all development activities for ocadusertib and other non-CNS disease development candidates. Under the Lilly Agreement, we have the right to opt-out of co-funding the ocadusertib development activities in the US, Europe and Japan at two different specified times

and as a result receive lesser royalties from sales. In September 2023, we provided the first opt-out notice to Lilly and our funding commitment was capped at a specified amount through April 1, 2024, as provided for in the Lilly Agreement, as amended in September 2023. We provided $21.4 million funding to Lilly throughout the periods for our share for ocadusertib development costs incurred through April 1, 2024. Under the Lilly Agreement as amended, we have the right to opt-in to co-funding of ocadusertib development, upon us providing notice to Lilly within 30 days of certain events, as specified in the Lilly Agreement. If we decide to exercise our opt-in right, we will be required to continue to share in global development costs, and if we later exercise our second opt-out right (no later than April 1, 2025), our share in global development costs will be up to a specified cap through December 31, 2025, as provided for in the Lilly Agreement.

Patent Infringement Lawsuit

In June 2022, we received a notice letter regarding an Abbreviated New Drug Application (ANDA) submitted to the FDA by Annora Pharma Private Limited (Annora) requesting approval to market a generic version of TAVALISSE. In July 2022, we filed a lawsuit in the US District Court for the District of New Jersey against Annora and its subsidiaries for infringement of certain of our US patents. Litigation continues, and no trial date is currently set. For a more detailed discussion of this litigation matter, see "Part I, Item 3, Legal Proceedings" of this Annual Report on Form 10-K.

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 recently expanded our hematology and oncology portfolio with our third commercialized product, GAVRETO, which we believe is highly synergistic with and complementary to our existing hematology and oncology focused commercial infrastructure. We continue to maintain a strong commercial and medical affairs team in the US to enable us to execute successfully on our commercialization strategy to grow TAVALISSE in chronic ITP, REZLIDHIA in mIDH1 R/R AML, and GAVRETO in NSCLC and advanced thyroid cancers. For the expansion of fostamatinib and olutasidenib outside of the US, we entered into partnerships and are currently exploring other partnership opportunities. We continue our development of novel therapies designed to significantly improve the lives of patients with hematological disorders and cancer. We will be focusing on the further development of our products in other indications on our own or through our partners. We aim to expand our portfolio with additional commercial products and/or additional candidates for our development pipeline, on our own and/or in partnership with pharmaceutical and biotechnology companies as well as academic institutions and government organizations.

In particular, the key elements that we believe are value drivers, which we plan to continue to execute include:

- growing sales of TAVALISSE in chronic ITP, REZLIDHIA in mIDH1 R/R AML, and GAVRETO in NSCLC and advanced thyroid cancers; and
- advancing our development pipeline on our own and/or with collaboration partner(s).

Our Product Portfolio

The following table summarizes our portfolio:

	Indication	Target	Stage	Partner
Commercialized Products				
TAVALISSE® (fostamatinib)[1,2]	Adult Chronic ITP	SYK	Approved	
REZLIDHIA® (olutasidenib)[3]	R/R AML	mIDH1	Approved	
GAVRETO® (pralsetinib)[4]	RET+ NSCLC & Advanced Thyroid Cancer	RET	Approved	
Clinical Trials				
R289*	Lower-risk MDS	IRAK1/4	Phase 1b	
Partnered Programs				
Bemcentinib*	NSCLC	AXL	Phase 2	BerGenBio
Ocadusertib (previously R552)*	Rheumatoid Arthritis	RIPK1	Phase 2	Lilly
Milademetan*	Cancer	MDM2	Phase 1	Daiichi-Sankyo
Rxxx (CNS penetrant)	CNS Diseases	RIPK1	Pre-clinical	Lilly

Company-Sponsored Trials

[1] Please see the TAVALISSE Full Prescribing Information
[2] The product is also commercially available in Europe and the UK (TAVLESSE) as well as Canada, Israel and Japan (TAVALISSE) for the treatment of adult chronic immune thrombocytopenia (ITP).
[3] Please see the REZLIDHIA Full Prescribing Information, including Boxed WARNING
[4] Please see the GAVRETO Full Prescribing Information
* Investigational compound in this indication and has not been submitted for FDA review

Commercial Products

TAVALISSE/Fostamatinib in ITP

TAVALISSE overview

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 (TPO) and splenectomy.

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 multicenter, 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 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. 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, increased aspartate aminotransferase, 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. 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. In addition, a report describing the long-term safety and durable efficacy of TAVALISSE with up to five years of treatment was published in Therapeutic Advances in Hematology in 2021.

The FDA granted orphan drug designation for fostamatinib for the treatment of ITP in August 2015. 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.

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 to TPO receptors on megakaryocyte precursors include PROMACTA® (Novartis International AG), Nplate® (Amgen, Inc.), DOPTELET® (Swedish Orphan Biovitrum AB) and ALVAIZ™ (Teva Pharmaceutical Industries Ltd.). In the longer term, we may eventually face competition from potential manufacturers of generic versions of our marketed products, including the proposed generic version of TAVALISSE that is the subject of an ANDA submitted to the FDA by Annora, which, if approved and allowed to enter the market, it could result in significant decreases in the revenue derived from sale of TAVALISSE and thereby materially harm our business and financial condition.

TAVALISSE commercial activities, including sales and marketing

Our marketing and sales efforts are focused on hematologists and hematologist-oncologists in the US who manage chronic adult ITP patients. We have a fully integrated commercial team consisting of sales, marketing, market access, and commercial operations functions. Our sales team promotes our products in the US using customary

pharmaceutical company practices. Our products are 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 our products, we have established a reimbursement and patient support program called Rigel OneCare ® (ROC). Through ROC, we provide co-pay assistance to qualified, commercially insured patients to help minimize out-of-pocket costs and provide free product 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.

We have entered into various license and commercial agreements to commercialize fostamatinib globally as discussed below, but we retain the global rights to fostamatinib outside of the respective territories under such license and commercial agreements.

Fostamatinib outside of the US

We have a commercialization license agreement with Grifols for exclusive rights to commercialize fostamatinib for human diseases, and non-exclusive rights to develop, fostamatinib in their territory. Grifols territory includes EU, the UK, Turkey, the Middle East, North Africa and Russia (including Commonwealth of Independent States). In January 2020, the European Commission (EC) granted a centralized MA for fostamatinib (TAVLESSE) valid throughout EU and which has been grandfathered in the UK, after the departure of the UK from the EU, for the treatment of chronic ITP in adult patients who are refractory to other treatments. Grifols has launched TAVLESSE in the UK and certain countries in EU including Germany, France, Italy and Spain, and continues a phased rollout across the rest of EU.

We have an exclusive license and supply agreement with Kissei to develop and commercialize fostamatinib in all current and potential indications in Japan, China, Taiwan and 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. Japan has the third highest prevalence of chronic ITP in the world behind the US and Europe. Kissei was granted orphan drug designation from the Japanese Ministry of Health, Labor and Welfare for R788 (fostamatinib) in chronic ITP in February 2020. In December 2022, Japan's Pharmaceuticals and Medical Devices Agency (PMDA) approved TAVALISSE for the treatment of chronic ITP, and in April 2023, Kissei launched TAVALISSE for chronic ITP in Japan. In January 2025, Kissei announced the Korean Ministry of Food and Drug Safety approved TAVALISSE for the treatment of thrombocytopenia in adult patients with chronic idiopathic thrombocytopenic purpura who have had an insufficient response to a previous treatment

We have exclusive commercial and license agreements with Medison to commercialize fostamatinib in all potential indications in Canada and Israel. 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. TAVALISSE is commercially available in Canada and Israel.

We have a commercial license agreement with Knight to exclusively commercialize fostamatinib for approved indications in Latin America, consisting of Mexico, Central and South America, and the Caribbean. We are also responsible for the exclusive manufacture and supply of fostamatinib for all future development and commercialization activities under a commercial and supply agreement. In August 2023, Knight submitted the MAA for regulatory approval in Mexico, Colombia and Brazil for fostamatinib for the treatment of adult patients with ITP who had insufficient response to a previous treatment. In December 2024, Knight announced the approval of TAVALISSE in Mexico for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment.

REZLIDHIA/Olutasidenib in R/R AML with mIDH1

REZLIDHIA overview

mIDH1 alterations are seen in AML, MDS, glioma, chondrosarcoma, and intrahepatic cholangiocarcinoma. It is estimated that there are approximately 1,000 adult patients, a well-identified patient population, with mIDH1 R/R AML, part of an AML market estimated to have an incidence of approximately 20,000 cases in the US and an estimated 120,000 cases globally. Despite having approved treatment options for R/R AML patients who are mIDH1 positive, an unmet need remains.

Olutasidenib, an oral, small molecule drug designed to selectively bind to and inhibit mIDH1, is a treatment option with durable remissions, reduced QTc potential, and a stable pharmacokinetics profile that enables a consistent drug exposure over time. This targeted agent has the potential to provide therapeutic benefit by reducing 2-hydroxyglutarate levels and restoring normal cellular differentiation. IDH1 is a natural enzyme that is part of the normal metabolism of all cells. When mutated, IDH1 activity can promote blood malignancies and solid tumors. Olutasidenib was granted orphan drug designation by the FDA for the treatment of AML, which provides orphan drug market exclusivity from the time of marketing approval on December 1, 2022.

REZLIDHIA is designed to bind to and inhibit mIDH1 to reduce 2-hydroxyglutarate levels and restore normal cellular differentiation of myeloid cells. REZLIDHIA is a novel, non-intensive monotherapy treatment in the R/R AML setting demonstrating a CR+CRh rate of 35% in patients with over 90% of those responders in complete remission.

We in-licensed REZLIDHIA from Forma pursuant to a license and transition services agreement entered in July 2022, with exclusive, worldwide rights for development, manufacturing and commercialization of REZLIDHIA for any uses, including for the treatment of AML and other malignancies. In accordance with the terms of the license and transition services agreement, we paid an upfront fee of $2.0 million, with the potential to pay up to $67.5 million additional payments upon achievement of specified development and regulatory milestones and up to $165.5 million additional payments upon achievement of certain commercial milestones. In 2022, certain milestones were met which entitled Forma to receive a $17.5 million milestone payments. No new milestone was met in 2023 and 2024. In addition, subject to the terms and conditions of the license and transition services agreement, Forma would be entitled to tiered royalty payments on net sales of licensed products at percentages ranging from low-teens to mid-thirties, as well as certain portions of our sublicensing revenue, subject to certain standard reductions and offsets.

In December 2022, the FDA approved REZLIDHIA capsules for the treatment of adult patients with R/R AML with IDH1 mutation as detected by an FDA-approved test, and we began the commercialization of REZLIDHIA and made it available to patients. The recommended dosage of REZLIDHIA is 150 mg taken orally twice daily until disease progression or unacceptable toxicity. The FDA approval was based on the NDA for olutasidenib for the treatment of m1DH1 R/R AML submitted by Forma, that had a PDUFA action date for the application of February 15, 2023. The NDA application was supported with a Phase 2 registrational trial for olutasidenib in mIDH1 R/R AML. Interim results from the Phase 2 registrational trial were reported at the American Society of Clinical Oncology (ASCO) annual meeting in June 2021. The interim results of this trial of 153 patients showed that olutasidenib demonstrated a favorable tolerability profile as a monotherapy in patients with R/R AML who have a susceptible mIDH1, and achieved a complete remission (CR) plus CR with partial hematologic recovery (CRh) rate of 33.3% (30% CR and 3% CRh), the primary efficacy endpoint. While a median duration of CR/CRh was not yet reached, a sensitivity analysis (with a hematopoietic stem cell transplant, as the end of a response) indicated the median duration of CR/CRh was 13.8 months**.** The overall response rate, comprised CR, CRh, Cri, partial response, and morphologic leukemia-free state (MLFS), was 46% and the median duration of overall response rate (ORR) was 11.7 months. The median overall survival was 10.5 months. For patients with CR/CRh, the median overall survival was not reached, but the estimated 18-month survival was 87%. The most frequently reported treatment emergent adverse events were nausea, constipation, increased white blood cell count, decreased red blood cell count, pyrexia, febrile neutropenia, and fatigue.

In January 2023, we announced that REZLIDHIA has been added by the National Comprehensive Cancer Network (NCCN) to the latest NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for AML. REZLIDHIA is now included as a recommended targeted therapy for adult patients with R/R AML with IDH1 mutation.

In February 2023, we announced peer-reviewed publication data in *Blood Advances*, which summarize clinical results from the Phase 2 registrational trial of REZLIDHIA in patients with mIDH1 R/R AML. The published data demonstrate that REZLIDHIA induced durable remissions and transfusion independence with a well-characterized safety profile. The observed efficacy is clinically meaningful and represents a therapeutic advance in this poor prognosis patient population with limited treatment options. REZLIDHIA demonstrated both a high rate of response and an extended median duration of complete response of 28.1 months, which is more than a year longer than what is reported with the standard of care. In June 2023, we announced the second REZLIDHIA publication in *Blood Advances*, a review article examining the preclinical and clinical development, and the positioning of REZLIDHIA in the mIDH1 AML treatment landscape. The review concluded that the approval of REZLIDHIA is a critical addition to the mIDH1 AML treatment landscape. Further, the available data support the use of REZLIDHIA as monotherapy in R/R AML patients who have failed intensive chemotherapy or venetoclax plus hypomethylating agents combination therapy.

In April 2024, we announced a peer-reviewed publication in *Leukemia & Lymphoma* on data from an analysis of the Phase 2 study evaluating REZLIDHIA in patients with mIDH1 AML who are R/R to prior venetoclax-based regimens. The findings from these analyses suggest that REZLIDHIA alone or in combination with azacitidine demonstrated potential efficacy in patients with AML following failure of venetoclax combination therapy.

In May 2024, we announced the presentation of the five-year results from the registrational Phase 2 trial of REZLIDHIA in R/R mIDH1 AML patients at the 2024 ASCO Annual Meeting and EHA 2024 Hybrid Congress. The data published reinforces REZLIDHIA's efficacy in heavily pretreated patients with mIDH1 AML, including those R/R to prior venetoclax. The safety profile was consistent with what was previously reported. Further, REZLIDHIA was generally well tolerated in elderly patients with R/R mIDH1 AML and induced durable remissions. Despite the challenges of treating elderly patients who had already failed prior AML treatment, the results suggest that elderly patients can benefit from therapy with REZLIDHIA. REZLIDHIA was also effective in achieving remission in patients with mIDH1 R/R AML and served as a bridging strategy towards potentially curative allogeneic transplantation in a substantial subset of these previously ineligible patients. Additionally, REZLIDHIA was well tolerated in a subset of patients with myeloproliferative neoplasms mlDH1 AML, a patient population often associated with poor responses to available therapies.

Competitive landscape for REZLIDHIA

There is currently one other product approved in the US for patients with IDH1 mutation. The FDA granted approval to TIBSOVO® (ivosidenib), an oral targeted IDH1 mutation inhibitor, (i) in July 2018, for adult patients with R/R AML with a susceptible IDH1 mutation, (ii) in May 2019, for newly diagnosed AML with a susceptible IDH1 mutation who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy, (iii) in August 2021, for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation as detected by an FDA-approved test, (iv) in May 2022, in combination with azacitidine (azacitidine for injection) for newly diagnosed AML with a susceptible IDH1 mutation, as detected by an FDA-approved test in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy, and (v) in October 2023, for adult patients with R/R MDS with a susceptible IDH1 mutation, as detected by an FDA-approved test. In addition, some clinicians may utilize non-targeted treatments for patients with mIDH1 R/R AML, including use of venetoclax combinations, hypomethylating agents, other chemotherapy regimens, or investigational agents that may be available to them.

REZLIDHIA commercial activities, including sales and marketing

We believe REZLIDHIA is highly synergistic with our existing hematology-oncology focused commercial and medical affairs infrastructure. Our commercial effort focuses on growing awareness of REZLIDHIA within key institutions, and among targeted HCPs who manage patients with R/R AML with mIDH1. We retain the global rights, excluding certain geographies as discussed below, to develop and commercialize olutasidenib for all indications, and we are currently exploring other ex-US partnership opportunities.

Olutasidenib outside of the US

In September 2024, we entered into a collaboration and license agreement with Kissei, pursuant to which Kissei

was granted exclusive rights to develop and commercialize olutasidenib in all human diseases in Japan, Korea and Taiwan. Kissei will initially seek approval for REZLIDHIA in Japan for R/R mIDH1 AML and will be responsible for conducting clinical studies as required by the Japanese PMDA. We remain responsible for the manufacture and supply of olutasidenib for all development and commercialization activities and will supply Kissei with bulk drug product for use under the license and supply agreements.

In November 2024, we entered into a commercial license agreement with Dr. Reddy's for an exclusive license to develop and commercialize olutasidenib in Dr. Reddy's territory which includes Latin America, South Africa, India, certain countries in the CIS, Southeast Asia region and North Africa, Australia, and New Zealand. We are responsible for the exclusive manufacture and supply of olutasidenib for all future development and commercialization activities under a supply agreement.

Under the license and services agreement with Forma as discussed in "Note 5 – In-Licensing and Acquisition" 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, Forma is entitled to a certain portion of sublicensing revenue, which include, but are not limited to upfront payment, milestone payments and royalties, that we receive from a third party sublicensee. Following the license agreements with Kissei and Dr. Reddy's as discussed above, Forma is entitled to a portion of the sublicensing revenue we receive from Kissei and Dr. Reddy's.

GAVRETO/Pralsetinib in metastatic RET fusion-positive NSCLC and advanced thyroid cancers

GAVRETO overview

RET is a receptor tyrosine kinase that activates multiple downstream pathways involved in cell proliferation and survival. RET can be activated by mutation or when a portion of the RET gene that encodes the kinase domain is joined to part of another gene creating a fusion gene that encodes an aberrantly activated RET fusion protein. RET alterations, such as fusions or mutations, drive the growth of multiple tumor types. It is estimated that over 226,000 adult patients in the US will be diagnosed with lung cancer in 2025. NSCLC is the most common type of lung cancer in the US accounting for 80-85% of all lung cancer diagnoses. RET activating fusions are key disease drivers in NSCLC. RET fusions are implicated in approximately 1-2% of patients with NSCLC.

We acquired the rights to research, develop, manufacture and commercialize GAVRETO from Blueprint, pursuant to an Asset Purchase Agreement entered in February 2024. GAVRETO is a once daily, small molecule, oral, kinase inhibitor of wild-type RET and oncogenic RET fusions. Currently, GAVRETO is one of only two approved RET inhibitors on the market for patients. GAVRETO is approved by the FDA for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA-approved test.

GAVRETO is also approved for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). This indication was approved by the FDA under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial. Discussions with the FDA regarding confirmatory requirements are ongoing.

In June 2024, we announced the completion of the transfer to us of the NDA for GAVRETO, and GAVRETO became commercially available from us in the US by prescription. GAVRETO was co-marketed by Blueprint and Genentech, a member of Roche, to patients in the US since September 2020 pursuant to a collaboration agreement between Blueprint and Roche, which agreement was terminated effective in February 2024.

The FDA granted GAVRETO new chemical entity exclusivity until September 2025 and orphan drug exclusivity until September 2027 with respect to the approval for treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA-approved test. The FDA also granted GAVRETO two orphan drug exclusivities until December 2027 with respect to FDA approval for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are

radioactive iodine-refractory (if radioactive iodine is appropriate), and for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid carcinoma who require systemic therapy.

Competitive landscape for GAVRETO

GAVRETO faces competition for RET fusion-positive NSCLC and advanced thyroid cancers from Lilly's selpercatinib (Retevmo®). In addition, other commercially available therapies used to treat RET fusion-positive NSCLC include cabozantanib and platinum-based chemotherapy regimens with or without pembrolizumab, atezolizumab, nivolumab/ipilumumab, cemiplimab or tremelimumab-durvalumab. GAVRETO may also face competition from other drug candidates in development for RET-altered cancers, as well as multi-kinase inhibitors with RET activity being evaluated in clinical trials.

GAVRETO commercial activities, including sales and marketing

We began our commercialization and started recognizing revenue from product sales of GAVRETO in June 2024. We believe GAVRETO is highly synergistic with our current product portfolio, and we expect to continue to leverage our existing commercial infrastructure to ensure current and newly prescribed GAVRETO patients have continued access to this important treatment option. We distribute and market GAVRETO for approved indications in RET fusion-positive NSCLC and advanced thyroid cancers.

Clinical Stage Programs

R289, an Oral IRAK 1/4 Inhibitor for Hematology-Oncology, Autoimmune, and Inflammatory Diseases

During the second quarter of 2018, we selected R835, a proprietary molecule from our dual IRAK 1/4 inhibitor 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 receptor (IL-1R) family 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. R835 prevents cytokine release in response to TLR and IL-1R activation in vitro, and 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 than inhibition of either one individually.

In October 2019, we announced results from a Phase 1 randomized, placebo-controlled, double-blind clinical study evaluating the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of R835 in 91 healthy adult subjects. The Phase 1 study showed that R835 had a favorable safety, tolerability and PK profile and established proof-of-mechanism by demonstrating the inhibition of inflammatory cytokine production in response to a lipopolysaccharide (LPS) challenge.

We advanced the development of our IRAK 1/4 inhibitor program, following evaluation of single and multiple ascending doses of R289, a new pro-drug formulation of R835 in healthy subjects. In January 2022, we initiated a Phase 1b open-label, multicenter study to evaluate the safety, tolerability and preliminary efficacy of R289 in patients with R/R lower-risk MDS. In December 2022, we announced the dosing of the first patient. This Phase 1b study is expected to enroll approximately 48 patients (up to 36 patients in the dose escalation phase, up to 40 patients in the dose expansion phase, and 10 less heavily pre-treated LR-MDS patients in an exploratory cohort). The primary objective of the study is safety, with secondary and exploratory objectives to assess preliminary efficacy and characterize the pharmacokinetic and pharmacodynamic profile of R289. The safety and efficacy data from this Phase 1b study is intended to inform the recommended dose of R289 for further clinical evaluation in lower-risk MDS. Enrollment in the fifth dose level (500 mg / 250 mg split dose) is complete and the new sixth dose level (500 mg twice daily) is now open for enrollment. In December 2024, initial data from the dose escalation part of the Phase 1b study was presented at the 66th ASH Annual Meeting and Exposition. In summary, R289 was generally well tolerated with preliminary signs of efficacy in this heavily pretreated lower-risk MDS patient population, the majority of whom were HTB at baseline. RBC-TI ≥8 weeks

was achieved by three patients (1 at 500 mg QD and 2 at 750 mg QD); two HTB patients achieved RBC-TI >24 weeks. The median duration of RBC-TI was 29 weeks (range 12.7-51.9 weeks). One HTB patient receiving 500 mg QD achieved a minor HI-E response, with a 64% reduction in RBC transfusions compared to baseline. The three patients that achieved RBC-TI had peak hemoglobin increases exceeding 2.0 g/dL compared to baseline.

R289 was granted Fast Track designation by the FDA for the treatment of patients with previously-treated transfusion dependent lower-risk MDS in November 2024. In January 2025, the FDA granted R289 orphan drug designation for the treatment of myelodysplastic syndromes.

Olutasidenib for mIDH1 AML, Other Heamtologic Cancers and HGG

We have a strategic collaboration agreement with MDACC to expand our evaluation of olutasidenib in AML and other hematologic cancers with IDH1 mutations. Under such collaboration agreement, we will jointly lead the clinical development efforts with MDACC to evaluate the potential of olutasidenib to treat newly diagnosed and R/R patients with AML, higher-risk MDS, and advanced myeloproliferative neoplasms, in combination with other agents. The collaboration will also support the evaluation of olutasidenib as monotherapy in patients with IDH1 mutated CCUS and lower-risk MDS, as well as maintenance therapy following hematopoietic stem cell transplant. MDACC has now opened for enrollment the four studies outlined in the multi-year strategic development alliance. In August 2024, MDACC opened enrollment for a Phase 1b/2 triplet therapy trial of decitabine and venetoclax in combination with olutasidenib in patients with mIDH1 AML. The Phase 1b part of the trial seeks to determine the safety and tolerability and recommended Phase 2 dose of decitabine and venetoclax in combination with olutasidenib. The primary objective of the Phase 2 part of the trial is to determine the complete remission rate in both newly diagnosed and R/R patients. The first patient was enrolled in the Phase 1b/2 triplet therapy trial in September 2024, and the trial is ongoing. In December 2024, MDACC opened enrollment for two trials, a Phase 2 study in patients with IDH1-mutated CCUS, lower-risk MDS and chronic myelomonocytic leukemia (CMML), and a Phase 1/2 study of olutasidenib maintenance therapy following an allogeneic stem cell transplant for patients with IDH1-mutated myeloid malignancies. In January 2025, MDACC opened for enrollment a Phase 2 study of olutasidenib in combination with hypomethylating agents (HMA) in patients with mIDH1 higher-risk myelodysplastic syndrome (HR-MDS)/ CMML or advanced myeloproliferative neoplasms.

We also have a collaboration with CONNECT to conduct a Phase 2 clinical trial to evaluate olutasidenib in combination with temozolomide in patients with HGG harboring an IDH1 mutation (TarGet-D). Under the collaboration, CONNECT will include the olutasidenib treatment arm (TarGet-D) within CONNECT's TarGet study, a molecularly guided Phase 2 umbrella clinical trial for HGG. In our sponsored arm, adolescents and young adult patients (<39 years old) with newly-diagnosed IDH1-mutation positive HGG will receive maintenance therapy with olutasidenib in combination with temozolomide for the first year after radiotherapy, followed by olutasidenib monotherapy for the second year. CONNECT recently opened for enrollment the TARGET-D study, a Phase 2 study evaluating olutasidenib in combination with temozolomide, followed by olutasidenib monotherapy, as maintenance therapy for newly diagnosed adolescent and young adult patients (ages 12 to 39 years) with HGG harboring an IDH1 mutation.

Partnered Clinical Programs

Ocadusertib – Lilly

Lilly is continuing to advance ocadusertib (previously R552) and has initiated the Phase 2a trial studying ocadusertib in adult patients with moderately to severely active rheumatoid arthritis. The Phase 2a enrollment of approximately 100 patients is ongoing, with preliminary analysis of the Phase 2a results anticipated in the first half of 2025. RIPK1 is implicated in a broad range of key inflammatory cellular processes and plays a key role in tumor necrosis factor 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.

Bemcentinib – BerGenBio

We have an exclusive, worldwide research, development and commercialization agreement with BerGenBio for our investigational AXL receptor tyrosine kinase inhibitor, R428 (now referred to as bemcentinib (BGB324)). In February 2023, BerGenBio announced positive data from the Phase 2 trial of bemcentinib in combination with pembrolizumab in patients with second-line NSCLC. The treatment with bemcentinib in combination with pembrolizumab demonstrated long survival benefit and sustained disease control, particularly in patients with AXL TPS > 5, substantiating the relevance of AXL as a target and bemcentinib's selective inhibition capabilities in NSCLC. Also in March 2023, BerGenBio announced its first patient dosed in a Phase 1b/2a trial evaluating bemcentinib in first-line NSCLC patients harboring STK11 mutations. In March 2024, BerGenBio announced initiation of the Phase 2a portion of the study following a positive decision by the Data and Safety Monitoring Board (DSMB) following review of the Phase 1b safety data. In July 2024, BerGenBio announced that the DSMB confirmed acceptable safety at the highest dose tested in Phase 1b and recommended that under the study protocol, no additional patients will be required for Phase 1b. In October 2024, BerGenBio announced the preliminary safety data from dose escalation Phase 1b in first-line NSCLC patients.

Milademetan – Daiichi

DS-3032 is an investigational oral selective inhibitor of the 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 trial of DS-3032 suggests that DS-3032 may be a promising treatment for hematological malignancies including R/R AML and high-risk MDS. In September 2020, worldwide rights to DS-3032 (milademetan) were out-licensed from Daiichi to Rain Oncology Inc. (Rain). In January 2024, Pathos Al, Inc. (Pathos) completed the acquisition of Rain. Pathos indicated that it has continued interest in further developing milademetan for cancer patients using its propriety PathOS Platform.

Research, Preclinical and Clinical Development Programs

We maintain expertise in drug development to leverage our existing proprietary collection of inhibitors, small-molecule compound libraries and large database of associated phenotypic and biochemical assay results of therapeutic interest. We also maintain leading expertise on specific areas of operation such as inhibition of SYK, IRAK 1/4, RIPK1 and mIDH1 kinases to assist clinical development and commercial affairs, as well as to expand and explore additional opportunities for such inhibitors in the clinical space. Our preclinical operations involve collaborations with clinical research organizations, leading investigators from universities and research organizations around the world, and strategic collaborations with other pharmaceutical companies.

We have experts in clinical 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 clinical development efforts.

We also have strategic development collaborations with MDACC and CONNECT to conduct evaluation of olutasidenib in AML, other hematologic cancers and glioma. Incrementally, we plan on initiating a Phase 2 clinical study in recurrent glioma. This, in combination with our strategic collaborations with MD Anderson and CONNECT, are aimed to expand our olutasidenib pipeline development programs.

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 Contracts" 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 actively seek patent protection for our marketed products and investigational candidates and associated technologies, in the US and in major market countries that we consider important to the development of our business worldwide. We strive to obtain and maintain proprietary protection for other discoveries, inventions, trade secrets and know-how that are critical to our business operations. We also strive to operate without infringing the proprietary rights of others, and aim to prevent others from infringing our proprietary rights. We hold global patent rights necessary for the continued development and commercialization of fostamatinib, olutasidenib and R289, and US patent rights necessary for the continued development and commercialization of pralsetinib in the US. We have developed and continue to develop an extensive patent portfolio in the US, Europe, Japan and other major market countries to protect our commercial and clinical programs.

TAVALISSE (fostamatinib). Fostamatinib is covered as a composition of matter in US Patent No. 7,449,458 having an earliest expiration date in 2026 and which was granted patent term extension extending the term to September 2031. In addition to the composition of matter patent, US patents covering our fostamatinib products directed to, among others, particular salts, crystalline forms, formulations and therapeutic uses, are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (referred to as the "Orange Book") and have patent expiration dates falling between 2026 and 2032. As of December 31, 2024, there are 43 issued US patents including the aforementioned Orange Book listed patents, and 4 pending applications which includes pending applications covering additional therapeutic uses, which, if issued, will have expiration dates to 2041.

In Europe and Japan, fostamatinib composition of matter patents are issued having an earliest patent expiration date in 2026 but which have been extended to 2031 through patent term extension in Japan and supplemental protection certificates in Europe. Additional patents covering fostamatinib salts, crystalline forms, formulations, as well as methods of use, are issued in Europe and Japan, with patent expiration to 2032, not including any patent term extensions.

REZLIDHIA (olutasidenib). Olutasidenib is covered as a composition of matter in US Patent No. 9,834,539 having an earliest expiration date in 2035 and for which a patent term extension application is pending which is expected to extend the expiration to December 2036. In addition to the composition of matter patent, additional US patents covering our olutasidenib products which are directed to, among others, particular salts, solid forms, formulations and therapeutic uses, are listed in the Orange Book and have patent expiration dates falling between 2035 and 2039. As of December 31, 2024, there are 18 issued US patents including the aforementioned Orange Book listed patents covering our olutasidenib marketed products, and 8 pending US patent applications including patent applications directed to therapeutic uses and combination therapies with olutasidenib, which, if issued, will have expiration dates to 2045.

In Japan and Europe, corresponding olutasidenib composition of matter patents have issued having an earliest expiration date in 2035, not including any patent term extensions. We intend to file additional foreign applications directed to new therapeutic uses and combination therapies for olutasidenib, which, if issued, will have expiration dates to 2045.

GAVRETO (pralsetinib). Pralsetinib is covered as a composition of matter in US Patent No. 10,030,005 having an expiration date in November 2036. As of December 31, 2024, we have 6 issued and 4 pending patent applications in the US covering our pralsetinib product including particular solid forms and formulations, as well as therapeutic uses. Collectively, these patents and patent applications, if issued, will have expiration dates between 2036 and 2041.

R289. We have developed and continue to develop our patent portfolio covering our investigational candidate R289. R289 is covered as a composition of matter in US Patent No. 11,370,787, having an earliest expiration date in 2040, not including any potential patent term extension. As of December 31, 2024, we have 4 issued and 5 pending patent applications in the US covering additional R289 composition of matter, including salts and solid forms, as well as R289 formulation and therapeutic uses. Collectively, these patents and patent applications, if issued, will have earliest expiration dates falling between 2036 and 2045. We are seeking global patent protection for R289 and currently have R289 composition of matter patents and patent applications covering R289 that are issued or pending in over 20 countries. We intend to file additional US and foreign applications based on our ongoing development programs directed

to new therapeutic uses and combination therapies as well as new formulations and methods of manufacture, to the extent they are discovered or invented.

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.

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 and biologics 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 our products 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;
- enter commercialization agreements for our new drug compounds; and
- obtain and maintain an appropriate reimbursement price and positive recommendations by HTA bodies.

ITP

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 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 was 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.

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, 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 International AG), Nplate (Amgen, Inc.), DOPTELET (Dova Pharmaceuticals) and ALVAIZ (Teva Pharmaceutical Industries Ltd.).

AML with IDH1 Mutation

There is currently one other product approved in the US for patients with IDH1 mutation. TIBSOVO (ivosidenib), an oral targeted IDH1 mutation inhibitor, is an FDA-approved drug for (i) adult patients with R/R AML with a susceptible IDH1 mutation, (ii) newly diagnosed AML with a susceptible IDH1 mutation who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy, (iii) for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation as detected by an FDA-approved test, and (iv) in combination with azacitidine (azacitidine for injection), for newly diagnosed AML with a susceptible IDH1 mutation, as detected by an FDA-approved test in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. TIBSOVO is a registered trademark of Servier Pharmaceuticals LLC, a wholly owned, indirect subsidiary of Les Laboratoires Servier. In addition, some clinicians may utilize non-targeted treatments for patients with mIDH1 R/R AML, including use of venetoclax combinations, hypomethylating agents, other chemotherapy regimens, or investigational agents that may be available to them.

Metastatic RET fusion-positive NSCLC and advanced thyroid cancers

GAVRETO faces competition for RET fusion-positive NSCLC and advanced thyroid cancers from Lilly's selpercatinib (Retevmo). In addition, other commercially available therapies used to treat RET fusion-positive NSCLC include cabozantanib and platinum-based chemotherapy regimens with or without pembrolizumab, atezolizumab, nivolumab/ipilumumab, cemiplimab or tremelimumab-durvalumab. GAVRETO may also face competition from other drug candidates in development for RET-altered cancers, as well as multi-kinase inhibitors with RET activity being evaluated in clinical trials.

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 regulations;
- submission to the FDA of an 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 EU and the UK, with a clinical trial application required to be submitted for each clinical trial to each EU Member State's national competent authority 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 as of January 31, 2023, 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 has not applied the CTR, and is currently revising its own clinical trials framework, 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 an sNDA, 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 review designations

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 EC.

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 the UK 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 the UK, 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.

However, the general pharmaceutical legislative framework, as well as the framework applicable to orphan and pediatric medicinal products in the EU, is under review. The EC expects to publish its position on this in March 2023. Although the final proposals are not yet formally known, it is expected that there will be a reduction in applicable regulatory exclusivities which will significantly affect all medicinal products that will be authorized after the legislative changes have taken effect, including a reduction in the 10-year orphan market exclusivity, which will be modulated according to certain parameters.

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.

In the EU and the UK, a six-month extension to a supplementary protection certificate may be granted, subject to certain circumstances, upon the completion of an agreed pediatric investigation plan (PIP). However, within the EU, regulatory protections afforded to medicinal products such as data exclusivity, marketing protection, market exclusivity for orphan indications and pediatric extensions are currently under review and could be curtailed in future years.

ANDA 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 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) NDA

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 EUA

Section 564 of the FDCA (21 U.S.C. § 360bbb-3) 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 US Department of Health and Human Services (DHHS) Secretary.

On February 4, 2020, then-DHHS Secretary Alex M. Azar II determined that a public health emergency exists for COVID-19 and declared that it justifies the authorization of emergency use of in vitro diagnostics for COVID-19, pursuant to Section 564 of the FDCA. On March 2, 2020, March 24, 2020, and March 27, 2020, Secretary Azar issued

corresponding declarations for personal respiratory protective devices; for medical devices, including alternative products used as medical devices; and, for drugs and biological products. The determination and these declarations were published in the Federal Register on February 7, 2020, March 10, 2020, March 27, 2020, and April 1, 2020, respectively.

While the emergency determination and declaration are 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; and
- 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, 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.

On May 11, 2023, the COVID-19 PHE declared under the Public Health Services Act expired. FDA officials have stated that this will not impact FDA's ability to authorize medical countermeasures for emergency use, such that existing EUAs will remain in effect and the agency may continue to issue new EUAs going forward when criteria for issuance are met. This is nonetheless subject to change.

Pharmaceutical Coverage, Pricing and Reimbursement

In the US and 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, in the US, 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. This includes the Consolidated Appropriations Act of 2021, which addressed several drug price reporting and transparency measures, such as a new requirement for prescription drug plan sponsors and Medicare Advantage organizations to develop tools to display Medicare Part D prescription drug benefit information in real time and for insurance companies and employer-based health plans 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 provision in the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act (collectively, the Affordable Care Act) that capped 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. As of January 1, 2024, manufacturers' MDRP rebate liability is no longer capped, potentially resulting in a manufacturer paying more in MDRP rebates than it receives on the sale of certain covered outpatient drugs. In August 2022, the Inflation Reduction Act of 2022 (IRA) was signed into law, which implements substantial changes to the Medicare program, including drug pricing reforms and changes to the Medicare Part D benefit design. Among other reforms, the IRA imposes inflation rebates on drug manufacturers for products reimbursed under Medicare Parts B and D if the prices of those products increase faster than inflation; implements changes to the Medicare Part D benefit that, beginning in 2025, cap beneficiary annual out-of-pocket spending at $2,000, while imposing new discount obligations for pharmaceutical manufacturers; and, beginning in 2026, establishes a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with the Centers for Medicare and Medicaid Services (CMS). CMS has also taken steps to implement the IRA, including: releasing the negotiated maximum prices, which will be effective in 2026, for the first ten drugs that were subject to the IRA's negotiation process; releasing quarterly lists of Medicare Part B products that are subject to adjusted coinsurance rates based on the inflationary rebate provisions of the IRA; and announcing a list of fifteen additional drugs that will be subject to price negotiations during 2025. While it remains to be seen how the drug pricing provisions imposed by the IRA will affect the broader pharmaceutical industry, several pharmaceutical manufacturers and other industry stakeholders have challenged the law, including through lawsuits brought against the DHHS, the Secretary of DHHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA's drug price negotiation provisions.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including limitations on reimbursement, discounts, restrictions on certain product access and marketing, cost disclosure (including disclosures for certain price increases or launches of costly drugs), 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. The new Regulation came into effect in January 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 federal and state fraud and abuse laws, anti-kickback laws, false claims laws, laws requiring 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, pharmacies, 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, 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 (FCA), 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 $14,308 to $28,619 per false claim or statement for penalties assessed after January 15, 2025, 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 HIPAA-covered entities and their business associates obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, accessibility and transmission of individually identifiable health information, including protected health information (PHI). While the vast majority of HIPAA obligations do not apply to pharmaceutical companies or clinical trial data, the requirements inform privacy and security practices across the industry and may impact interactions with health care providers. Moreover, HITECH created 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 payment transparency tracking and reporting 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 CMS, within the DHHS, information related to payments and other transfers of value made by that entity to US-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors),

physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, certified nurse midwives, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to timely, accurately, and completely submit the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties;

- state laws that require the reporting of certain pricing information, including information pertaining to and justifying price increases, prohibit prescription drug price gouging; or impose payment caps on certain pharmaceutical products deemed by the state to be "high cost"; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may be broader in scope than analogous federal laws and may apply to sales or marketing arrangements and claims involving healthcare items or services regardless of payor.

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 federal 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. This law was designed to expand access to health insurance coverage for uninsured and underinsured individuals while containing overall healthcare costs. There have been numerous 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, the Tax Cuts and Jobs Act of 2017 included 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 certain high-cost employer-sponsored health coverage and the medical device excise tax on non-exempt medical devices, 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." Under the IRA, this coverage gap has been eliminated as of January 1,

2025. The IRA also requires pharmaceutical manufacturers to pay 10% of the negotiated price of brands, biologics, and biosimilar products, when Medicare Part D beneficiaries are in the initial coverage phase, and 20% of the negotiated price during the catastrophic phase of Medicare Part D coverage. 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 June 17, 2021, the US Supreme Court dismissed a judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the law. It is unclear how any future litigation and other healthcare reform efforts 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 through the first eight months of the fiscal year 2032 sequestration order, unless additional Congressional action is taken (with the exception of a temporary suspension, and later a temporary reduction, instituted during the COVID-19 pandemic that expired on July 1, 2022). 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 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. For example, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which among other changes, eliminated 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, as of January 1, 2024. The American Rescue Plan Act also temporarily increased premium tax credit assistance for individuals eligible for subsidies under the Affordable Care Act 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 IRA extended this increased tax credit assistance and removal of the 400% federal poverty limit through 2025. In August 2022, the IRA was signed into law, which implements substantial changes to the Medicare program, including drug pricing reforms and changes to the Medicare Part D benefit design. Among other reforms, the IRA imposes inflation rebates on drug manufacturers for products reimbursed under Medicare Parts B and D if the prices of those products increase faster than inflation; implements changes to the Medicare Part D benefit that, beginning in 2025, will cap benefit annual out-of-pocket spending at $2,000, while imposing new discount obligations for pharmaceutical manufacturers; and, beginning in 2026, establishes a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with CMS. On February 14, 2023, the DHHS issued a report, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a "high-value drug list" setting the maximum co-payment amount for certain common generic drugs at $2; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements for certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments. It remains to be seen how these drug pricing initiatives will affect the broader pharmaceutical industry. 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. For example, several recently passed state laws require disclosures to state agencies and/or commercial purchasers with respect to price increases and new product launches that exceed certain pricing thresholds as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and

their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations. Some states have also established prescription drug affordability boards that are tasked with identifying certain high-cost prescription products that may pose affordability challenges for consumers and payors, conducting cost reviews on such products, and, in some circumstances, imposing upper payment limits on such products.

Policy changes, including potential modification or repeal of all or parts of the Affordable Care Act or the implementation of new health care legislation, could result in significant changes to the health care system, which may prevent us from being able to generate revenue, attain profitability or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or lower pricing for our product candidates, or additional pricing pressures.

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.

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.

Manufacturing and Raw Materials

We currently do not have the manufacturing capabilities or experience necessary to produce our products or any product candidates for clinical trials. We currently use three active pharmaceutical ingredient manufacturing facilities and three finished goods manufacturing facilities for our products. 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 ingredients 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, 2024, we have 162 full-time and 2 part-time employees. Of these employees, 88 were engaged in commercial activities, 43 were engaged in development activities, and 33 were engaged in general and administrative activities. We also engage 8 temporary employees and consultants.

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 all welcoming and a 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.

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.

Environmental, Social and Governance (ESG)

Our approach to ESG factors is consistent with our mission and our corporate values. We are committed to conducting our business in a safe and environmentally sustainable manner that promotes the health of patients, our employees, our community and the environment. ESG oversight is exercised both at the Board of Directors level and through our executive leadership. The Corporate Governance, Health Care Compliance Oversight and Nominating Committee has oversight responsibility over our ESG strategy and policies and is briefed by management on matters related to ESG as appropriate. For more information and the latest on our ESG efforts, please refer to our Proxy Statement for the 2025 Annual Meeting of Stockholders to be filed with the SEC. Additionally, our full ESG report is available on our website at *www.rigel.com/investors/esg*. Information in our ESG Report is not incorporated by reference into this Form 10-K.

Corporate Information

Our principal executive office is currently located at 611 Gateway Boulevard, Suite 900, South San Francisco, CA 94080. Our telephone number is (650) 624-1100.

Available Information

We electronically file with the 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 our products 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 our products 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 our products 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.

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.

While we have substantially increased the size of our organization particularly in our sales force in 2021, we also implemented reductions in workforce particularly in our research and development group in 2021 and 2022. We may need to add additional qualified personnel and resources to support our commercial activities and expected growth. 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 our products and development of our other product candidates.

Our future financial performance and our ability to sustain successful commercialization of our products 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 our products, 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 a potential pandemic or global economic slowdown, could adversely affect our business and operations.

Our strategy to expand our hematology and oncology pipeline on our own, or through acquisitions or in-licensing of early or late-stage products or companies, or through partnerships with pharmaceutical and biotechnology companies, as well as academic institutions and government organizations, may not be successful.

Our business is focused on the development and commercialization of novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. In this regard, we continue to pursue internal drug discovery efforts or partnerships with pharmaceutical and biotech companies, as well as academic institutions and government organizations, with the goal of identifying new product candidates to advance into clinical trials. Our discovery efforts to identify new product candidates require substantial technical, financial and human resources. These 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 trial, 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 discovery efforts, we continue to seek to broaden and diversify our product portfolio through acquisition or in-licensing of a product. This strategy is dependent on our ability to successfully identify and acquire or in-license relevant product candidates. In July 2022, we entered into a license and transition services agreement with Forma for an exclusive license to develop, manufacture and commercialize olutasidenib, a proprietary inhibitor of mIDH1, for any uses worldwide, including for the treatment of AML and other malignancies. On December 1, 2022, the FDA approved REZLIDHIA capsules for the treatment of adult patients with R/R AML with a susceptible IDH1 mutations as detected by an FDA-approved test. REZLIDHIA is our second commercial product and we believe is highly synergistic with our existing hematology-oncology focused commercial and medical affairs infrastructure. Further, in February 2024, we entered into an Asset Purchase Agreement with Blueprint to purchase certain assets comprising the right to research, develop, manufacture and commercialize GAVRETO, Blueprint's proprietary RET inhibitor of tyrosine kinase for the treatment of metastatic RET fusion-positive NSCLC and advanced thyroid cancer, in the US. Simultaneously and in connection with entering into the Asset Purchase Agreement, we also entered into certain supporting agreements with Blueprint, including a customary transition agreement, pursuant to which, during a transition period, Blueprint will transition regulatory and distribution responsibility for pralsetinib to us. On June 24, 2024, we announced the completion of the transfer of GAVRETO NDA to us, and GAVRETO became commercially available from us in the US by prescription beginning on June 27, 2024. The in-licensing and acquisition of a product 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. The success of this strategy depends partly upon our ability to identify, select and acquire or in-license promising product candidates and technologies. The process of proposing, negotiating and implementing a license or acquisition of a product candidate is lengthy and complex, and we may be unable to in-license or acquire the rights to any such products, product candidates or technologies from third parties for several reasons. We may also be unable to in-license or acquire additional relevant product candidates on acceptable terms. Further, even if we identify acquisition or in-licensing targets, we may not be able to complete the transactions or we may determine after due diligence investigation not to pursue identified targets. Even if we succeed in our efforts to obtain rights to suitable product candidates, the success of our investments in these areas, our investment strategy will remain subject to the inherent risks associated with the development and commercialization of the product, and with the competitive business environment in which we operate.

In addition, acquisitions and in-licensing may entail numerous operational, financial and legal risks, including:

- potential failure of the due diligence process to identify significant problems, liabilities or other shortcomings or challenges of an acquired or licensed product candidate or technology, including problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, partner disputes or issues and other legal and financial contingencies and known and unknown liabilities;
- inability to integrate the target company or in-licensed asset successfully into our existing business and inability to maintain the key business relationships of the target;

- in an in-licensing or an asset acquisition of a product that is commercially available in the market, we may not be able to successfully transition the existing patients who are dependent to the acquired or in-licensed product, or successfully enter into a reimbursement coverage contracts that the existing patients were previously dependent into, or successfully enter into a contract with contract manufacturers to continue the production of the in-licensed or acquired product;
- assumption of unknown or contingent liabilities or incurrence of unanticipated expenses;
- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- incurrence of large one-time expenses and acquiring intangible assets that could result in significant future amortization expense and significant write-offs;
- higher than expected acquisition and integration costs; and
- inability to maintain uniform standards, controls, procedures and policies;

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

We currently have product candidates in the clinical testing stage and may further pursue to expand our clinical testing efforts. 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 clinical development. 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 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, obtaining and maintaining reimbursement in national markets and positive recommendation from HTA bodies, maintaining regulatory compliance, manufacturing, competition and costs and expenses that may exceed current estimates. In future clinical trials, we, our partners or others 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. For example, in October 2024, we issued a Dear Healthcare Provider Letter for GAVRETO related to a new safety signal identified in an ongoing Phase 3 clinical trial of pralsetinib in first-line treatment of RET fusion-positive, metastatic NSCLC patients, being conducted by Roche. The letter advises healthcare providers to apply certain measures to protect patient safety, including enhanced ongoing monitoring for signs and symptoms of infection as well as guidance for withholding treatment to patients in the presence of active infection. 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 (pharmacokinetic, 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, we conducted a Phase 3 pivotal trial of fostamatinib in patients with warm auto immune hemolytic anemia (wAIHA) initiated in March 2019 and completed in April 2022. In June 2022, we announced top-line

efficacy and safety data results of the trial, and the results did not demonstrate statistical significance in the primary efficacy endpoint of durable hemoglobin response in the overall study population. We conducted an in-depth analysis of these data to better understand differences in patient characteristics and outcomes and submitted these findings to the FDA. In October 2022, we announced that we received guidance from the FDA's review of these findings. Based on the result of the trial and the guidance from the FDA, we did not file an sNDA for this indication. Further, we may experience errors in the analysis of our clinical trial results. For example, we conducted our Phase 3 clinical trial to evaluate safety and efficacy of fostamatinib in hospitalized COVID-19 patients launched in November 2020 and completed enrollment in July 2022. We previously announced in November 2022 the top-line results did not meet statistical significance in the primary efficacy endpoint. Upon further analysis, we discovered an error by the biostatistical contract research organization (CRO) in the application of a statistical stratification factor. After correcting for this statistical error, the primary endpoint of the study was met. However, given the end of the federal COVID-19 PHE in May 2023, and based on feedback from the FDA, DOD and other advisors regarding the program's regulatory requirements, costs, timeline and potential for success, we decided not to submit an Emergency Use Authorization (EUA) or sNDA.

Foreign regulatory requirements governing clinical trials may diverge and impose additional regulatory burdens, which may result in delays. For instance, the new EU Clinical Trials Regulation (EU) No 536/2014 (CTR) has amended the system of approval for clinical trials in the EU and has established a new clinical trials portal and database for application for authorizations, called the Clinical Trials Information System (CTIS). All ongoing clinical trials in the EU will be subject to the provisions of the CTR as of January 31, 2025. In addition, on June 18, 2024, new CTIS transparency rules came into effect, requiring scheduled publication of certain key clinical trial information.

If the results of our clinical trials fail to meet the primary efficacy endpoints, or otherwise do not ultimately meet the requirements for an NDA approval by the FDA, 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 are subject 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 payors 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 may 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, certain 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 "Business – Government Regulation – Healthcare and Privacy Law and Regulation and Healthcare Reform" contained in Part I, Item 1 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 FTC has brought several cases alleging violations of Section 5 of the FTC Act with respect to health information, and has proposed rulemaking on a variety of privacy and data security topics. Additionally, the FTC published an advance notice of proposed rulemaking in 2022 on commercial surveillance and data security, and may propose regulation concerning the ways in which companies collect, aggregate, protect, use, analyze, and retain consumer data, as well as transfer, share, sell, or otherwise monetize that data in the coming years. The FTC has also been active with respect to enforcement of its Health Breach Notification Rule and in scrutinizing the use and disclosure of sensitive personal information. The FTC finalized changes to the Health Breach Notification Rule in April 2024. Moreover, 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, including, but not limited to: the Electronic Communications Privacy Act, the Computer Fraud and Abuse Act, the Health Insurance Portability and Accountability Act (HIPAA), the Health Information Technology for Economic and Clinical Health Act, the Telephone Consumer Protection Act, the CAN-SPAM Act, and other laws and regulations, and continues to consider comprehensive federal privacy legislation.

In addition, state legislatures have enacted statutes to address privacy and information security issues, including the California Consumer Privacy Act of 2018 (the CCPA). For example, the CCPA, as amended by the California Privacy Rights Act (CPRA), 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 (as consumers, business contacts and employees), 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 disclosures to California residents and to provide them with rights with respect to their personal information, including the right to opt out of the sale of such information. Moreover, the CPRA, among other things, imposes requirements relating to data minimization and correction, and gives California residents additional rights over their personal information, including the right to opt-out of the use of their personal information in online behavioral advertising and to opt-out of certain types of consumer profiling. The CPRA also provides for penalties for CPRA violations concerning California residents under the age of 16, and established the California Privacy Protection Agency to implement and enforce the law. Although there are exemptions for PHI, clinical trial and other research-related data under the CCPA, the CCPA could impact our business depending on how it is interpreted by the California Privacy Protection Agency, as well from new regulations issued by the Agency to further implement the law. Compliance with the CCPA may increase our compliance costs and potential liability.

Multiple other states have followed California and enacted comprehensive privacy laws, or are considering similar legislation. While these new laws and proposals generally include exemptions for HIPAA-covered PHI and clinical trial data, they add layers of complexity to compliance in the US market, and could increase our compliance costs and adversely affect our business. Moreover, some states have enacted laws specific to health data privacy, which may cause additional compliance costs such as the Washington My Health My Data Act and Nevada's Consumer Health Data Privacy Law. For example, the Washington My Health My Data Act regulates "consumer health data" which is defined as "personal information that is linked or reasonably linkable to a consumer and that identifies a consumer's past, present, or future physical or mental health." However, the My Health My Data Act provides exemptions for personal data used or shared in research, including data subject to 45 C.F.R. Parts 46, 50, and 56. States, such as Colorado, Utah and California, have passed or are considering legislation or regulation governing the development or use of artificial intelligence technologies, supplementing the existing consumer protection, FDA and other regulatory guidance that may apply to the use of AI technologies in our business, and which may impact our use of technology. Moreover, 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.

Laws and regulations relating to privacy, data protection, consumer protection, AI and information security are evolving and subject to potentially differing interpretations. These requirements may be interpreted and applied in a manner that varies from one jurisdiction to another and/or may conflict with other laws or regulations. New laws and regulations 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 those 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, in the EU, the collection, use, disclosure, transfer and other processing of personal data (i.e., data which identifies an individual or from which an individual is identifiable) is governed by the EU General Data Protection Regulation 2016/679 (the EU GDPR), which came into direct effect in all EU Member States on and from May 25, 2018. The UK has implemented the EU GDPR as the UK GDPR which sits alongside the UK Data Protection Act 2018 (the UK GDPR, and together with the EU GDPR, the GDPR). In October 2024, the UK government introduced to Parliament the Data (Use and Access) Bill (the DUA Bill) which is set to introduce reforms to the UK GDPR. The DUA Bill is currently progressing through the legislative process and is expected to be finalized during 2025. The GDPR has direct effect where an entity is established in the European Economic Area (EEA) or the UK (as applicable) and has extraterritorial effect, including where an entity established outside of the EEA or the UK processes personal data in relation to the offering of goods or services to individuals in the EEA and/or the UK or the monitoring of their behavior.

The GDPR imposes obligations on controllers, including, among others:

- accountability and transparency requirements, requiring controllers to demonstrate and record compliance with the GDPR and to provide more detailed information to data subjects regarding the processing of their personal data;

- requirements to process personal data lawfully including specific requirements for obtaining valid consent where consent is the lawful basis for processing;

- obligations to consider data protection when any new products or services are developed and designed (including e.g., to limit the amount of personal data processed);

- obligations to comply with data protection rights of data subjects including a right: (i) of access to, erasure of, or rectification of personal data, (ii) to restriction of processing or to withdraw consent to processing, (iii) to object to processing or to ask for a copy of personal data to be provided to a third party, and (iv) not to be subject to solely automated decision-making; and

- an obligation to report personal data breaches to: (i) the data protection supervisory authority without undue delay (and no later than 72 hours) after becoming aware of the personal data breach, where feasible, unless the personal data breach is unlikely to result in a risk to the data subjects' rights and freedoms; and (ii) affected data subjects, where the personal data breach is likely to result in a high risk to their rights and freedoms.

In addition, the EU GDPR prohibits the international transfer of personal data from the EEA to jurisdictions that the European Commission does not recognize as having an 'adequate' level of data protection unless a data transfer mechanism has been put in place or a derogation under the EU GDPR can be relied on. In certain cases (e.g., where transfers are made in reliance on EU SCCs) a company must also carry out a so-called transfer privacy impact assessment (TIA). A TIA, among other things, assesses laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under EU SCCs will need to be implemented to ensure an 'essentially equivalent' level of data protection to that afforded in the EEA.

On July 10, 2023, the European Commission adopted its Final Implementing Decision granting the US adequacy (Adequacy Decision) for EU-US transfers of personal data for entities self-certified to the EU-US Data Privacy Framework (DPF). Entities relying on EU SCCs for transfers to the US. are also able to rely on the analysis in the Adequacy Decision as support for their TIA regarding the equivalence of US national security safeguards and redress.

The UK GDPR also imposes similar restrictions on transfers of personal data from the UK to jurisdictions that the UK Government does not consider adequate, including the US. The UK Government has published its own form of the EU SCCs, known as the International Data Transfer Agreement and an International Data Transfer Addendum to the EU SCCs. The UK Information Commissioner's Office (ICO) has also published its version of the TIA and guidance on international transfers, although entities may choose to adopt either the EU or UK style TIA. Further, on September 21, 2023, the UK Secretary of State for Science, Innovation and Technology established a UK-US data bridge (i.e., a UK adequacy decision) and adopted UK regulations to implement the UK-US data bridge (UK Adequacy Regulations). Personal data may be transferred from the UK under the UK-US data bridge through the UK extension to the DPF, from October 12, 2023, to organizations self-certified under the UK extension to the DPF.

Data protection supervisory authorities have the power under the GDPR to (amongst other thing) impose fines for serious breaches of up to the higher of 4% of the organization's annual worldwide turnover or €20 million (under the EU GDPR) or £17.5 million (under the UK GDPR). The GDPR identifies a list of points to consider when determining the level of fines for data supervisory authorities to impose (including the nature, gravity and duration of the infringement). Data subjects also have a right to compensation, as a result of an organization's breach of the GDPR which has affected them, for financial or non-financial losses (e.g., distress).

Privacy and data protection compliance has and may in the future require substantial amendments to our procedures and policies and the changes could adversely impact our business by increasing operational and compliance costs or impact business practices. Further, there is a risk that the amended policies and procedures will not be implemented correctly or that individuals within the business will not be fully compliant with the new procedures. If there are breaches of these measures, we could face significant litigation, government investigations, administrative and monetary sanctions as well as reputational damage which may have a material adverse effect on our operations, financial condition and prospects. There is a risk that we could be impacted by a cybersecurity incident that results in loss or unauthorized disclosure of personal data, potentially resulting in us facing harms similar to those described above.

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, cybersecurity requirements are laid down in various laws in the EU and the UK, the key ones being: (i) the GDPR (as discussed above), which requires controllers and processors to implement appropriate technical and organizational measures to safeguard personal data to a level of security appropriate to the data protection risk; (ii) the UK Network and Information Systems Regulation 2018 (NIS Regulations), and (iii) the EU Network and Information Systems Security 2 Directive (NISD2).

The GDPR does not provide for a specific set of cybersecurity requirements or measures to be implemented, but rather requires a controller or processor to implement appropriate cyber and data security measures in accordance with the then-current risk, the state of the art, the costs of implementation and the nature, scope, context and purposes of the processing. The GDPR however does explicitly require that controllers notify personal data breaches, within the meaning of the GDPR as described above.

In the UK, the NIS Regulations apply to 'operators of essential services' (OES) and 'relevant digital service providers' (RDSP) and following the UK General Election in July 2024, the new UK Government has announced it intends to introduce a Cyber Security and Resilience Bill to the UK Parliament. The NIS Regulations require that appropriate and proportionate technical and organizational measures are implemented to manage the risk of network and information systems, and impose requirements related to incident handling and notification in relation to incidents with significant disruptive effect. Under the NIS Regulations, the ICO may issue fines of up to £17 million and take other action following non-compliance.

In the EU, the NISD2 (and the implementing laws at a national EU Member State level) impose stringent cybersecurity and incident reporting requirements on 'essential' and 'important' entities, which include ICT managed service providers (MSP), cloud service providers as well as entities carrying out research and development activities of medicinal products, and certain specific medical device manufacturers. Our entities may be in scope of the NISD2 where they qualify as a MSP, cloud provider, R&D entity and/or medical device manufacturer within the meaning of NISD2 and offer those services in the EU.

The NISD2 empowers the EU Member States to define all rules regarding penalties applicable to infringements, provided that they are effective, proportionate, and dissuasive. NISD2 states that any maximum fine which national implementing law provides for should at least be set at €10 million or 2% of total worldwide turnover, whichever is higher, where essential entities are concerned. Other sanctions may include (i) a temporary suspension to provide services in the EU (by suspending relevant authorizations/certifications); (ii) an order to make public certain elements of the infringement and/or inform customers; and (iii) injunctions to immediately cease infringing conduct. Importantly, NISD2 also provides that senior members of staff can be held personally liable, and face administrative fines or be temporarily suspended from exercising managerial functions at the legal representative or chief executive officer level. The NISD2 has not to date been transposed by all EU Member States despite the deadline for doing so having passed.

In addition, the EU Critical Entities Resilience Directive (CER) is aimed at strengthening the resilience of 'critical infrastructure' against specific threats including cyber incidents, natural hazards, terrorist attacks, insider threats, and sabotage. The scope of CER includes entities designated as 'critical' under CER and includes (among other things) the health sector and the manufacturers of medical devices as 'essential services.' The CER imposes cybersecurity and resilience requirements in particular in relation to incidents with so-called 'significant disruptive effects' – which are incidents that are able to significantly impact the continuation of the critical infrastructure service offering in the EU. Requirements include to: (i) identify relevant risks that may significantly disrupt the provision of essential services (i.e., pursuant to a risk assessment); (ii) take appropriate and proportionate technical, security and organizational measures to ensure resilience (i.e., based on the outcome of the risk assessment); and (iii) notify disruptive incidents to the competent authorities within 24 hours after becoming aware of an incident. The CER is enforceable on a national EU Member State level by the competent authorities, and allows EU Member States to set penalties as long as they are effective, proportionate, and dissuasive. Our entities may be in scope of the CER where they qualify as critical entities within the meaning of CER. The CER has not to date been transposed by all EU Member States despite the deadline for doing so having passed.

In the EU, a number of new laws related to digital data and AI have recently entered into force, are expected to enter into force in the foreseeable future, or have been proposed and are being considered. We are still assessing the scope of application, impact, and risk of these recent EU laws on our business, and will continue to assess this moving forward, including for example: (i) the EU's Data Act, which – came into force on January 11, 2024 and which seeks to, among other things regulate the use of, and access to, data generated through connected (or Internet-of-Things) devices and introduces a new means for public sector bodies to access, use and re-use private sector data. EU Member State competent authorities are empowered to enforce the Data Act and determine the appropriate sanction provided penalties are "effective, proportionate and dissuasive"; and (ii) the European Health Data Space Regulation (EHDS), which was

formally adopted on January 8, 2025 and is expected to enter into force during 2025 and which seeks to, among other things, provide individuals with more control over their electronic health data (EHD), enable cross-border sharing of EHD between national EU healthcare systems and facilitate the sharing of EHD for secondary research purposes.

The EU has developed a standalone law to govern the offering and use of AI systems in the EU (the "AI Act") which entered into force on August 1, 2024 and will become applicable in a gradual manner between 2025-2027 depending on the requirement. The AI Act imposes regulatory requirements onto AI system providers, importers, distributors, and deployers, in accordance with the level of risk involved with the AI system ("unacceptable", "high", "limited", and "minimal" risk). Unacceptable-risk AI systems are banned from being offered and used in the EU, and high-risk AI systems (which include AI used as part of medical devices in certain instances) are subject to a set of regulatory requirements under the AI Act including to establish quality and post-marketing monitoring and risk assessment systems, requirements related to the training of AI systems and training data, and requirements related to human oversight. Limited-risk AI systems are subject mainly to transparency requirements only and minimal-risk AI systems are not subject to obligations under the AI Act. General-purpose AI systems are subject to a number of requirements – mostly akin to the requirements that apply to high-risk AI systems under the AI Act.

Non-compliance with the AI Act may be subject to regulatory fines of up to 7% of annual worldwide turnover. In parallel, on October 10, 2024, the EU adopted the EU Product Liability Directive to regulate non-contractual and non-fault based liability for defective products, including digital products and AI, and has introduced a new EU AI Liability Directive to facilitate claims for damages brought by EU users of AI systems.

The UK to date has not adopted dedicated AI legislation, instead looking to rely on a principles-based, sector-specific approach to AI regulation. However, in July 2024 it was announced that new AI regulation would in fact be introduced.

Further, 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 (which the UK has not implemented, as the law entered into force following the UK's exit from the EU), 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 MAA 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.

Significant changes or developments in US laws or policies, including changes in US healthcare regulation, may have a material adverse effect on our business.

There is uncertainty surrounding potential changes to the regulatory environment in the US, particularly as it relates to healthcare regulation and related programs, following the outcome of the recent US Presidential election which may have an adverse effect on our business. For example, the new administration issued an executive order establishing an agency to reform federal government processes and reduce expenditures. Pressures on and uncertainty surrounding the US federal government's budget, and potential changes in budgetary priorities, could adversely affect the funding for individual programs, including Medicare and other government programs upon which our business depends. Additionally, changes in legislation and regulations (including those related to taxation, trade and importation), economic and monetary policies, geopolitical matters, among other potential impacts, could adversely impact the global economy and our operating results. The potential impact of new policies that may be implemented as a result of the new administration is currently uncertain.

The biopharmaceutical industry is subject to extensive regulatory obligations and policies that may be subject to change, including due to judicial challenges, election cycles, and resulting regulatory updates and changes in policy priorities.

On June 28, 2024, the US Supreme Court issued an opinion holding that courts reviewing agency action pursuant to the Administrative Procedure Act "must exercise their independent judgment" and "may not defer to an agency interpretation of the law simply because a statute is ambiguous." The decision will have a significant impact on how lower courts evaluate challenges to agency interpretations of law, including those by the FDA, DHHS, CMS and other agencies with significant oversight of the biopharmaceutical industry. The new framework is likely to increase both the frequency of such challenges and their odds of success by eliminating one way in which the government previously prevailed in such cases. As a result, significant regulatory policies will be subject to increased litigation and judicial scrutiny.

In addition, federal agency priorities, leadership, policies, rulemaking, communications, spending and staffing may be significantly impacted by election cycles. For example, the current presidential administration aims to significantly reduce government spending through cuts to federal healthcare programs and reductions in the workforces of key government agencies, such as the FDA, DHHS, and CMS. Efforts by the current administration to limit federal agency budgets or personnel may result in reductions to agency budgets, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates. Any resulting changes in regulation may result in unexpected delays, increased costs, or other negative impacts on our business that are difficult to predict.

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 manufacturer-sponsored patient assistance program that helps financially needy patients in the US access our therapies. This type of program has become the subject of enforcement scrutiny in recent years. For example, some pharmaceutical manufacturers have been named in lawsuits challenging the legality of their patient assistance programs under a variety of federal and state laws. In addition, certain state and federal enforcement authorities continue to pursue investigations and enter into settlements related to manufacturers' support of patient assistance programs, and members of Congress have also initiated inquiries on topics that include, for example, manufacturer-sponsored patient assistance programs, co-payment assistance programs, and manufacturer contributions to independent charitable patient assistance programs. Moreover, the DHHS, Office of the Inspector General continues to publish advisory opinions and other agency guidance on the topic of patient assistance, which reflects the government's continued scrutiny of manufacturer sponsored or supported patient assistance programs. 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 or restrictions with respect to these programs and/or support that would affect pharmaceutical manufacturers.

Our patient assistance program could become the target of similar inquiries, litigation, enforcement, and/or legislative proposals. 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. 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 our products, or of products with which we compete, our business may be harmed.

Under the FDCA, the FDA can approve an 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 our products.

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 FDA's 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 our products or products with which it competes, our business would be harmed.

In June 2022, we received a notice letter regarding an ANDA submitted to the FDA by Annora, requesting approval to market a generic version of TAVALISSE. The notice letter included a Paragraph IV certification with respect to our US Patent Nos. 7,449,458; 8,263,122; 8,652,492; 8,771,648 and 8,951,504, which are listed in the Orange Book. The notice letter asserts that these patents will not be infringed by Annora's proposed product, are invalid and/or are unenforceable. Annora's notice letter does not provide a Paragraph IV certification against our other patents listed in the Orange Book. On July 25, 2022, we filed a lawsuit in the US District Court for the District of New Jersey against Annora and its affiliates, Hetero Labs Ltd., and Hetero USA, Inc., for infringement of our US patents identified in Annora's Paragraph IV certification. On September 21, 2022, Annora and its affiliates answered and counterclaimed for declaratory judgment of non-infringement and invalidity of the '458, '122, '492, '648, and '504 patents. We filed an answer to Annora's counterclaims on October 12, 2022. Annora served invalidity and non-infringement contentions on December 31, 2022. We filed an answer to Annora's invalidity and non-infringement contentions in March 2023. Litigation continues, and no trial date is currently set. We intend to vigorously enforce and defend our intellectual property related to TAVALISSE. We cannot be assured that such lawsuit will prevent the introduction of a generic version of TAVALISSE for any particular length of time, or at all. If an ANDA from Annora or any other generic manufacturer is approved, and a generic version of TAVALISSE is introduced, whether following the expiration of our patents, the invalidation of our patents as a result of any litigation, or the determination that the proposed generic product does not infringe on our patents, our sales of TAVALISSE would be adversely affected. In addition, we cannot predict what additional ANDAs could be filed by Annora or other potential generic competitors requesting approval to market generic forms of our products, which would require us to incur significant additional expense and result in distraction for our management team, and if approved, result in significant decreases in the revenue derived from sales of our marketed products and thereby materially harm our business and financial condition.

Unforeseen safety issues could emerge with our products 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 our products 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 our products after approval:

- regulatory authorities may require the addition of labeling statements, specific warnings, contraindications, Dear Healthcare Provider letters, press releases, field alerts, or other communications containing warnings or other safety information about our products to physicians and pharmacies;

- regulatory authorities may withdraw their approval of the product and require us to take our approved drugs off the market or suspend their commercialization until the identified issues have been satisfactorily addressed;
- 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 (REMS);
- we may have additional limitations on how we promote our drugs;
- third-party payors may limit coverage or reimbursement for our products;
- sales of our products 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 our products and could substantially increase our operating costs and expenses, which in turn could delay or prevent us from generating significant revenue from sale of our products. For example, in October 2024, we issued a Dear Healthcare Provider letter related to a new safety signal for GAVRETO. The letter advises healthcare providers to apply certain measures to protect patient safety, including enhanced ongoing monitoring for signs and symptoms of infection as well as guidance for withholding treatment to patients in the presence of active infection. This and other communications containing warnings or other safety information to physicians and pharmacies, or required updates to labeling statements, including specific warnings or contradictions, could limit the commercial success of GAVRETO or any of our other drug products.

Side effects and toxicities associated with our products, as well as the warnings, precautions and requirements listed in the prescribing information for our products, could affect the willingness of physicians to prescribe, and patients to utilize, our products and thus harm commercial sales of our products. For example, for REZLIDHIA, the FDA-approved label contains a boxed warning describing the risk of differentiation syndrome, which can be fatal, in patients receiving the drug. This and other restrictions could limit the commercial success of the product.

If a safety issue emerges post-approval, we may become subject to costly product liability litigation by our customers, their patients or payors. 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 our products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- 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.

Our business could be materially and adversely affected by pandemics as a result of their potential 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.

Pandemics may result in extended travel and other restrictions in order to reduce the spread of diseases. Government measures taken in response to pandemics could have a significant impact, both direct and indirect, on our business and commerce, as significant reductions in business related activities may occur, supply chains may be disrupted, and manufacturing and clinical development activities may be curtailed or suspended.

For example, during the COVID-19 pandemic, we observed reduced patient-doctor interactions and our representatives had fewer visits with health care providers, which negatively affected our product sales. Physicians with practices severely impacted by the COVID-19 pandemic, or a pandemic occurring in the future, and who currently prescribe our products, may eventually decide to close their independent practices and join a larger medical organization with a practice that does not prescribe our products. Additionally, a pandemic, including COVID-19 or any resurgence thereof, may impact commercial-related activities, such as our marketing programs, speaker bureaus, and market access initiatives which may be required to be conducted virtually, delayed or cancelled, all of which occurred as a result of the COVID-19 pandemic. During the COVID-19 pandemic, we had to deploy resources to enable our field-based employees to continue to engage with health care providers in hybrid virtual and in-person interactions, which may be required in the event a pandemic occurs in the future.

With respect to clinical development, in response to the COVID-19 pandemic, we took measures to implement remote and virtual approaches, including remote patient monitoring where possible and working with our investigators for appropriate care of these patients in a safe manner. Due to the effects of COVID-19 pandemic, we experienced a number of our clinical trial investigators either paused, postponed or delayed new patient enrollment and restricted site visits of existing patients enrolled. In the event that a global pandemic, or a resurgence of the COVID-19 pandemic, occurs in the future, we may need to make decisions on a country-by-country basis to minimize risk to the patients and clinical trial sites. We may 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. We experienced slower than anticipated enrollment in some of our clinical trials due to adverse effects of COVID-19 pandemic, and in the future, we may experience adverse impacts of a global pandemic on our clinical trials, including the timing thereof, or our ability to continue to treat patients enrolled in our trials, enroll and assess new patients, supply study drugs and obtain complete data points in accordance with study protocol.

Pandemics may cause significant disruption in the supply chain for our commercial products. We 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. While 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 our products and to remain informed of any challenges within our supply chain, we may face disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of our products. Such supply disruptions would adversely impact our ability to generate sales of and revenues from our products and our business, financial condition, results of operations and growth prospects could be adversely affected.

Pandemics may affect our collaboration and licensing partners for the commercialization of our products globally, as well as our ability to advance our various clinical stage programs. We cannot predict the impact of such disruptions on our partners' ability to advance commercialization of our products 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 pandemics. For example, in response to the COVID-19 pandemic, the FDA delayed inspections and evaluations of certain drug manufacturing facilities and clinical research sites We cannot predict whether, and when, health regulatory agencies will decide to pause or resume inspections due to pandemics. 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, as seen in the COVID-19 pandemic, pandemics could result in a significant disruption of global financial markets. We could experience an inability to access additional capital or 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, or we may not be able to meet the requirements under our Credit and Security Agreement (Credit Agreement) with MidCap Financial Trust (MidCap). While we expect pandemics to adversely affect our business, financial condition, results of operations and growth prospects in the future periods, 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 circumstances that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration and severity of pandemics, 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 diseases. To the extent pandemics 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.

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 rebate or discount 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, the 340B Drug Pricing Program, as administered by the Health Resources and Services Administration, 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 payors and/or required covered entities 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. For example, in September 2024, CMS published a final rule that included significant revisions to certain Medicaid Drug Rebate Program provisions, including, but not limited to: (i) new definitions for key terms under the Medicaid Drug Rebate Program, such as "covered outpatient drug" and "market date"; (ii) revised processes for identifying drug misclassifications, as well as additional penalties that can be imposed against manufacturers in connection with such misclassifications; and (iii) a new 12-quarter time limit for manufacturers to initiate disputes, hearing requests, and audits for state-invoiced rebate amounts. 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 DHHS, Office of Inspector General and other governmental enforcement and administrative bodies have increased their focus, including through recent enforcement actions against manufacturers, on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate average manufacturer price and best price 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 payors. 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.

Finally, we may be affected by developments relating to the 340B Drug Pricing Program (340B Program). For example, since 2021, multiple manufacturers have implemented policies to reduce diversion and inappropriate claims for discounts by placing restrictions on 340B pricing for drugs dispensed through contract pharmacies. The DHHS sent several of these manufacturers' letters claiming that the policies violate the 340B statute and referring the manufacturers for potential enforcement action. Manufacturers challenged these letters in federal court, and the US Court of Appeals for the Third Circuit and the District of Columbia Circuit have ruled in favor of several manufacturers, finding that the policies were consistent with the 340B statute. Multiple states have recently enacted laws that require manufacturers to ship 340B drugs to certain contract pharmacies and impose various civil and criminal penalties on manufacturers that do not comply. These laws have been challenged in federal court and many of the cases are pending. In March 2024, the US Court of Appeals for the Eight Circuit upheld the Arkansas law prohibiting drug makers for restricting 340B drug discounts for providers using contract pharmacies. DHHS also issued a final rule on procedures for the 340B Program's administrative dispute resolution process in April 2024. It is unclear how the other pending litigation, proposed legislation, or future administrative action relating to the 340B Program will impact our business.

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, third-party 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, third-party 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;
- any additional support that may be required to administer the treatment to patients;
- 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, third-party 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, 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 commercialization of our products. We may seek another collaborator or licensee in the future for further clinical development and commercialization of our products, 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 commercialization of our products 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 commercialization of our products, 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 our products. 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 a global pandemic and the global tensions arising from the Russia-Ukraine war and the Hamas-Israel war. 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 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.

We entered into a Credit Agreement with MidCap on September 27, 2019, amended on March 29, 2021, February 11, 2022, July 27, 2022, and April 11, 2024. The Credit Agreement provides for a $60.0 million term loan credit facility. As of December 31, 2024, the outstanding principal balance of the loan was $60.0 million, and no remaining funds were available under the term loan credit facility. 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 11 – 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.

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

Our distribution operations for the sale of our products are 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. Further, climate change may increase both the frequency and severity of extreme weather conditions and natural disasters, which may affect our business operations. If we encounter difficulties with any of our distribution facilities, whether due to the potential future impacts of a global 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;
- potential future impacts, if any, including a global 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 products 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. We make estimates for provisions for sales discounts, returns and allowances. Our estimates are based on available customer and payor data received from the specialty pharmacies and distributors, as well as third party market research data. In part, our estimates are dependent on our distribution channel and payor mix. If actual results in the future vary from our estimates, we adjust these estimates, which would affect our net product revenue and earnings in the period such variances become known. 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 our products and product candidates we licensed to our collaboration partners.

We do not and will not have access to all information regarding our products 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 our collaboration partners. In addition, we have confidentiality obligations under our respective agreements with our collaboration partners. Thus, our ability to keep our shareholders informed about the status of our products and other product candidates will be limited by the degree to which our collaboration partners keep us informed and allows us to disclose such information to the public. If our collaboration partners fail to keep us informed about commercialization efforts related to our products, 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 our products 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;
- our ability to secure patent and regulatory protection;
- our ability to secure a favorable price or a positive HTA assessment;
- potential future impacts, if any, of a global 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.

For the year ended December 31, 2024, we recognized income from operations of $24.2 million primarily due to higher net product sales and collaboration revenues, partially offset by our operating expenses. Historically, we have 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 and costs of our ongoing commercial efforts. Although we recognized income from operations for the current period, there can be no assurance that we will generate annual operating income in the foreseeable future. Currently, our potential sources of revenues include sales of our products, as well as upfront, milestones and royalty payments pursuant to our collaboration arrangements, all of which may never materialize if sales of our products decline or if our collaboration partners 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, 2024, we had an accumulated deficit of approximately $1.4 billion. The extent of our future losses or profitability, if any, 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 may seek another collaborator or licensee in the future for clinical development and commercialization of our products, 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 expiration date of September 2031, olutasidenib is covered as a composition of matter in a US issued patent that has an expected expiration date of December 2036, after taking into account patent term extension rules, and pralsetinib is covered as a composition of matter in a US issued patent that has an expiration date in November 2036 and subject to extensions.

In the future, our patent position might be highly uncertain and involve complex legal and factual questions, and the cost to defend may also be significant. 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 our products 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.

An adverse outcome may allow third parties to use our intellectual property without a license and/or allow third parties to introduce generic and other competing products, any of which would negatively impact our business. For example, in June 2022, we received a notice letter from Annora advising that it has filed an ANDA with the FDA for a generic version of TAVALISSE and asserting that certain patents related to TAVALISSE that are listed in the Orange Book will not be infringed by Annora's proposed product, are invalid and/or are unenforceable. In July 2022, we filed a lawsuit in the US District Court for the District of New Jersey against Annora and its subsidiaries for infringement of those US patents. In September 2022, Annora and its subsidiaries answered and counterclaimed for declaratory judgment of non-infringement and invalidity of those patents. We filed an answer to Annora's counterclaims on October 12, 2022. Annora served invalidity and non-infringement contentions on December 31, 2022. We filed an answer to Annora's invalidity and non-infringement contentions in March 2023. Litigation continues, and no trial date is currently set. We intend to vigorously enforce and defend our intellectual property rights related to TAVALISSE. Should Annora or any other third parties receive FDA approval of an ANDA for a generic version of fostamatinib or a 505(b)(2) NDA with respect to fostamatinib, and if our patents covering fostamatinib were held to be invalid (or if such competing generic versions of fostamatinib were found to not infringe our patents), then they could introduce generic versions of fostamatinib or other such 505(b)(2) products before our patents expire, and the resulting competition would negatively affect our business, financial condition and results of operations. Please also see the risk factor entitled, "If manufacturers obtain approval for generic versions of our products, or of products with which we compete, our business may be harmed." In the future, there might be other claims that are subject to substantial uncertainties and unascertainable damages or other remedies, and the cost to defend may also be significant.

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 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;
- we will obtain a supplementary protection certificate that will extend the protection afforded by the patent to the product with a marketing authorization; 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, partnering and commercialization activities.

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. 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. In June 2024, California Senate Bill 167 was signed into law which suspends NOL deductions for tax years beginning on or after January 1, 2024 and before January 1, 2027 for taxpayers with net business income or modified adjusted gross income of at least $1.0 million for the tax year. The legislation also limits the aggregate use of otherwise allowable business credits to $5.0 million for each tax year beginning on or after January 1, 2024 but before January 1, 2027 (except for certain credits not subject to the limitation). Further, the Tax Act requires the taxpayers to capitalize Research and Experimental (R&E) expenditures under Section 174 of the Internal Revenue Code, as amended (Code), effective for taxable years beginning after December 31, 2021, which will reduce our NOLs beginning in 2022. R&E expenditures attributable to US-based research must be amortized over a period of 5 years and R&E expenditures attributable to research conducted outside of the US must be amortized over a period of 15 years.

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 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.

Changes in valuation allowance of deferred tax assets may affect our future operating results

We continue to record a full valuation allowance on our deferred tax assets considering our cumulative losses in prior years. In assessing the need for a valuation allowance, we consider historical levels of income, expectations and risks associated with estimates of future taxable income. We periodically evaluate our deferred tax asset balance for realizability. To the extent we believe it is more-likely-than-not that our deferred tax assets will not be realized, we will continue to maintain the valuation allowance against the deferred tax assets. Realization of our deferred tax assets is

dependent primarily upon future taxable income. If our assumptions and consequently our estimates change in the future, the valuation allowances may be increased or decreased, resulting in a respective increase or decrease in income tax expense.

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 current collaborations including Lilly, Grifols, Kissei, Medison, Knight, BerGenBio, and Daiichi. Under several 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 recognized material amount of revenue from royalties for the commercial sale of drugs, and we do not know when we will be able to generate such meaningful revenue in the future.

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 our products in which there are existing therapies and drug candidates in development for the treatment of hematologic disorders and cancer that may be alternative therapies to our products. 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 payors. 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 our products 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 developing 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;
- obtain access to manufacturing resources of the sufficient standard and scale;
- enter commercialization agreements for our new drug compounds; and
- obtain and maintain appropriate reimbursement price and positive recommendations by HTA bodies.

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 our products 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;
- the announcement of regulatory applications, such as Annora's ANDA, seeking approval of generic versions of our marketed products;
- 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.

We completed a reverse stock split of our shares of common stock, which may reduce and may limit the market trading liquidity of the shares due to the reduced number of shares outstanding and may potentially have an anti-takeover effect.

We completed a reverse stock split of our common stock by a ratio of 1-for-10 effective June 27, 2024. The primary objective of the reverse stock split was to attempt to raise the per share trading price of our common stock. We believe that a low per share market price of our common stock impairs our marketability to, and acceptance by, institutional investors and other members of the investing public and creates a negative impression of us. Among other benefits, the effectuation of the reverse stock split seeks to help us maintain compliance with the minimum bid continued listing requirement of $1.00 per share required to maintain continued listing on The Nasdaq Global Select Market (the Bid Price Requirement). Prior to us effecting a reverse stock split, the closing bid price of our common stock at certain periods fell below $1.00 per share for 30 consecutive trading days. We received deficiency letters from the Listing Qualifications Department of Nasdaq on November 22, 2022 and November 27, 2023, notifying us that, for 30 consecutive business days, the bid price for our common stock had closed below the Bid Price Requirement. We received notification from the Listing Department of Nasdaq on January 5, 2023 and December 12, 2023 that we had regained our compliance with the Bid Price Requirement because the closing price of our common stock closed at $1.00 or more for over 10 consecutive days. Although we regained compliance with the Nasdaq Bid Price Requirement, in the future, Nasdaq may initiate a delisting process with a notification letter if we were to again fall out of compliance. If we were to receive such a notification, we would be afforded a grace period of 180 calendar days to regain compliance with the Bid Price Requirement. In order to regain compliance, shares of our common stock would need to maintain a minimum closing bid price of at least $1.00 per share for a minimum of 10 consecutive trading days. Additionally, we may be unable to meet other applicable Nasdaq listing requirements, including maintaining minimum levels of stockholders' equity or market values of our common stock in which case, our common stock could be delisted. If our common stock were to be delisted, the liquidity of our common stock would be adversely affected and the market price of our common stock could decrease.

Reducing the number of outstanding shares of our common stock through the reverse stock split increased the per share trading price of our common stock. However, there is no assurance that:

- the market price per share of our common stock after the reverse stock split will rise in proportion to the reduction in the number of shares outstanding before the reverse stock split;

- the reverse stock split will result in a per-share price that would attract brokers and investors who do not trade in lower-priced stocks;
- the reverse stock split will result in a per-share price that will increase our ability to attract and retain employees and other service providers; or
- the reverse stock split will promote greater liquidity for our stockholders with respect to their shares.

In addition, the reverse stock split reduced the number of outstanding shares of our common stock without reducing the authorized number of shares of our common stock. Therefore, the number of shares of our common stock that are authorized and unissued has increased relative to the number of issued and outstanding shares of our common stock following the reverse stock split. Our Board of Directors may authorize the issuance of the remaining authorized and unissued shares without further stockholder action for a variety of purposes, except as such stockholder approval may be required in particular cases by our Amended and Restated Certificate of Incorporation, applicable law or the rules of any stock exchange on which our securities may then be listed. The issuance of additional shares would be dilutive to our existing stockholders and may cause a decline in the trading price of our common stock. The issuance of authorized but unissued shares of common stock could be used to deter a potential takeover of us that may otherwise be beneficial to stockholders by diluting the shares held by a potential suitor or issuing shares to a stockholder that will vote in accordance with our Board of Directors' desires. A takeover may be beneficial to independent stockholders because, among other reasons, a potential suitor may offer such stockholders a premium for their shares of stock compared to the then-existing market price. We do not have any plans or proposals to adopt provisions or enter into agreements that may have material anti-takeover consequences.

The market price of our common stock is based on our performance and other factors, some of which are unrelated to the number of shares outstanding. If the market price of our common stock declines, the percentage decline as an absolute number and as a percentage of our overall market capitalization may be greater than would occur in the absence of the reverse stock split.

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

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). The UK Government and the EU recently adopted a new agreement, the "Windsor Framework" which will replace the Northern Ireland Protocol. According to the Windsor Framework, medicinal products intended for the UK market including Northern Ireland will be authorized by the MHRA, and will bear a "UK only" label. This means that Medicinal products placed on the market in Northern Ireland will no longer need to be compliant with EU law. These new measures will be implemented from January 1, 2025.

A separate marketing authorization will be required to market drugs in Great Britain. The MHRA has launched the Innovative Licensing and Access Pathway (ILAP), a new accelerated assessment procedure for marketing authorization applications facilitating the interaction with pricing authorities and HTA bodies and aiming to enable companies to enter the UK market faster. On January 1, 2024, the MHRA launched a new International Recognition Procedure for Great Britain (England, Scotland and Wales) marketing authorization applications whereby the MHRA

will, when considering such applications, recognize the approval of medicines by trusted reference regulators in Australia, Canada, Switzerland, Singapore, Japan, United States and EU following its own abbreviated assessment. 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 the UK following Brexit is granted on an essentially identical basis as in the EU but is based on the prevalence of the condition in the UK. It is therefore possible that conditions that are currently designated as orphan conditions in the UK will no longer be, and conditions that are not currently designated as orphan conditions in the EU will be designated as such in the UK.

In April 2023, the European Commission adopted a wide ranging proposal for a new Directive and a new Regulation to revise and replace the existing general pharmaceutical legislation. This change will likely result in significant changes to the pharmaceutical industry. In particular, it is expected that the new Directive and Regulations will, if made into law, affect the duration of the period of regulatory protection afforded to medicinal products including regulatory data protection (also called “data exclusivity”), marketing exclusivity afforded to orphan medicinal products, as well as the conditions of eligibility to the orphan designation. The legislation is not expected to be adopted before 2026/2027.

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 with competing pharmaceutical or biotechnology companies, any of which may 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 process in place to ensure we are complying with all requirements of law, our consulting or advisory contracts with our scientific consultants and advisors may be scrutinized under the Anti-Kickback Statute, the UK Bribery Act 2010, and other similar national and state-level legislation, which prohibit, among other things, companies from offering or paying anything of value as remuneration for ordering, purchasing, or recommending the ordering or purchasing of pharmaceutical and biological products that may be paid for, in whole or in part, by Medicare, Medicaid, or another federal healthcare program. 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 available 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 dependent upon information technology systems, infrastructure, and data to operate our business. While we believe our cybersecurity measures are adequate, our cybersecurity risk management, strategy and governance may be found to be inadequate that could harm our business. We 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 breakdowns, 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 trial 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. Notably, on July 26, 2023, the SEC adopted a final rule on cybersecurity risk management, strategy, governance and incident disclosure (SEC Cyber Rule). The SEC Cyber Rule requires public companies to make current disclosures about material cybersecurity incidents as well as annual disclosures of material information about their cybersecurity risk management, strategy and governance. The SEC Cyber Rule became effective on September 5, 2023. 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, we may conduct additional equity offerings. We have an Open Market Sale Agreement with Jefferies LLC (Jefferies) entered on August 4, 2020, and amended and restated on August 2, 2024, 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. We had a shelf registration statement (the Prior Registration Statement) filed with the SEC that expired on August 3, 2024. The Prior Registration Statement included a base prospectus registering the offering, issuance, and sale by us of up to $250.0 million in the aggregate of the securities identified from time to time in one or more offerings, including the $100.0 million of shares of our common stock that may be offered, issued and sold under the Open Market Sale Agreement. On August 2, 2024, we filed a new shelf registration statement (the New Registration Statement) with the SEC to replace the Prior Registration Statement. The New Registration Statement was declared effective on August 9, 2024 by the SEC. The New Registration Statement includes a base prospectus to register the offering, issuance and sale by us of up to $250.0 million in the aggregate of securities identified from time to time in one or more offerings, including up to $100.0 million of shares of our common stock that may be offered, issued and sold under the Open Market Sale Agreement. As of December 31, 2024, we have not sold any shares of common stock under such Open Market Sale Agreement.

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 our products 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 our products, 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 a legal challenge to the Affordable Care Act brought by several states (which argued that, without the individual mandate, the entire Affordable Care Act was unconstitutional) without specifically ruling on the constitutionality of the law. It is unclear how future actions before the Supreme Court, other such litigation, and the healthcare reform measures of future presidential administrations 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 our products, 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.

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 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.

On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other changes, eliminated the statutory Medicaid drug rebate cap, which was previously set at 100% of a drug's average manufacture price, for single source and innovator multiple source drugs, as of January 1, 2024. The American Rescue Plan Act also temporarily increased premium tax credit assistance for individuals eligible for subsidies under the Affordable Care Act 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 Inflation Reduction Act (IRA) extended this increased tax credit assistance and removal of the 400% federal poverty limit through 2025. Additionally, beginning in April 2013, the Budget Control Act of 2011 created an automatic reduction of Medicare payments to providers of up to 2%. As a result of the COVID-19 pandemic, this reduction was temporarily suspended from May 1, 2020 through March 31, 2022, with subsequent reductions to 1% from April 1, 2022 through June 30, 2022. The 2% reduction was then reinstated and has been in effect since July 1, 2022, and will remain in effect through the first eight months in which the fiscal year 2032 sequestration order is in effect, unless additional Congressional action is taken. Moreover, on June 16, 2022, the Federal Trade Commission issued a policy statement stating its intent to increase enforcement scrutiny of "exclusionary rebates" to PBMs and other intermediaries that "foreclose competition." On August 16, 2022, the IRA was signed into law, which, among other reforms, allows Medicare to: beginning in 2026, establish a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation with CMS; beginning in 2023, penalize drug companies that raise prices for products covered under Medicare Parts B and D faster than inflation; and beginning in 2025, impose new discount obligations on pharmaceutical and biological manufacturers for products covered under Medicare Part D. CMS continues to take steps to implement the IRA, including: releasing the negotiated maximum prices, which will be effective in 2026, for the first ten drugs that were subject to the IRA's negotiation process; releasing quarterly lists of Medicare Part B products that are subject to adjusted coinsurance rates based on the inflationary rebate provisions of the IRA; and announcing a list of fifteen additional drugs that will be subject to price negotiations during 2025. While it remains to be seen how the drug pricing provisions imposed by the IRA will affect the broader pharmaceutical industry, several pharmaceutical manufacturers and other industry stakeholders have challenged the law, including through lawsuits brought against the DHHS, the Secretary of the DHHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA's drug price negotiation provisions.

There have also been healthcare reform efforts carried out via administrative agencies. For example, on February 14, 2023, the DHHS issued a report, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a "high-value drug list" setting the maximum out-of-pocket costs for certain common generic drugs at $2 per month per drug; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements for certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments. Additionally, consistent with former President Biden's previous announcements in connection with the Cancer Moonshot initiative, on June 27, 2023,

the Center for Medicare Innovation at CMS announced a new model, the Enhancing Oncology Model, that is designed to make high-quality cancer care more affordable to both patients and Medicare.

Other proposed administrative actions may affect our government pricing responsibilities. For example, there are pending legal and legislative developments relating to the 340B Drug Pricing Program, including ongoing litigation challenging federal enforcement actions against manufacturers and recently introduced and enacted state legislation. It remains to be seen how these drug pricing initiatives will affect the broader pharmaceutical industry.

The results of the 2024 Presidential and Congressional elections, and potential subsequent developments further increase the uncertainty related to the healthcare regulatory environment. In addition, on June 28, 2024, the U.S. Supreme Court issued an opinion holding that courts reviewing agency action pursuant to the Administrative Procedure Act (APA) "must exercise their independent judgment" and "may not defer to an agency interpretation of the law simply because a statute is ambiguous." The decision will have a significant impact on how lower courts evaluate challenges to agency interpretations of law, including those by CMS and other agencies with significant oversight of the healthcare industry. The new framework is likely to increase both the frequency of such challenges and their odds of success by eliminating one way in which the government previously prevailed in such cases. As a result, significant regulatory policies may be subject to increased litigation and judicial scrutiny. Any resulting changes in regulation may result in unexpected delays, increased costs, or other negative impacts that are difficult to predict but could have a material adverse effect on our business and financial condition. For example, certain of these changes could impose additional limitations on the rates we will be able to charge for our future products or the amounts of reimbursement available for our future products from governmental agencies or third-party payors.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. Specifically, several US states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports, and/or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Other state laws prohibit certain marketing-related activities, including the provision of gifts, meals or other items to certain healthcare providers, and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Several state laws require disclosures related to state agencies and/or commercial purchasers with respect to price increases and new product launches that exceed certain thresholds as identified in the relevant statutes. Another emerging trend at the state level is the establishment of prescription drug affordability boards, some of which will prospectively permit certain states to establish upper payment limits for drugs that the state has determined to be "high-cost." Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

Furthermore, the increased emphasis on managed healthcare in the US and on country and regional pricing and reimbursement controls in the EU and the UK 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, 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.

We cannot predict the likelihood, nature, or extent of health reform initiatives that may arise from future legislation or administrative action. 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, for additional information.

Regulatory approval for any approved product is limited by the FDA, the EC 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 our products 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 EC 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 and for REZLIDHIA is only approved for use in adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. Further, GAVRETO is approved by the FDA for the treatment of adult patients with metastatic RET fusion-positive NSCLC and has a conditional approval for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer. 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, or if we are not able to maintain a conditional approval or transition a conditional approval to full approval, 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 our products 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 us. 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 a global pandemic, global tensions arising from the Russian-Ukrainian war and Hamas-Israel war 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. 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 potential future impacts of a global pandemic, the global tensions arising from the Russian-Ukrainian war and Hamas-Israel war 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 effects of the COVID-19 pandemic, for several of our development programs, we experienced disruption or delay in our ability to enroll and assess patients, maintain patient enrollment, supply study drugs, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in employee resources or otherwise. In addition, in the event that a global pandemic occurs in the future, some patients in our clinical trial 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 may be adversely affected if a global pandemic continues and persists for an extended period of time, and we may experience significant disruptions to our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects in the future.

We have conducted in the past and are currently conducting or may conduct in the future clinical trials in the US and outside the US. In the past, we had clinical trial sites in Russia and Ukraine for our wAIHA trial, which trials have concluded. Recent actions taken by the Russian Federation in Ukraine and surrounding areas have destabilized the region and caused the adoption of comprehensive sanctions by, among others, the EU, the US and the UK, which restrict a wide range of trade and financial dealings with Russia and Russian persons, as well as certain regions in Ukraine. Also, the recent global tensions arising from the Hamas-Israel war may result in disruptions in the broader global economic environment. Further, some patients may not be able to comply with clinical trial protocols if the conflict impedes patient movement or interrupts healthcare services. In addition, clinical trial site initiation and patient enrollment may be delayed, and we may not be able to access sites for initiation and monitoring in regions affected by the Russian-Ukrainian war or the Hamas-Israel war including due to the prioritization of hospital resources away from clinical trials or as a result of warfare, violence, government-imposed curfews, or events or other governmental actions that restrict movement. We could also experience disruptions in our supply chain or limits our ability to obtain sufficient materials for our drug products in certain regions.

Public perception of the risk-benefit balance for our product candidates may be affected by adverse events in clinical trials involving our product candidate or other 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, 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 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 our products or any product candidates for clinical trials. We currently use three active pharmaceutical ingredient manufacturing facilities and three finished goods manufacturing facilities for our products. 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 active pharmaceutical ingredients 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. In the ordinary course of business, we enter into agreements with contract manufacturers to manufacture our inventory products. For example, in October 2024, we entered into an agreement with a third-party contract manufacturer to manufacture TAVALISSE that is expected to be delivered starting in fiscal year 2026 through 2029. Although the agreement provides a cancellation clause with or without cause upon written notice, we may or may not be subject to payment of cancellation fees. The level of cancellation fees is generally dependent on the timing of the written notice in relation to the commencement date of work, with the maximum cancellation fees equal to the full price of the work order. 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. Our third-party manufacturers import certain materials from China to produce our products. The tensions between the US and China have led to a series of tariffs and sanctions being imposed by the US on imports from China mainland, as well as other business restrictions. Geopolitical developments, including changes arising as a result of the recent US presidential election, may lead to further developments with respect to the imposition or threat of imposition of trade policies, tariffs, taxes and other limitations on cross-border operations. Such tensions could adversely impact us and our third-party manufacturers. 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 investigational new drug (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 EMA, 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 a global 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 us, 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, MHRA 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.

We commercialize our products in the US and we have entered into commercialization agreements with third parties to commercialize fostamatinib outside the US. 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, 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 our products or any of our product candidates, when and if approved, whether due to the impacts of a global 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 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.

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 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 have orphan drug designations from the FDA but we may not be able to obtain additional orphan drug designations in the future, or maintain the orphan drug designations or exclusivity for the approved drugs for the treatment of respective indications, or we may be unable to maintain the benefits associated with orphan drug designations, including the potential for market exclusivity.

We have an orphan drug designation in the US for fostamatinib for the treatment of ITP and wAIHA, and for olutasidenib for the treatment of AML. Also, pralsetinib has an orphan drug designation in the US for the treatment of adult patients with metastatic RET fusion-positive NSCLC, for the treatment of advanced or metastatic RET fusion-positive thyroid cancer, and for the treatment of advanced or metastatic RET-mutant medullary thyroid carcinoma. In January 2025, the FDA granted R289 orphan drug designation for the treatment of myelodysplastic syndromes. We may also 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 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 in the US, we may not be the first to obtain marketing approval for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products or we might not maintain our orphan drug designation. 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.

In addition, Congress is considering updates to the orphan drug provisions of the FDCA in response to a recent 11th Circuit decision. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug exclusivity and would materially adversely affect our business, financial condition, results of operations, cash flows and prospects.

Risks Related to Commercialization

Our prospects are highly dependent on our commercial products. To the extent that the commercial success of our products 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.

We are focusing a significant portion of our activities and resources on our products, 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 our products in the US. We have also entered into exclusive commercialization agreements with third parties to commercialize fostamatinib outside the US, and we plan to further enter partnership with existing or other third parties to commercialize our products outside the US in the future.

Sustained successful commercialization of our products is subject to many risks and uncertainties, including the impact of a global pandemic on the successful commercialization in the US, as well as the successful commercialization efforts for our products through our collaborative partners. 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.

There are many factors that could cause the commercialization of our products to be unsuccessful, including a number of factors that are outside our control. The commercial success of our products depends on the extent to which patients and physicians accept and adopt our products to treat the related diseases. We also do not know how physicians, patients and payors will respond to our future price increases of our products. Physicians may not prescribe our products and patients may be unwilling to use our products if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Our products compete, 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 our products in clinical development in additional indications may adversely impact the commercialization and potential of fostamatinib. Thus, significant uncertainty remains regarding the commercial potential of our products.

Market acceptance of our products 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;
- potential future impacts, if any, due to the effects of a global pandemic and the global tensions arising from

the Russian-Ukrainian war and Hamas-Israel war;

- 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;
- a positive HTA concluding that the product is cost-effective and the HTA bodies issuing a positive recommendation for the use of the product as a first or second line of treatment for the granted therapeutic indication;
- 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 our products, 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 our products 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 development and commercialization of fostamatinib in Kissei, Grifols, Medison and Knight's territories, and of olutasidenib in Kissei and Dr. Reddy's territories. As a consequence of our license agreements with our collaboration partners, 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 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 our products 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 may 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 payors to contain or reduce their costs, including by taking the following steps, among others: decreasing the portion of costs payors will cover, ceasing to provide full payment for certain products depending on outcomes, and/or not covering certain products at all. If payors 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 our products 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 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 payors 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.

On January 12, 2025, the new HTA Regulation, Regulation No 2021/2282 on Health Technology Assessment (HTA Regulation) started applying to new cancer medicines and advanced therapy medicinal products, and imposes a new procedure for the assessment of the pricing and reimbursement of medicinal products. The HTA Regulation intends to foster cooperation among EU member states in assessing health technologies and provide a procedure for joint clinical assessments of medicinal products at a centralized level. It requires companies applying for products in scope to make relevant submissions for the joint clinical assessment, in line with a number of prespecified criteria. By 2030 it will apply to all medicinal products.

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 effects of a global pandemic, depending on its scale and duration, may 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 our products 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 our products and retain experienced commercial personnel, our business will be substantially harmed.

We continuously expend significant time and resources to maintain a sales force that is credible and compliant with applicable laws in marketing our products. In addition, we must continually train our sales force to ensure that an appropriate and compliant message about our products 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 our products, our efforts to successfully commercialize our products 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 our products. As a result, we will be required to expend significant time and resources to market, sell, and distribute our products to hematologists and hematologist-oncologists. There is no guarantee that the marketing strategies we have developed, 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 our products. 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.

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, we may be unable to realize the commercial potential of our products. Also, to the extent that the commercial opportunities for our products 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 our products, 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 our products 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 our products for any individual, additional indications. For example, in June 2022, we announced that the top-line results from our Phase 3 trial in wAIHA did not demonstrate statistical significance in the primary efficacy endpoint of durable hemoglobin response in the overall study population. While we conducted an in-depth analysis of these data to better understand differences in patient characteristics and outcomes and submitted these findings to the FDA, in October 2022, we announced that we received guidance from the FDA of these findings. Based on the result of the trial and the guidance from the FDA, we did not file an sNDA for wAIHA.

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 public health emergencies including a global pandemic, 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 our products 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 force majeure events;
- 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.

Further, evolving FDA standards may cause additional setbacks. In 2023, FDA published guidance documents and a final rule which all concern clinical trial requirements. In June 2023, FDA published a draft guidance, E6(R3) Good Clinical Practice, which seeks to unify standards for clinical trial data for the International Council for

Harmonisation of Technical Requirements of Pharmaceuticals for Human Use member countries and regions. In August 2023, FDA published a guidance document, Informed Consent, Guidance for IRBs, Clinical Investigators, and Sponsors, which supersedes past guidance and finalizes draft guidance on informed consent. Further, in December 2023, FDA published a final rule, Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations, which allows exceptions from informed consent requirements when a clinical investigation poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of human subjects.

Alterations to clinical trial requirements, including due to judicial challenges, may affect recruitment and retention of patients and may hinder or delay a clinical trial. Further, changes to data requirements may cause FDA or comparable foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and may require further studies. Changes to trial requirements or trial data may increase costs and delay product development.

General Risk Factors

Global economic conditions could adversely impact our business.

Deterioration in the macroeconomic economy could lead to losses or defaults by our customers or suppliers, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. The global financial markets and economy are currently, and have from time to time experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability.

Any significant deterioration in the US economy would likely affect the operation of our business and ability to raise capital. In addition, US debt ceiling and budget deficit concerns have increased the possibility of additional credit-rating downgrades and economic slowdowns, or a recession in the US. Although US lawmakers passed legislation to raise the federal debt ceiling on multiple occasions, ratings agencies have lowered or threatened to lower the long-term sovereign credit rating on the US. The impact of this or any further downgrades to the US government's sovereign credit rating or its perceived creditworthiness could adversely affect the US and global financial markets and economic conditions.

The global financial markets and economy may also be adversely affected by the current or anticipated impact of military conflict, including the ongoing Russian-Ukrainian war, and the Hamas-Israel war, terrorism or other geopolitical events. Sanctions imposed by the US and other countries in response to such conflicts, including the Russian-Ukrainian war and the Hamas-Israel war, may also adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability.

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 or global economy or certain sectors thereof and, thus, could adversely impact our businesses.

Bank failures or other events affecting financial institutions could adversely impact our liquidity and other business.

Financial institutions have recently experienced, and may experience in the future, industry instability and failures which have led to disruptions in access to bank deposits or lending commitments. In 2023, the closures of Silicon Valley Bank (SVB) and Signature Bank and their placement into receivership with the Federal Deposit Insurance Corporation (FDIC), as well as the FDIC's seizure and sale of First Republic Bank, created bank-specific and broader financial institution liquidity risk and concerns. On March 12, 2023, federal regulators announced that the FDIC would

complete its resolution of SVB in a manner that fully protects all depositors. On March 27, 2023, First Citizens Bank (FCB) announced that it has entered into an agreement with FDIC to purchase all of the asset and liabilities of SVB. Customers of SVB automatically become customers of FCB following the acquisition.

We maintain a depository relationship with SVB/FCB and other banking institutions. All of our cash deposits are accessible to us, and we do not anticipate any losses with respect to such funds. Since the March 2023 financial institution failure, there has been a heightened risk and greater focus on the potential failures of other banks in the future. If these banks fail in the future, we may not be able to immediately (or ever) recover our cash in excess of the FDIC insured limits which would adversely impact our operating liquidity and could negatively impact our operations, results of operations and financial performance. Although we believe our exposure is limited, if in the future any of the financial institutions that we maintain depository or lending relationships were to be placed into receivership, we may be unable to access such funds to meet our working capital requirements. In addition, if any of our customers, suppliers or other parties with whom we conduct business are unable to access funds, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impacted by factors that affect us, the financial institutions with which we have credit agreement or arrangements directly, or the financial services industry or economy in general.

Shareholder activism and private securities-related litigation could cause material disruption to our business.

Publicly traded companies have increasingly become subject to campaigns by our stakeholders, including investors, and more recently regulatory organizations advocating corporate actions such as actions related to ESG matters, impacts of climate change, 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.

There is a growing emphasis from select investors, regulators, and other stakeholders on corporate responsibility, particularly regarding ESG factors. Some investors and advocacy groups utilize these factors to shape investment strategies, potentially opting out of investing in our company if they perceive our corporate responsibility policies as insufficient. Third-party providers offering corporate responsibility ratings and reports have surged to meet rising investor demand, with numerous organizations evaluating companies on ESG matters, and these evaluations receive widespread attention. A low ESG or sustainability rating from such providers could lead certain investors to overlook our common stock in favor of competitors. Institutional investors, in particular, use these ratings to compare companies, and any perceived lag in our ESG efforts might prompt voting decisions or other actions to hold our Board of Directors accountable. Furthermore, evolving assessment criteria for corporate responsibility practices may raise expectations, compelling us to undertake costly initiatives to meet new standards. Failure to meet these evolving criteria could reinforce the perception of inadequate corporate responsibility policies. Non-compliance could also lead to reputational damage if our procedures or standards fall short of stakeholder expectations.

Securities-related class action lawsuits and/or derivative lawsuits have often been brought against companies, including biotechnology and biopharmaceutical companies, that experience volatility in the market price of their securities. It is possible that such lawsuit will be filed, or allegations from stockholders with this matter. Such lawsuits and any other related lawsuits are subject to inherent uncertainties, and the actual defense and disposition costs will depend upon many unknown factors. The outcome of such lawsuits is necessarily uncertain. We could be forced to expend significant resources in the defense of the pending lawsuits and any additional lawsuits, and we may not prevail.

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 our Amended and Restated Bylaws (our 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 our 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 our Board of Directors or for proposing matters that can be acted upon at stockholder meetings;
- provide for staggered terms for our Board of Directors; 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 (DGCL), which imposes certain restrictions relating to transactions with major stockholders, may discourage, delay or prevent a third party from acquiring us.

Our Bylaws designate a state or federal court located within the State of Delaware as the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our current or former directors, officers, stockholders, or other employees.

Our Bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of us under Delaware law, (ii) any action asserting a claim of breach of a fiduciary duty by any current or former director, officer, or other employee of ours that is owed to us or our stockholders, (iii) any action asserting a claim against us or any of our directors, officers, or other employees arising pursuant to any provision of the DGCL or our Amended and Restated Certificate of Incorporation and our Bylaws (as either may be amended from time to time), (iv) any action asserting a claim against us governed by the internal affairs doctrine, or (v) any other action asserting an "internal corporate claim," as defined under Section 115 of the DGCL. The forgoing provisions do not apply to any claims arising under the Securities Act and, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the sole and exclusive forum for resolving any action asserting a claim arising under the Securities Act.

These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our current or former directors, officers, or other employees, which may discourage lawsuits with respect to such claims. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find the choice of forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations, and financial condition.

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, regulations and national and EU codes of conduct, 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 future success depends on our ability to attract and retain key employees and relationships.

We are highly dependent on the commercial, research and development, clinical, business development, financial and legal expertise of our executive officers, as well as the other principal members of our management. We expect to continue hiring and retaining qualified personnel which is critical to our success. Replacing key employees and executive officers may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. 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.

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 1C. Cybersecurity

Risk Management and Strategy

Cybersecurity and privacy incidents in the pharmaceutical industry are growing in frequency and severity, prompting organizations to invest heavily in people, processes, and technology to bolster their cybersecurity risk management capabilities.

We assess the integrity of our information technology and cybersecurity platforms to help ensure proper safety measures are implemented. We understand the extensive responsibility associated with safeguarding our systems and data. Our processes for assessing, identifying, and managing material risks from cybersecurity threats include:

- *Detection and Prevention:* We utilize various securities tools and technologies designed to prevent, identify, protect, detect, escalate, respond and recover from cyber threats in a timely manner. Our approach includes real-time monitoring, threat analysis, and regular security evaluations to identify and mitigate potential vulnerabilities.
- *User Training & Education:* We realize that human error can be a significant cybersecurity risk, so we have implemented education and training programs for our staff to raise awareness about cybersecurity best practices. By promoting a culture of security consciousness, we empower our staff to identify potential threats and respond effectively, in a way that is designed to enhance the overall cybersecurity posture of our organization.
- *Incidence Response and Business Continuity:* We have comprehensive Incidence Response and Business Continuity plans in place designed to ensure the continuity, availability and accessibility of our systems and data, even in the face of unforeseen events such as natural disasters or cyber incidents, which plans and systems we test regularly.

  We rely upon the capacity, availability and security of our information technology hardware and software infrastructure. We maintain comprehensive compliance and security programs designed to help safeguard and ensure the integrity of the confidential information we possess, which includes both organization and technical control measures. We routinely conduct employee trainings on important information security procedures and test and measure compliance with these security measures. In addition, we maintain cyber insurance policies that mitigate the financial risk of any potential incident.

  We engage consultants, auditors, and other third parties in connection with such processes. We work with third-party service providers to assist us in our cybersecurity risk management to identify areas that may potentially impact our business, develop and implement control framework to mitigate such cybersecurity risks, and to be prepared to respond to and report (as required) applicable cybersecurity incidents.

  We face a number of risks including the growing threat of cybersecurity attacks. Despite our implementation of security measures to combat the threats of cybersecurity attacks, any system failure, accident or security breach could result in disruptions to our operations. To the extent that any disruption, cybersecurity attack or other security breach results in a loss or damage to our data or inappropriate disclosure of confidential information, our business could be harmed. In addition, we may be required to incur significant costs to protect against damaged caused by these disruptions or security breaches in the future.

While we have not, as of the date of this Annual Report on Form 10-K, experienced cybersecurity incidents that have materially affected us, our business strategy, our results of operations or our financial condition, there can be no

guarantee that we will not experience such an incident in the future. For additional information regarding risks from cybersecurity threats, please refer to "Item 1A. Risk Factors" of this annual report on Form 10-K.

Governance

Our Corporate Governance, Healthcare Compliance Oversight, and Nominating committee oversees our cybersecurity risk management. This committee periodically reviews and assesses the risk exposure of our risks related to data privacy, technology and information security, including cyber-security, and back-up of information systems and makes recommendations to our Board of Director pertaining to monitoring and minimizing findings in such assessment. This committee periodically reports to the Board of Directors.

While the Corporate Governance, Healthcare Compliance Oversight, and Nominating committee oversees our cybersecurity risk management, our management also plays an integral role in cybersecurity oversight. Our management is responsible for day-to-day risk management processes. This includes periodic updates from the Executive Director of Information Technology who has over 24 years of work experience in the life science industry, and holds an undergraduate degree in Industrial Technology. The Executive Director of Information Technology is responsible for managing the daily measures of safeguarding the information technology infrastructure from potential threats and vulnerabilities, which includes monitoring the prevention, detection, mitigation, and remediation of cybersecurity incidents. Additionally, we have established a Crisis Management Team (CMT), which is a team of cross-functional participants who are prepared to review and assess any potential cybersecurity incidents. The CMT team is led by our CFO and our General Counsel who will advise the Corporate Governance, Healthcare Compliance Oversight, and Nominating committee of the Board accordingly in the event of any incident. We believe this division of responsibilities is the most effective approach for addressing our cybersecurity risks and that the Board leadership structure supports this approach.

Item 2. Properties

We lease a 13,670 rentable square feet office space located at 611 Gateway Boulevard, Suite 900, South San Francisco, California. We currently sublease the office from Atara Biotherapeutics, Inc. (Atara), which sublease will expire in May 2025. In February 2025, we entered into a lease agreement with 611 Gateway Center LP (611 Gateway) to lease the same office space currently subleased from Atara, which lease will commence following the expiration of the sublease with Atara and expire in July 2027. This leased facility is currently held as our Headquarters. We believe that this leased facility is in good operating condition and is adequate for all our present and near term uses.

Item 3. Legal Proceedings

From time to time, we may be a party or subject to legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. Some of these proceedings that we may be involved in the future are claims that are subject to substantial uncertainties and unascertainable damages or other remedies.

Our threshold for disclosing material environmental legal proceedings involving a government authority where potential monetary sanctions are involved is $1.0 million.

In June 2022, we received a notice letter regarding an ANDA submitted to the FDA by Annora, requesting approval to market a generic version of TAVALISSE. The notice letter included a Paragraph IV certification with respect to our US Patent Nos. 7,449,458; 8,263,122; 8,652,492; 8,771,648 and 8,951,504, which are listed in the FDA's Orange Book. The notice letter asserts that these patents will not be infringed by Annora's proposed product, are invalid and/or are unenforceable. Annora's notice letter does not provide a Paragraph IV certification against our other patents listed in the Orange Book. On July 25, 2022, we filed a lawsuit in the US District Court for the District of New Jersey against Annora and its affiliates, Hetero Labs Ltd., and Hetero USA, Inc., for infringement of our US patents identified in Annora's Paragraph IV certification. On September 21, 2022, Annora and its affiliates answered and counterclaimed for declaratory judgment of non-infringement and invalidity of the '458, '122, '492, '648, and '504 patents. We served an answer to Annora's counterclaims in October 2022. Annora served invalidity and non-infringement contentions in December 2022. We served an answer to Annora's invalidity and non-infringement contentions in March 2023.

Litigation continues, and no trial date is currently set. We intend to vigorously enforce and defend our intellectual property related to TAVALISSE.

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.

On June 27, 2024, we effected a 1-for-10 reverse stock split. As a result of the reverse stock split, every ten issued and outstanding shares of our common stock were automatically combined into one issued and outstanding share of common stock. No fractional shares were issued in connection with the reverse stock split. As a result of the reverse stock split, proportionate adjustments were made to the number of shares underlying (and as applicable, the exercise or conversion prices of) our outstanding equity awards and to the number of shares of common stock issuable under our equity incentive plans. The reverse stock split did not change the par value of our common stock, which remains $0.001, or the authorized number of shares of our common stock. All share amounts and per share amounts disclosed in this Annual Report on Form 10-K have been adjusted to reflect the reverse stock split on a retroactive basis for the respective periods presented.

Holders of Record

As of February 25, 2025, there were approximately 28 holders of record of our common stock.

Dividend Policy

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.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

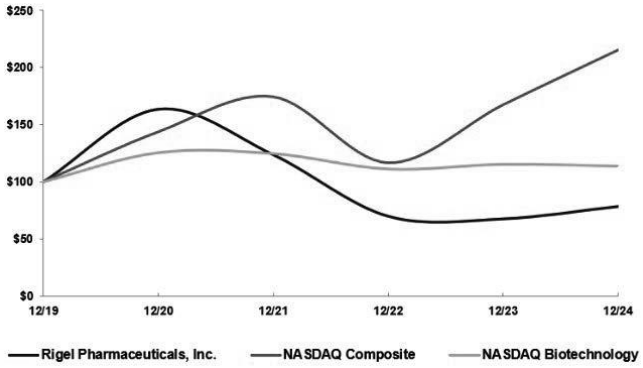
None.

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, 2019 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



Item 6. [Reserved]

Not applicable.

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 2024 and 2023 items and 2024 and 2023 year-to-year comparisons. This section does not discuss 2022 items and 2023 to 2022 year-to-year comparisons. Discussions of 2022 items and 2023 to 2022 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 our Annual Report on Form 10-K for the year ended December 31, 2023.

Overview

We are a biotechnology company dedicated to developing and providing novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. We focus on products that address signaling pathways that are critical to disease mechanisms.

TAVALISSE (fostamatinib disodium hexahydrate) is our first product approved by the FDA. TAVALISSE is the only approved 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 and the UK (as TAVLESSE), and in Canada, Israel and Japan (as TAVALISSE) for the treatment of chronic ITP in adult patients.

REZLIDHIA (olutasidenib) is our second FDA-approved product. REZLIDHIA capsules are indicated for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. We in-licensed REZLIDHIA from Forma with exclusive, worldwide rights for its development, manufacturing and commercialization.

GAVRETO (pralsetinib) is our third FDA-approved product which we began commercializing in June 2024. GAVRETO is a once daily, small molecule, oral, kinase inhibitor of wild-type RET and oncogenic RET fusions. GAVRETO is approved by the FDA for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA-approved test. GAVRETO is also approved under accelerated approval based on overall response rate and duration response rate, for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). We acquired the rights to research, develop, manufacture and commercialize GAVRETO in the US from Blueprint pursuant to an Asset Purchase Agreement entered in February 2024.

We continue to advance the development of R289, our dual IRAK 1/4 inhibitor program, in an open-label, Phase 1b study to determine the tolerability and preliminary efficacy of the drug in patients with lower-risk MDS who are relapsed, refractory or resistant to prior therapies.

We have strategic development collaborations with MDACC to expand our evaluation of olutasidenib in AML and other hematologic cancers with IDH1 mutations, and with CONNECT to conduct a Phase 2 clinical trial to evaluate olutasidenib in combination with temozolomide in patients with HGG harboring an IDH1 mutation.

We have a RIPK1 inhibitor program in clinical development with our partner Lilly. We also have product candidates in clinical development with partners BerGenBio and Daiichi.

For discussions of recent business updates, please refer to "Part I, Item 1, Business – Business Updates" 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 as described below.

Our revenues from product sales are recognized at net sales price when our customers obtain control of our product, which occurs at a point in time, upon delivery. 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, 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 payor 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.

Recent Accounting Pronouncements

For a discussion of recent 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

Revenues

	Year Ended December 31,		$ Change
	2024	2023	
		(in thousands)	
Product sales, net	$ 144,902	$ 104,294	$ 40,608
Contract revenues from collaborations	34,376	11,488	22,888
Government contracts	—	1,100	(1,100)
Total revenues	$ 179,278	$ 116,882	$ 62,396

The following table summarizes revenues from each of our customers who individually accounted for 10% or more of the total net product sales and revenues from collaborations:

	Year Ended December 31,	
	2024	2023
McKesson Corporation	45%	43%
Cencora Inc. (formerly ASD Healthcare)	20%	21%
Cardinal Health, Inc.	13%	25%
Kissei	11%	*

* Denotes less than 10%

Revenue from product sales is related to our sale of our products in the US, net of chargebacks, discounts and fees, government and other rebates and returns. Typically, our first quarter net sales are impacted by the first quarter reimbursement issues such as the resetting of co-pays and the Medicare donut hole.

TAVALISSE net product sales in 2024 was $104.8 million, increased by 12% compared to $93.7 million in 2023. The increase was primarily due to increased quantities sold, as well as increased price per bottle, partially offset by higher revenue reserves driven by increased government and private payor rebates. REZLIDHIA net product sales in 2024 was $23.0 million, increased by 118% compared to $10.6 million in 2023. The increase was primarily due to increased quantities sold primarily driven by increased number of patients under therapy, partially offset by the higher revenue reserves primarily due to increased government rebates. Following the commercialization of GAVRETO in June 2024, we started recognizing revenue from shipments to our distributors. In 2024, we recognized $17.1 million of GAVRETO net product sales.

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

	Year Ended December 31,		
	2024	2023	$ Change
		(in thousands)	
Kissei	$ 20,414	$ 2,186	$ 18,228
Grifols	9,085	8,782	303
Dr. Reddy's	4,000	—	4,000
Medison	502	520	(18)
Other third parties	375	—	375
Total revenues from collaborations	$ 34,376	$ 11,488	$ 22,888

In 2024, contract revenues from collaborations consisted primarily of revenue from Kissei of $20.4 million, $10.0 million of which was the upfront fee we received from sublicensing olutasidenib, and the remainder was related to the delivery of drug supplies. In addition, we recognized revenue from Grifols of $9.1 million related to delivery of drug supplies and earned royalty, and $4.0 million from Dr. Reddy’s related to an upfront fee from sublicensing olutasidenib. In 2023, contract revenues from collaborations consisted primarily of revenue from Grifols of $8.8 million related to the delivery of drug supplies and earned royalty, and revenue from Kissei of $2.2 million related to the delivery of drug supplies.

No government contract revenue was recognized in 2024. Government contracts revenue in 2023 comprised $1.0 million of government award granted to us by the US Department of Defense (DOD) to support our Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib in hospitalized COVID-19 patients, and $0.1 million award granted to us by Biomedical Advanced Research and Development (BARDA), part of the Office of the Assistant Secretary for the Preparedness and Response at the DHHS for our evaluation of fostamatinib in mitigating the impact of long-term respiratory distress.

We expect our future revenues to include product sales of our existing commercial products and product sales from new commercial products we may have in the future. Our net product sales may be impacted by the demand from our customers, changes to government and private payor rebate programs, chargeback and discount programs, co-payment assistance programs, and any other rebate and discount programs we may enter in the future. In addition, our future revenues may include payments from our existing and new collaboration partners and government grants. As of December 31, 2024, we have deferred revenue of $1.4 million associated with our collaboration agreement with Kissei, which amount will be recognized as revenue upon satisfaction of our remaining performance obligation.

Cost of Product Sales

	Year Ended December 31,		
	2024	2023	$ Change
		(in thousands)	
Cost of product sales	$ 18,647	$ 7,110	$ 11,537

The cost of product sales includes the cost of inventories sold to our customers and to our collaborative partners. Certain inventories sold for the periods presented include inventory quantities acquired or produced prior to the FDA approval of the product, and do not reflect the full cost of the inventories sold, since such costs incurred prior to FDA approval were previously expensed and charged to research and development expense. In particular, we still utilize active pharmaceutical ingredients with zero cost for our TAVALISSE inventories, which we expect to make use of for the next 1 to 2 years. As such, we recognize lower cost of product sales in the periods where we sell inventory quantities acquired or produced prior to the FDA approval of the product. As we acquire or produce more FDA approved inventory quantities in the future, our inventory cost in the balance sheet and cost of product sales will reflect the full cost of acquiring or producing such products. Cost of product sales may also include reserves for potential excess, dated or obsolete inventories, estimated based upon assumptions about future demand and market conditions as well as product shelf lives. Cost of product sales also includes amortization of intangible assets acquired from in-licensing or acquisition of commercialized products, as well as sublicensing revenue fees and royalty expense.

The increase in cost of product sales in 2024 compared to 2023 was primarily due to increased royalty expense and sublicensing revenue fee of $6.8 million, and increased amortization of intangible assets of $1.0 million. In addition, cost of product sales also increased by $3.7 million due to increase in product sales and delivery of drug supplies pursuant to our supply agreements with our collaborative partners.

Research and Development Expense

	Year Ended December 31,		
	2024	2023	$ Change
		(in thousands)	
Research and development expense	$ 23,380	$ 24,522	$ (1,142)
Stock-based compensation expense included in research and development expense	$ 1,514	$ 2,094	$ (580)

The decrease in research and development expense in 2024 compared to 2023 was primarily due to decreased personnel related costs and stock-based compensation expense of $0.9 million, decreased consulting related expenses of $0.9 million, and decreased other various research and development expenses of $0.8 million. These decreases were partially offset by increased clinical trial related expenses of $1.5 million primarily driven by increased research development activities on our ongoing clinical development programs for olutasidenib, which was partly offset by decreased clinical expenses due to the timing of study progress activities on our ongoing IRAK 1/4 inhibitor program, and timing of trial completion activities on our Phase 3 trials of fostamatinib in patients with COVID-19 and wAIHA.

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 clinical studies including IRAK 1/4 inhibitor program; our collaborative partnerships with MDACC and CONNECT to evaluate olutasidenib in AML, other hematologic cancers and glioma; and any other clinical programs we may pursue in the future.

We do not track fully burdened research and development costs separately for each of our drug candidates. 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 expense 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.

Preclinical testing and clinical development are long, expensive and uncertain processes, and we cannot reliably predict the timing of such clinical trial activities. 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 expense by category (in thousands):

	Year Ended December 31,		From January 1, 2007* to December 31, 2024
	2024	2023	
Categories:			
Research	$ 1,217	$ 1,773	$ 270,273
Development	20,141	19,655	582,616
Other	2,022	3,094	279,272
	$ 23,380	$ 24,522	$ 1,132,161

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

“Other” expenses in 2024 and 2023 consisted of allocated facilities costs of $0.5 million and $1.0 million, respectively, and stock-based compensation expense of $1.5 million and $2.1 million, respectively.

Selling, General and Administrative Expense

	Year Ended December 31,		
	2024	2023	$ Change
		(in thousands)	
Selling, general and administrative expense	$ 113,059	$ 105,741	$ 7,318
Stock-based compensation expense included in selling, general and administrative expense	$ 10,879	$ 6,712	$ 4,167

The increase in selling, general and administrative expense in 2024 compared to 2023 was primarily due to increased personnel-related costs and stock-based compensation expense of $7.4 million primarily driven by increased headcount, and increased commercial related expenses of $2.5 million primarily due to expansion of commercial activities. These increases were partially offset by decreased consulting and third party services of $0.9 million and decreased other various sales, general and administrative expenses of $1.7 million.

We expect to incur significant selling, general and administrative expenses, as we expect our commercial related expenses to increase as we continue to expand our commercial activities for our commercial products. We continue to deploy resources to enable our field-based employees to engage with healthcare providers. These engagements have enabled our field team to cover existing prescribers, as well as develop relationships with new prescribers to identify appropriate patients for our products.

Interest Income and Expense

	Year Ended December 31,		
	2024	2023	$ Change
		(in thousands)	
Interest income	$ 2,092	$ 2,272	$ (180)
Interest expense	$ (7,918)	$ (6,872)	$ (1,046)

Interest income is related to our interest-bearing cash and investment balances. The decrease in interest income in 2024 compared to 2023 was primarily driven by lower interest rates.

Interest expense comprised primarily of interest on the outstanding term loans with MidCap. The increase in interest expense in 2024 compared 2023 was primarily due to higher interest rate applicable to the term loans, as well as higher principal outstanding balance of the term loans as additional $20.0 million (Tranche 5) was funded in March 2023.

Provision for income tax

	Year Ended December 31,		
	2024	2023	$ Change
		(in thousands)	
Provision for income taxes	$ 881	$ —	$ 881

The provision for income tax for the year ended December 31, 2024 was related to foreign withholding tax and state taxes. We have not recorded 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. For the year ended December 31, 2023, there was no foreign withholding tax, and we have not recorded state and federal income taxes due to our pre-tax book losses and a full valuation allowance was recorded against our deferred tax assets.

Liquidity and Capital Resources

Liquidity

As of December 31, 2024 and 2023, we had approximately $77.3 million and $56.9 million, respectively, in cash, cash equivalents and short-term investments. We continue to maintain investment portfolios primarily in money market funds, US treasury bills, government-sponsored enterprise securities, 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,	
	2024	2023
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ 31,471	$ (5,743)
Investing activities	4,130	(4,297)
Financing activities	(11,641)	18,367
Net increase in cash and cash equivalents	$ 23,960	$ 8,327

Net cash provided by operating activities in 2024 was primarily due the proceeds from sales of our products, and cash received from our collaboration partners including the $10.0 million upfront payment from Kissei pursuant to the collaboration and license agreement, partially offset by the payments of operating expenses. Net cash used in operating activities in 2023 was primarily due to payments of operating expenses, partially offset by the proceeds from sales of our products, cash received from our collaboration partners including the $20.0 million regulatory milestone payment from Kissei received in January 2023, as well as cash received from government grants.

Net cash provided by investing activities in 2024 comprised primarily of net maturities of short-term investments of $4.4 million, proceeds from sale of property and equipment of $0.1 million, partially offset by payments for acquisition of intangible assets and capital expenditures of $0.4 million. Net cash used in investing activities in 2023 comprised payment of milestone obligations to Forma recorded as intangible assets of $15.0 million, partially offset by net maturities of short-term investments of $10.4 million and proceeds from sale of property and equipment of $0.3 million.

Net cash used in financing activities in 2024 comprised payment of the closing purchase price to Blueprint of $10.0 million and cost share payments to a collaboration partner of $3.6 million, partially offset by the net proceeds from issuance of common stock upon exercise of stock options and participation in the Purchase Plan of $2.0 million. Net cash provided by financing activities in 2023 was primarily due to the net cash proceeds from term loan financing (Tranche 5) of $20.0 million and proceeds from exercise of stock options and participation in the Purchase Plan of $1.0 million, partially offset by our cost share payments to Lilly of $2.6 million.

We believe that our existing capital resources are sufficient to support our current and projected funding requirements, including the continued commercialization of our products, through at least the next 12 months from the date of issuance of this Annual Report on Form 10-K. We used estimates and assumptions that may differ from actual, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with commercializing our products, 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

We finance our operations primarily through sales of our products, and contract payments under our collaboration agreements, as well as through equity securities and debt financing.

Under our existing collaboration agreements that we entered 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. As of December 31, 2024, total future contingent payments to us under our existing agreements with our collaboration partners was approximately $1.5 billion, if all potential product candidates achieved all of the payment triggering events under all of our current agreements. 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. See further discussion in "Note 4 - Sponsored Research and License Agreements

and Government Contracts" 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.

We have an Open Market Sale Agreement with Jefferies, as a sole agent, entered on August 4, 2020, and amended and restated on August 2, 2024. Pursuant to such Open Market Sale Agreement, 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. We have an active Registration Statement filed with the SEC, which registered, among other securities, a base prospectus which covers the offering, issuance, and sale by us of up to $250.0 million in the aggregate of the securities identified from time to time in one or more offerings, which include the $100.0 million of shares of our common stock that may be offered, issued and sold under the Open Market Sale Agreement. As of December 31, 2024, we have not sold any shares of common stock under such Open Market Sale Agreement.

We have a Credit Agreement with MidCap that provides for $60.0 million term loan credit facility, which was fully funded as of December 31, 2024.

Our operations will require significant additional funding in the foreseeable future. Unless and until we can generate sufficient cash from our operating activities, we may choose to raise additional funds through public and/or private offerings of equity securities, debt financings, or from other sources. However, certain external factors such as global pandemics, the global tensions arising from the Russia-Ukraine war and Hamas-Israel war, political and economic legislations, and other factors may continue to rapidly evolve which could significantly disrupt the global financial markets. Our ability to raise additional funds may be adversely impacted by potential worsening of global economic conditions and volatility in the credit and financial markets in the US and worldwide. We could experience an inability to access additional funds, which could in the future negatively affect our capacity for certain corporate development transactions or our ability to make important, opportunistic investments. To the extent that we raise additional funds through the sale of equity, our shareholders' ownership interest may experience substantial dilution. Our current credit facility with MidCap and any debt financing that we can 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 our products, 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 secure and maintain our patent protection and regulatory rights;
- 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, including regulatory rights such as regulatory data exclusivities; 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 with third parties that include, among others, arrangements with vendors, consultants, CROs and universities. Our contract arrangements with these third parties are generally cancellable on reasonable notice, and our obligations under such arrangements are generally based on services performed. We have agreements with certain clinical research organizations to conduct our clinical trials including our strategic development collaborations with MDACC and CONNECT. The timing of payments for any amounts owed under the respective agreements depends on various factors including, but not limited to, patient enrollment and other progress of the clinical trials. 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. We expect to continue entering into contracts in the normal course of business with various third parties to support our commercial activities and research and development programs.

In the ordinary course of business, we enter into agreements with contract manufacturers to manufacture our inventory products. Although the agreements generally provide a termination clause with or without cause, we may still be subjected to payment of cancellation fees. The level of cancellation fees is generally dependent on the timing of the written notice in relation to the commencement of work, with the maximum cancellation fees equal to the full price of the work order. In October 2024, we entered into an agreement with a third-party contract manufacturer to manufacture TAVALISSE that is expected to be delivered starting in 2026 through 2029. As of December 31, 2024, the contractual obligation not included in our financial statements related an agreement that may potentially be subjected to cancellation fees amounted to approximately $24.1 million, with approximately $6.8 million due in one year and $9.3 million due within two to three years. As of December 31, 2024, we have not incurred any cancellation fees under our agreements with contract manufacturers.

As discussed in detail in “Note 4 – Sponsored Research and License Agreements and Government Contracts” 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, under the Lilly Agreement, although our co-funding obligation for development of ocadusertib (previously R552) in the US, Europe, and Japan ended on April 1, 2024, we have the right to opt-in to co-funding, upon us providing notice to Lilly within 30 days of certain events, as specified in the agreement. If we decide to exercise our opt-in right, we will be required to continue to share in the global development costs with Lilly, and if we later exercise our second opt-out right (no later than April 1, 2025), our share in global development costs will be up to a specified cap through December 31, 2025, as provided for in the Lilly Agreement.

Also, as discussed in detail in “Note 4 – Sponsored Research and License Agreements and Government Contracts” and “Note 5 – In-Licensing and Acquisition” 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 license and transition services agreement with Forma, Forma is entitled to potential development and regulatory milestone payment and tiered royalty payments on net sales as well as certain portion of sublicensing revenue. Further, following our olutasidenib sublicensing agreements with Kissei and Dr. Reddy’s, Forma is entitled to the portion of the sublicensing revenue we receive from Kissei and Dr. Reddy’s under such respective agreements.

Additionally, as discussed in detail in "Note 5 – In-Licensing and Acquisition" 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 an Asset Purchase Agreement with Blueprint, in addition to unpaid purchase price consideration, Blueprint is entitled to potential commercial and regulatory milestone payments, as well as tiered royalty payments.

We have a contractual commitment with respect to our credit facility with MidCap. Under the amended Credit Agreement, the term loans mature on September 1, 2027, and the interest-only period is through October 1, 2025. As of December 31, 2024, the outstanding principal amount of the loan was $60.0 million, of which $7.5 million principal payments are due within 12 months. As of December 31, 2024, future interest calculated using the base interest rate as per the amended Credit Agreement, and the final fee payments associated with the credit facility amounted to $14.3 million, with approximately $6.5 million payable within 12 months.

As of December 31, 2024, we have a contractual commitment related to our sublease agreement with Atara for approximately $0.3 million, payable through the expiration of the sublease agreement in May 2025. In February 2025, we entered into a lease agreement with 611 Gateway to lease the same office space currently subleased from Atara. Our contractual commitment related to the lease agreement with 611 Gateway was $1.4 million, of which $0.3 million is payable in the next 12 months from December 31, 2024.

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. 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.

Interest on our outstanding loan from MidCap is subject to changes in Secured Overnight Financing Rate (SOFR). Fluctuations in SOFR above the contractual floor rate may have a material effect on our interest payment obligations in the future.

Item 8. Financial Statements and Supplementary Data

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Rigel Pharmaceuticals, Inc.

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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, 2024 and 2023, the related statements of operations, comprehensive income (loss), stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, 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, 2024, 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 4, 2025 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 account or disclosure 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 and/or privately-negotiated 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, 2024, the Company has recorded net liabilities for product sales allowances and discounts of $26.4 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, which include product sold, contractual terms and discount rates, 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 over material ending accrual balances. 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 4, 2025

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

	As of December 31,	
	2024	2023
Assets		
Current assets:		
Cash and cash equivalents	$ 56,746	$ 32,786
Short-term investments	20,575	24,147
Accounts receivable, net	41,615	30,550
Inventories	6,002	5,522
Prepaid and other current assets	10,165	6,261
Total current assets	135,103	99,266
Property and equipment, net	92	165
Intangible assets, net	27,100	13,878
Operating lease right-of-use assets	246	861
Other assets	1,435	3,055
Total assets	$ 163,976	$ 117,225
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 3,339	$ 7,142
Accrued compensation	10,139	8,676
Accrued research and development	4,073	3,513
Revenue reserves and refund liability	26,440	15,684
Loans payable, net, current portion	7,272	7,229
Other accrued liabilities	10,396	5,334
Deferred revenue	1,355	1,355
Lease liabilities, current portion	285	692
Other long-term liabilities, current portion	—	3,642
Total current liabilities	63,299	53,267
Acquisition-related liabilities	5,000	—
Long-term portion of lease liabilities	—	285
Long-term portion of loans payable, net	52,408	52,373
Other long-term liabilities	39,981	39,944
Total liabilities	160,688	145,869
Commitments		
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; none issued and outstanding as of December 31, 2024 and 2023	—	—
Common stock [(1)], $0.001 par value; 400,000,000 shares authorized; 17,710,216 and 17,482,513 shares issued and outstanding as of December 31, 2024 and 2023, respectively	18	17
Additional paid-in capital [(1)]	1,393,325	1,378,881
Accumulated other comprehensive income	10	8
Accumulated deficit	(1,390,065)	(1,407,550)
Total stockholders' equity (deficit)	3,288	(28,644)
Total liabilities and stockholders' equity (deficit)	$ 163,976	$ 117,225

(1) Shares issued and outstanding, including appropriate reclassifications between common stock and additional paid-in capital, have been restated to reflect the 1-for-10 reverse stock split effected on June 27, 2024 on a retroactive basis for the respective periods presented.

See Accompanying Notes to Financial Statements.

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

	Year Ended December 31,		
	2024	2023	2022
Revenues:			
Product sales, net	$ 144,902	$ 104,294	$ 76,718
Contract revenues from collaborations	34,376	11,488	39,024
Government contracts	—	1,100	4,500
Total revenues	179,278	116,882	120,242
Costs and expenses:			
Cost of product sales	18,647	7,110	1,749
Research and development	23,380	24,522	60,272
Selling, general and administrative	113,059	105,741	112,451
Restructuring charges	—	—	1,320
Total costs and expenses	155,086	137,373	175,792
Income (loss) from operations	24,192	(20,491)	(55,550)
Interest income	2,092	2,272	684
Interest expense	(7,918)	(6,872)	(3,707)
Income (loss) before income taxes	18,366	(25,091)	(58,573)
Provision for income taxes	881	—	—
Net income (loss)	$ 17,485	$ (25,091)	$ (58,573)
Net income (loss) per share[(1)]			
Basic	$ 0.99	$ (1.44)	$ (3.44)
Diluted	$ 0.99	$ (1.44)	$ (3.44)
Weighted average shares used in computing net income (loss) per share [(1)]			
Basic	17,579	17,401	17,049
Diluted	17,687	17,401	17,049

(1) Share and per share amounts have been restated to reflect the 1-for-10 reverse stock split effected on June 27, 2024 on a retroactive basis for the respective periods presented.

See Accompanying Notes to Financial Statements.

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

	Year Ended December 31,		
	2024	2023	2022
Net income (loss)	$ 17,485	$ (25,091)	$ (58,573)
Other comprehensive income (loss):			
Net unrealized gain (loss) on short-term investments	2	161	(51)
Comprehensive income (loss)	$ 17,487	$ (24,930)	$ (58,624)

See Accompanying Notes to Financial Statements.

RIGEL PHARMACEUTICALS, INC.
STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except number of shares)

	Common Stock [1]		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital [1]	Income (Loss)	Deficit	Equity (Deficit)
Balance as of January 1, 2022	17,160,175	$ 17	$ 1,354,345	$ (102)	$ (1,323,886)	$ 30,374
Net loss	—	—	—	—	(58,573)	(58,573)
Net change in unrealized loss on short-term investments	—	—	—	(51)	—	(51)
Issuance of common stock upon exercise of options and participation in Purchase Plan	158,016	—	2,124	—	—	2,124
Issuance of common stock upon vesting of restricted stock units (RSUs)	21,625	—	—	—	—	
Stock-based compensation expense	—	—	12,510	—	—	12,510
Balance as of December 31, 2022	17,339,816	17	1,368,979	(153)	(1,382,459)	(13,616)
Net loss	—	—	—	—	(25,091)	(25,091)
Net change in unrealized loss on short-term investments	—	—	—	161	—	161
Issuance of common stock upon exercise of options and participation in Purchase Plan	99,196	—	1,049			1,049
Issuance of common stock upon vesting of RSUs	43,501	—	—			—
Stock-based compensation expense	—	—	8,853			8,853
Balance as of December 31, 2023	17,482,513	17	1,378,881	8	(1,407,550)	(28,644)
Net income	—	—	—	—	17,485	17,485
Net change in unrealized gain on short-term investments	—	—	—	2	—	2
Issuance of common stock upon exercise of options and participation in Purchase Plan	158,795	1	1,963	—	—	1,964
Issuance of common stock upon vesting of RSUs	68,908	—	—	—	—	—
Stock-based compensation expense	—	—	12,481	—	—	12,481
Balance as of December 31, 2024	17,710,216	$ 18	$ 1,393,325	$ 10	$ (1,390,065)	$ 3,288

(1) All share amounts in this column, including appropriate reclassifications between common stock and additional paid-in capital, have been restated to reflect the 1-for-10 reverse stock split effected on June 27, 2024 on a retroactive basis for the respective periods presented.

See Accompanying Notes to Financial Statements.

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

	Year Ended December 31,		
	2024	2023	2022
Operating activities			
Net income (loss)	$ 17,485	$ (25,091)	$ (58,573)
Adjustments to reconcile net income (loss) to net cash provided by operating activities:			
Stock-based compensation expense	12,393	8,806	12,385
(Gain) loss on sale and disposal of fixed assets	(79)	266	(138)
Depreciation and amortization	2,228	1,238	998
Non-cash interest expense	—	—	682
Net amortization of discount on short-term investments and term loans	(709)	(479)	(63)
Changes in assets and liabilities:			
Accounts receivable, net	(11,065)	9,770	(24,848)
Inventories	764	1,172	(2,377)
Prepaid and other current and non-current assets	(3,440)	2,054	(513)
Right-of-use assets	615	1,069	7,773
Accounts payable	(3,803)	(366)	3,788
Accrued compensation	1,463	(190)	(1,824)
Accrued research and development	560	(4,195)	(2,676)
Revenue reserves and refund liability	10,756	3,539	4,230
Other accrued liabilities	4,995	(1,151)	1,709
Lease liability	(692)	(1,128)	(8,546)
Deferred revenue	—	(14)	(1,227)
Other current and long-term liabilities	—	(1,043)	(4,538)
Net cash provided by (used in) operating activities	31,471	(5,743)	(73,758)
Investing activities			
Maturities of short-term investments	39,700	41,650	101,228
Purchases of short-term investments	(35,272)	(31,206)	(28,894)
Capital expenditures	(36)	—	(450)
Payments for acquisition of intangible assets	(360)	(15,000)	—
Proceeds from sale of property and equipment	98	259	893
Net cash provided by (used in) investing activities	4,130	(4,297)	72,777
Financing activities			
Net proceeds from term loan financing	—	19,950	19,542
Net proceeds from issuance of common stock from equity plans	1,964	1,049	2,124
Closing purchase price payment related to asset acquisition	(10,000)	—	—
Cost share payments to a collaboration partner	(3,605)	(2,632)	(15,116)
Net cash (used in) provided by financing activities	(11,641)	18,367	6,550
Net increase in cash and cash equivalents	23,960	8,327	5,569
Cash and cash equivalents at beginning of period	32,786	24,459	18,890
Cash and cash equivalents at end of period	$ 56,746	$ 32,786	$ 24,459
Supplemental disclosure of cash flow information			
Interest paid	$ 7,039	$ 5,848	$ 2,495
Income taxes paid	331	—	—
Purchases of intangible asset included within accounts payable	—	—	15,000
Acquisition-related liabilities	5,000	—	—

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 developing and providing novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. We focus on products that address signaling pathways that are critical to disease mechanisms.

TAVALISSE (fostamatinib disodium hexahydrate) is our first product approved by the FDA. TAVALISSE is the only approved 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 and the UK (as TAVLESSE), and in Canada, Israel and Japan (as TAVALISSE) for the treatment of chronic ITP in adult patients.

REZLIDHIA (olutasidenib) is our second FDA-approved product. REZLIDHIA capsules are indicated for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. We in-licensed REZLIDHIA from Forma with exclusive, worldwide rights for its development, manufacturing and commercialization.

GAVRETO (pralsetinib) is our third FDA-approved product which we began commercializing on June 27, 2024. GAVRETO is a once daily, small molecule, oral, kinase inhibitor of wild-type RET and oncogenic RET fusions. GAVRETO is approved by the FDA for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA-approved test. GAVRETO is also approved under accelerated approval based on overall response rate and duration response rate, for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). We acquired the rights to research, develop, manufacture and commercialize GAVRETO in the US from Blueprint pursuant to an Asset Purchase Agreement entered in February 2024.

We continue to advance the development of R289, our dual IRAK 1/4 inhibitor program, in an open-label, Phase 1b study to determine the tolerability and preliminary efficacy of the drug in patients with lower-risk MDS who are relapsed, refractory or resistant to prior therapies.

We have strategic development collaborations with MDACC to expand our evaluation of olutasidenib in AML and other hematologic cancers with IDH1 mutations, and with CONNECT to conduct a Phase 2 clinical trial to evaluate olutasidenib in combination with temozolomide in patients with HGG harboring an IDH1 mutation.

We have a RIPK1 inhibitor program in clinical development with our partner Lilly. We also have product candidates in clinical development with partners BerGenBio and 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).

Reverse Stock Split

We filed with the Secretary of State of the State of Delaware a certificate of amendment to our Amended and Restated Certificate of Incorporation, to effect a 1-for-10 reverse stock split, effective June 27, 2024. As a result of the reverse stock split, every ten issued and outstanding shares of our common stock were automatically combined into one issued and outstanding share of common stock. Accordingly, an amount equal to the par value of the decreased shares resulting from the reverse stock split was reclassified from common stock to additional paid-in capital on the balance sheet and statement of changes in stockholders' equity (deficit). No fractional shares were issued in connection with the reverse stock split. Stockholders who otherwise would be entitled to receive fractional shares of common stock were entitled to receive the cash value equal to the fraction to which the stockholder would otherwise be entitled, multiplied by the closing price of the common stock as reported by Nasdaq on the last trading day prior to the effective date of the split. As a result of the reverse stock split, proportionate adjustments were made to the number of shares underlying (and as applicable, the exercise or conversion prices of) our outstanding equity awards and to the number of shares of common stock issuable under our equity incentive plans. The reverse stock split did not change the par value of our common stock, which remains $0.001, or the authorized number of shares of our common stock. All share amounts and per share amounts disclosed in this Annual Report on Form 10-K have been adjusted to reflect the reverse stock split on a retroactive basis for the respective periods presented.

Liquidity

As of December 31, 2024, we had approximately $77.3 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 through 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 certain judgments, estimates and assumptions that could affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Critical accounting estimates and assumptions made by management include those relating to estimates around our product sales allowances and discounts; estimates around accounting for collaboration arrangements; and estimates around research and development accruals. Other accounting estimates also include but not limited to allowance for credit losses, inventory reserves, estimated general accruals, valuation of our stock option awards and probability of achievement of corporate performance-based milestones for our performance-based stock option awards, valuation allowance on deferred tax asset, estimated useful lives of long-lived assets, and any potential impairment loss. We base our estimates and assumptions on historical experience and on various other assumptions we believe to be applicable, and evaluate them on an ongoing basis to ensure they remain reasonable under current conditions. Actual results could differ significantly from those estimates, which could have a material impact on our business, results of operations, and financial condition.

Segment Reporting

Operating segments are defined as components of an enterprise about which separate financial information is available that is evaluated regularly by the chief operating decision maker (CODM), or decision making-group, in deciding how to allocate resources and in assessing performance. Our CODM is our chief executive officer. We view our operations and manage our business as one operating segment.

In November 2023, FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, which expands public entities' segment disclosures, among others, requiring disclosure of significant segment expenses that are regularly provided to the CODM and included within each reported measure of segment profit or loss; an amount and description of its composition for other segment items; and interim disclosures of a reportable segment's profit or loss and assets. This new guidance was effective for us beginning on this annual report on Form 10-K for the year ended December 31, 2024, and applied retrospectively to all prior periods presented. The impact

of the adoption of this guidance was not material to our financial position or results of operations, as the requirements impact only segment reporting disclosures in our notes to financial statements. See ‘Note 15 – Segment Information” for further details.

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) we satisfy our 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 our customers obtain control of our product, which occurs at a point in time upon delivery. Our specialty distributors resell our products to specialty pharmacy providers, health care providers, hospitals and clinics. In addition to distribution agreements with our specialty distributors, we also have arrangements with certain 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 specialty distributors 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. We also have rebate program agreements with certain PBMs for certain product, 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 revenue reserves and refund liability 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 specialty distributors who directly purchase the product from us. These specialty distributors 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 specialty distributors. The estimated obligations arising from these chargebacks and discounts are recorded as revenue reserves within revenue reserves and refund liability 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 Contracts

There is limited US GAAP accounting guidance for for-profit business entities that receives government assistance. We utilized other accounting standards, and have elected to analogize to International Financial Reporting Standards, specifically International Accounting Standards (IAS) 20, *Accounting for Government Grants and Disclosures of Government Assistance.* Following IAS 20, we account for government assistance as government contracts revenue within 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. Following the guidance of ASU 2021-10, *Disclosures by Business Entities about Government Assistance,* we disclose the nature of the transactions and the related accounting policy used, the line items on the balance sheet and income statement that are affected by the transaction and the amounts applicable to each financial statement line item, and the significant terms and conditions of the transactions, including commitment and contingencies. See "Note 4 – Sponsored Research and License Agreements and Government Contracts" for further discussions of government assistance we received.

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. We estimate volatility using the historical share price performance over the expected life of the option. We use historical data to determine the applicable expected term for each of the other option groups. 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. The expected dividend yield is 0% as we have not paid and do not expect to pay dividends in the future. We segregate option awards into the following three homogenous groups for the purpose of determining fair values of options: officers and directors, all other employees, and consultants.

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 the RSU grant is based on the market price of our common stock on the date of grant.

Accounts Receivable

Accounts receivable are recorded net of customer allowances for prompt payment discounts and any allowance for doubtful accounts. We monitor the financial performance and creditworthiness of our customers so that we can properly assess and respond to changes in their credit profile. We have not historically experienced credit losses and no amounts were reserved for estimated losses as of the balance sheet dates presented.

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

	Year Ended December 31,		
	2024	2023	2022
Balance at the beginning of the year	$ 180	$ 136	$ 106
Provision for prompt payment discount	1,035	686	557
Reduction in prompt payment discount	(969)	(642)	(527)
Balance at end of the year	$ 246	$ 180	$ 136

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. We have not historically experienced any significant credit losses related to these financial instruments and do not believe that we are exposed to any significant credit risk related to these instruments.

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 our product to our customers. Accounts receivable may also include outstanding invoices from our collaboration partners with respect to the related sponsored research and license agreements and government contracts. As of December 31, 2024, 81% of our accounts receivable are outstanding invoices to our customers related to product sales in the US, and the remaining 19% are outstanding invoices from our collaboration partners, mainly Dr. Reddy's and Grifols. As of December 31, 2023, 87% of our accounts receivable are outstanding invoices to our customers related to product sales in the US, and the remaining 13% are outstanding invoices from our collaboration partners, mainly Grifols.

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

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 (deficit) and comprehensive income (loss). The cost of securities sold is based on the specific identification method.

We periodically evaluate our available-for-sale marketable debt securities for impairment. When the fair value of a marketable debt security is below its amortized cost, the amortized cost is reduced to its fair value if it is more likely than not that we are required to sell the impaired security before recovery of our amortized cost basis, or we have the intention to sell the security. If neither of these conditions are met, we determine whether the impairment is due to credit losses by comparing the present value of the expected cash flows of the security with its amortized cost basis. The

amount of impairment recognized is limited to the excess of the amortized cost over the fair value of the security. An allowance for credit losses for the excess of amortized cost over the expected cash flows is recorded in other income (expense), net on the statements of operations. Impairment losses that are not credit-related are included in accumulated other comprehensive income (loss) in stockholders' equity (deficit).

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.

- 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.

Inventories and Cost of Product Sales

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, and is valued using the first-in, first-out method. Inventory costs primarily consist of active pharmaceutical ingredients, third-party manufacturing costs and allocated internal overhead costs. We capitalize inventory costs when the product is approved by the FDA, or when based on management's judgment, future commercialization was considered probable, and the future economic benefits are expected to be realized. Prior to FDA approval of a product, costs to purchase active pharmaceutical ingredients including costs to manufacture a product are charged to research and development expense when incurred. Our physical inventories as of balance sheet dates include inventory quantities where costs have been previously charged to research

and development expense since such costs were incurred prior to FDA approval of the product.

We provide reserves for potential excess, dated or obsolete inventories based upon assumptions about future demand and market conditions, as well as product shelf life. Inventories that are not expected to be consumed beyond our normal operating cycle are classified as non-current inventories and included within other assets in the balance sheet.

Cost of product sales primarily includes cost of inventories sold, and product shipping and handling costs. Cost of product sales also include amortization of intangible assets and royalty expense incurred pursuant to our agreements with Forma and Blueprint.

Property and Equipment

Property and equipment are stated at cost net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which range from three to seven years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful lives of the assets. Maintenance and repairs are charged to expense as incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in statements of operations in the period realized.

Intangible Assets

Intangible assets are amortized over the estimated useful life of the assets. We perform an impairment review of intangible assets whenever events or changes in business circumstances indicate the carrying amount of such asset may not be fully recoverable. If events or changes in circumstances suggest that the carrying amount of the intangible assets may not be recoverable, we will estimate the future cash flows expected to be generated from its use or eventual disposition. If the expected future undiscounted cash flows are less than the carrying amount of the asset, we will recognize an impairment loss based on the excess of the carrying amount over the fair value of such asset.

Research and Development Expenses

Research and development expenses include costs incurred to conduct research and development, including scientific personnel wages and associated employee benefits, research and development supplies and equipment, payments to collaborative clinical research partners, consulting fees and other various research and development related costs.

We have various contracts with third parties related to our research and development activities, including strategic development collaborations. Costs 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 an approved drug are charged to research and development expenses at the time of purchase.

We make accounting 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.

Research and development expenses also include milestone payment obligations incurred prior to regulatory approval of the product, which are accrued when the event requiring payment of the milestone occurs.

Advertising Expense

Advertising costs are expensed as incurred and are included within selling general and administrative expenses in the statements of operations. Advertising costs for the years ended December 31, 2024, 2023 and 2022 amounted to $2.1 million, $3.1 million, and $2.7 million, respectively.

Leases

We account for leases in accordance with ASU No. 2016-02*, Leases (Topic 842)*. Topic 842 requires a lessee to determine if an arrangement is a lease or contains a lease at contract inception. Right-of-use lease assets represent the right to use the underlying asset for the lease term and the lease liability represents the obligation 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 future minimum lease payments over the term of the lease. The operating right-of-use lease asset may also include initial direct costs and prepaid lease payments less lease incentives. In measuring the present value of the future minimum lease payments, we generally use our incremental borrowing rate as our lease agreement do not provide an implicit borrowing rate and we deemed that our incremental borrowing rate would be the rate of interest that we would have to pay to borrow on a collateralized basis over a similar term of the lease payments in a similar economic environment. If a lease includes options to extend the lease term, we do not assume the option will be exercised in the initial lease term assessment unless there is reasonable certainty that we will renew based on an assessment of economic factors present as of the lease commencement date. Leases with an initial term of 12 months or less are not recorded on the balance sheet. Lease expense for our operating leases 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.

Restructuring

Restructuring costs comprised severance, other termination benefit costs, and stock-based compensation expense for stock award and stock option modifications related to workforce reductions. 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.

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.

Recent Accounting Pronouncements

In November 2024, FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures.* This new guidance improves the disclosures about a public business entity's expenses by requiring more detailed information about the types of expenses (including purchases of inventory, employee compensation, depreciation and amortization) included within income statement expense captions. This guidance is effective for our annual reporting for the fiscal year ending December 31, 2027, and interim reporting periods beginning on fiscal year ending December 31, 2028, with early adoption is permitted. Upon adoption, this guidance may be applied prospectively to reporting periods after the effective date or retrospectively to all periods presented in the financial statements. We are currently evaluating this guidance and assessing the potential impact on our

financial statements and disclosures.

In December 2023, FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures*, which enhance the annual disclosure requirements regarding the tax rate reconciliation and incomes taxes paid information. This update is effective for our fiscal year ending December 31, 2025, and maybe adopted on a prospective or retrospective basis. Early adoption is permitted. We are currently assessing the impact of adopting this guidance but does not expect to have a significant impact to our financial statements and disclosures.

Other recently issued accounting guidance not discussed in this Annual Report on Form 10-K are either not applicable or did not have, or are not expected to have, a material impact on us.

2. NET INCOME (LOSS) PER SHARE

Basic net income (loss) per share is computed by dividing net income (loss) by the weighted-average number of shares of common stock outstanding during the period. Diluted net income (loss) per share is computed by dividing net income (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, RSUs and shares issuable under our Employee Stock Purchase Plan (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 earnings per share (in thousands except per share amounts):

	Year Ended December 31,		
	2024	2023	2022
EPS Numerator:			
Net income (loss)	$ 17,485	$ (25,091)	$ (58,573)
EPS Denominator—Basic:			
Weighted-average common shares outstanding	17,579	17,401	17,049
EPS Denominator—Diluted:			
Weighted-average common shares outstanding	17,579	17,401	17,049
Dilutive effect of stock options, RSUs and shares under Purchase Plan	108	—	—
Weighted-average shares outstanding and common stock equivalents	17,687	17,401	17,049
Net income (loss) per share			
Basic	$ 0.99	$ (1.44)	$ (3.44)
Diluted	$ 0.99	$ (1.44)	$ (3.44)

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,		
	2024	2023	2022
Stock options	3,391	3,411	3,469
RSUs	108	186	110
Total	3,499	3,597	3,579

3. REVENUES

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

	Year Ended December 31,		
	2024	2023	2022
Product sales:			
Gross product sales	$ 209,924	$ 147,058	$ 108,523
Discounts and allowances	(65,022)	(42,764)	(31,805)
Total product sales, net	144,902	104,294	76,718
Revenues from collaborations:			
License revenue	14,000	—	7,932
Milestone revenue	—	75	25,000
Delivery of drug supplies, royalty and others	20,376	11,413	6,092
Total revenues from collaborations	34,376	11,488	39,024
Government contracts	—	1,100	4,500
Total revenues	$ 179,278	$ 116,882	$ 120,242

Revenue from product sales is related to sales of our commercial products to our customers. For detailed discussions of our revenues from collaboration and government contracts, see "Note 4 – Sponsored Research and License Agreements and Government Contracts."

Our product sales revenue is net of chargebacks, discounts and fees, government and other rebates and returns. Of the total discounts and allowances from gross product sales for the years ended December 31, 2024, 2023 and 2022, $64.0 million, $41.5 million and $30.9 million, respectively, was accounted for as additions to revenue reserves and refund liability, and $1.0 million, $1.3 million and $0.9 million, respectively, 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. The following tables summarize the activities in chargebacks, discounts and fees, government and other rebates and returns that were accounted for revenue reserves and refund liability, for each of the periods presented (in thousands):

	Chargebacks, Discounts and Fees	Government and Other Rebates	Returns	Total
Balance as of January 1, 2024	$ 8,236	$ 3,517	$ 3,931	$ 15,684
Provision related to current period sales	49,071	13,586	1,315	63,972
Credit or payments made during the period	(43,933)	(8,760)	(523)	(53,216)
Balance as of December 31, 2024	$ 13,374	$ 8,343	$ 4,723	$ 26,440

	Chargebacks, Discounts and Fees	Government and Other Rebates	Returns	Total
Balance as of January 1, 2023	$ 6,213	$ 2,636	$ 3,296	$ 12,145
Provision related to current period sales	32,330	8,299	869	41,498
Credit or payments made during the period	(30,307)	(7,418)	(234)	(37,959)
Balance as of December 31, 2023	$ 8,236	$ 3,517	$ 3,931	$ 15,684

The following table summarizes revenues from each of our customers who individually accounted for 10% or more of the total net product sales and revenues from collaborations:

	Year Ended December 31,		
	2024	2023	2022
McKesson Corporation	45%	43%	31%
Cencora Inc. (formerly ASD Healthcare)	20%	21%	17%
Cardinal Health, Inc.	13%	25%	19%
Kissei	11%	*	24%

* Denotes less than 10%

4. SPONSORED RESEARCH AND LICENSE AGREEMENTS AND GOVERNMENT CONTRACTS

Sponsored Research and License Agreements

We conduct research and development programs independently and in connection with our corporate collaborators. As of December 31, 2024, we are a party to collaboration agreements with Lilly to develop and commercialize ocadusertib (previously R552), a RIPK1 inhibitor, for the treatment of non-CNS diseases and collaboration aimed at developing additional RIPK1 inhibitors for the treatment of CNS diseases; with Grifols to commercialize fostamatinib for human diseases in all indications, in Grifols territory which includes Europe, the UK, Turkey, the Middle East, North Africa and Russia (including Commonwealth of Independent States); with Kissei to develop and commercialize fostamatinib in Japan, China, Taiwan and Korea and olutasidenib in Japan, Korea and Taiwan; with Medison to commercialize fostamatinib in all indications, in Medison territory which includes Canada and Israel; with Knight to commercialize fostamatinib in all indications, in Knight territory which includes Latin America, consisting of Mexico, Central and South America, and the Caribbean; and with Dr. Reddy's to commercialize olutasidenib in Dr. Reddy's territory which includes Latin America, South Africa, India, Australia, New Zealand, and certain countries in the CIS, Southeast Asia region and North Africa.

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.

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. As of December 31, 2024, total future contingent payments to us under all of above existing agreements was approximately $1.5 billion, if all potential product candidates achieved all of the payment triggering events under all of our current agreements. Of this amount, approximately $279.5 million relates to the achievement of development events, $313.6 million relates to the achievement of regulatory events and $902.0 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.

We account for the milestone payments when such 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 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.

Global Exclusive License Agreement with Lilly

We have a global exclusive license and collaboration agreement with Lilly (Lilly Agreement) entered in February 2021, which became effective on March 27, 2021, upon clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, to develop and commercialize ocadusertib (previously R552) 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 Lilly agreement, we granted Lilly the exclusive rights to develop and commercialize ocadusertib and related RIPK1 inhibitors in all indications worldwide. The parties' collaboration is governed through a joint governance committee and appropriate subcommittees.

Under the terms of Lilly 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. We are also entitled to additional milestone payments for non-CNS disease products consisting of up to $330.0 million milestone payments upon the achievement of specified development and regulatory milestones, and up to $100.0 million in sales milestone payments on a product-by-product basis. In addition, depending on the extent of our co-funding of ocadusertib 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 are also eligible to receive milestone payments for CNS disease products consisting of up to $255.0 million in milestone payments upon the achievement of specified development, regulatory and commercial milestones, and up to $150.0 million in sales milestone payments on a product-by-product basis. 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.

Under 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. We are responsible for 20% of development costs for ocadusertib in the US, Europe, and Japan, up to a specified cap. Lilly is responsible for funding the remainder of all development activities for ocadusertib and other non-CNS disease development candidates. Pursuant to the terms of the Lilly Agreement, we have the right to opt-out of co-funding the ocadusertib development activities in the US, Europe and Japan at two different specified times and as a result receive lesser royalties from sales. Prior to us providing our first opt-out notice and the amendment to the Lilly Agreement as discussed below, under the Lilly Agreement, we were required to fund our share of the ocadusertib development activities in the US, Europe, and Japan up to a maximum funding commitment of $65.0 million through April 1, 2024.

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.

At the inception of the Lilly Agreement, given our rights to opt-out from the development of ocadusertib, we believed at the minimum, we had 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 accreted on such liability over the expected commitment period and adjusted for timing of expected cost share payments. No interest was accreted during the years ended December 31, 2024 and 2023, and $0.7 million of interest was accreted during the year ended December 31, 2022. At the inception, 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. 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. The transaction price allocated to the CNS penetrant IP of $6.7 million was recognized as revenue from the effective date of the Lilly Agreement through the eventual acceptance by Lilly in June 2022 using the input method. There was no

outstanding deferred revenue related to Lilly Agreement as of December 31, 2024 and 2023.

On September 28, 2023, we entered into an amendment to the Lilly Agreement which provided, among others that if we exercise our first opt-out right, we have the right to opt-in to the co-funding of ocadusertib development, upon us providing notice to Lilly within 30 days of certain events as specified in the Lilly Agreement, and as a result receive greater royalties from sales. If we decide to exercise our opt-in right, we will be required to continue to share in global development costs, and if we later exercise our second opt-out right (no later than April 1, 2025), our share in global development costs will be up to a specified cap through December 31, 2025, as provided for in the Lilly Agreement.

We paid Lilly $21.4 million for our share of development costs incurred through April 1, 2024. As of December 31, 2024 and 2023, the outstanding liability to Lilly reported within other long-term liabilities (current and non-current) in the balance sheets amounted to $40.0 million and $43.6 million, respectively. As discussed above, following the amendment to the Lilly Agreement, and us providing the first opt-out notice to Lilly, our cost share obligation for ocadusertib development ended on April 1, 2024. Although currently we are no longer obligated to share in the ocadusertib development costs incurred subsequent to April 1, 2024, the outstanding liability reported in our balance sheet as of December 31, 2024 amounting to $40.0 million has not been recognized as revenue because we cannot conclude that it is probable that a significant reversal of the amount of revenue, if recognized, will not occur until the likelihood of us exercising our opt-in right becomes remote, or when the opt-in right period lapses.

Grifols License Agreement

We have a commercialization license agreement with Grifols entered in January 2019 with exclusive rights to commercialize fostamatinib for human diseases, and non-exclusive rights to develop, fostamatinib in Grifols territory. 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 are also entitled to receive stepped double-digit royalty payments based on tiered net sales which may reach 30% of net sales. In January 2020, the EC granted a centralized MA for fostamatinib valid throughout the EU, and in the UK after the departure of the UK from the EU, for the treatment of chronic ITP in adult patients who are refractory to other treatments. With this approval, in February 2020, we received $20.0 million non-refundable payment, consisted 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, based on the terms of our collaboration agreement with Grifols. We accounted for this agreement under ASC 606 and recognized the corresponding revenue in the period we satisfied the performance obligations. As of December 31, 2024 and 2023, there was no outstanding deferred revenue.

We have a Commercial Supply Agreement with Grifols entered in October 2020 to supply and sell our drug product priced at a certain markup specified in the agreement, in quantities Grifols shall order from us pursuant to and in accordance with the agreement. For the years ended December 31, 2024, 2023, and 2022, we recognized $4.0 million, $5.6 million and $1.6 million, respectively, of revenue related to delivery of drug supply to Grifols.

We recognized royalty revenue from Grifols of $5.1 million, $3.2 million and $0.7 million for the years ended December 31, 2024, 2023 and 2022, respectively.

Kissei License Agreement – Olutasidenib

On September 3, 2024, we entered into a collaboration and license agreement with Kissei, pursuant to which Kissei was granted exclusive rights to develop and commercialize olutasidenib in all human diseases in Japan, Korea and Taiwan. Kissei is responsible for performing and funding the development activities for olutasidenib in the Kissei territory and we retained the co-exclusive right to conduct development activities in the Kissei territory solely for the purpose of supporting and obtaining regulatory approval of and commercializing olutasidenib in the world outside the Kissei territory. Under the terms of the agreement, we received a one-time, non-refundable, and non-creditable upfront cash payment of $10.0 million, with the potential for up to an additional $152.5 million in development, regulatory and commercial milestone payments, and will receive mid twenty to lower thirty percent, tiered, escalated net sales-based payments for the supply of olutasidenib, subject to certain standard reductions and offsets. Pursuant to the agreement, Kissei is responsible for companion diagnostic development in Japan, for which we will share 50% of the costs incurred

by Kissei, up to $3.0 million, which are creditable against future milestones and transfer price payments owed to us. We remain responsible for the manufacture and supply of olutasidenib for all development and commercialization activities under the agreement. Pursuant to the concurrently executed supply agreement, we will supply Kissei with bulk drug product for use under the collaboration and license agreement.

We accounted for this agreement following ASC 606 and concluded at the inception of the agreement, the upfront cash payment of $10.0 million was the consideration for granting the license right to Kissei, and there are no other material deliverables associated with the upfront payment. Accordingly, we recognized the upfront payment as revenue during the year ended December 31, 2024. The variable considerations related to future development, regulatory and commercial milestones were fully constrained because it was probable that a significant reversal of cumulative revenue would occur, given the inherent uncertainty of success with these future milestones. We will re-evaluate the transaction price in each reporting period as uncertain events are resolved or other changes in circumstances occur. We will recognize revenues related to the supply of olutasidenib upon delivery and when we are entitled to receive the product transfer price payments.

Under the license and services agreement with Forma as discussed in "Note 5 – In-Licensing and Acquisition", Forma is entitled to a certain portion of sublicensing revenue, which include, but are not limited to, upfront payments, milestone payments and royalties, that we receive from a third party sublicensee. Following the collaboration and license agreement with Kissei as discussed above, Forma is entitled to a portion of the sublicensing revenue we receive from Kissei. With the receipt of the upfront payment from Kissei, we recognized a $2.3 million sublicense revenue fee payable to Forma during the year ended December 31, 2024, which we recorded within cost of product sales.

Kissei License Agreement - Fostamatinib

We have an exclusive license and supply agreement with Kissei entered in October 2018, amended in November 2022, October 2023, August 2024, September 2024 and October 2024, to develop and commercialize fostamatinib in all current and potential indications in Japan, China, Taiwan and Korea. Kissei is responsible for performing and funding all development activities for fostamatinib in Kissei territories. At the inception of the agreement, we received an upfront cash payment of $33.0 million. Further, the agreement provides for up to $115.0 million in potential 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 Kissei territory 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.

In April 2022, Kissei announced that an NDA was submitted to Japan's PMDA for fostamatinib in chronic ITP, which entitled us to receive a $5.0 million non-refundable and non-creditable milestone payment. In December 2022, Kissei announced that Japan's PMDA approved the NDA for fostamatinib in chronic ITP, which entitled us to receive a $20.0 million non-refundable and non-creditable milestone payment. We accounted for this agreement under ASC 606, and recognized the corresponding revenue in the period we satisfied the performance obligations. As of December 31, 2024 and 2023, the remaining deferred revenue was related to the material right associated with discounted fostamatinib supply which amounted to $1.4 million. There was no material revenue recognized associated with the remaining performance obligation during the years ended December 31, 2024, 2023 and 2022. In January 2025, Kissei announced the Korean Ministry of Food and Drug Safety approved fostamatinib for the treatment of chronic ITP, which entitled us to receive a $3.0 million non-refundable and non-creditable milestone payment that we will recognize as revenue in the first quarter of 2025.

Pursuant to our supply agreement with Kissei, during the years ended December 31, 2024, 2023 and 2022, we recognized $10.4 million, $2.2 million, and $2.6 million, respectively, of revenue related to delivery of drug supplies to Kissei.

Medison Commercial and License Agreements

We have exclusive commercial and license agreements with Medison entered in October 2019 for the commercialization of fostamatinib for chronic ITP in Medison territory. Pursuant to which, we received a $5.0 million upfront payment with respect to the agreement in Canada. We accounted for this agreement 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. 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 auto immune hemolytic anemia in Canada. We determined that the non-refundable upfront fee represented the transaction price, however, due to the buyback provision, we accounted this upfront payment as financing arrangement under ASC 606. In 2022, management concluded that the likelihood of exercising the buyback option right was remote considering the top-line results from our Phase 3 trial of fostamatinib in wAIHA which showed that the trial did not demonstrate statistical significance in the primary efficacy endpoint, and the guidance received from the FDA. As such, in accordance with ASC 606, we relieved the outstanding financing liability of $5.7 million, which include the upfront payment and accreted interest, and recognized such amount as revenue in 2022. There was no outstanding deferred revenue related to Medison commercial and license agreement as of December 31, 2024 and 2023.

During the years ended December 31, 2024, 2023 and 2022, we recognized $0.5 million, $0.5 million, and no revenue, respectively, from Medison primarily related to the delivery of drug supplies and earned royalties.

Knight Commercial License and Supply Agreement

We have commercial license and supply agreements with Knight entered in May 2022 for the exclusive commercialization of fostamatinib for approved indications in Knight territory. Pursuant to such commercial license agreement, we received a $2.0 million one-time, non-refundable, and non-creditable upfront payment, with potential for up to an additional $20.0 million in regulatory and sales-based commercial milestone payments, and will receive twenty- to mid-thirty percent, tiered, escalated net-sales based royalty payments for products sold in the Knight territory. We accounted for this agreement under ASC 606 and identified that the upfront payment was a consideration for granting Knight the license to commercialize fostamatinib for approved indication in the Knight territory, and no further material deliverables associated to such upfront payment. As such, we recognized the upfront payment as revenue during the year ended December 31, 2022. No revenue was recognized during the years ended December 31, 2024 and 2023 from Knight. We are also responsible for the exclusive manufacture and supply of fostamatinib for all future development and commercialization activities under the agreement.

Dr. Reddy's Commercial License Agreement

In November 2024, we entered into a commercial license agreement with Dr. Reddy's Laboratories, Ltd. (Dr. Reddy's) to grant Dr. Reddy's an exclusive license to develop and commercialize olutasidenib in Dr. Reddy's territory which includes Latin America, South Africa, India, certain countries in the CIS, Southeast Asia Region and North Africa, Australia, and New Zealand. Pursuant to the commercial license agreement, we were entitled to receive a $4.0 million one-time, non-refundable and non-creditable upfront payment, which amount, net of applicable foreign withholding taxes was received in February 2025. In addition, we are also entitled to a potential for up to an additional $36.0 million in regulatory and sales-based commercial milestone payments, and will receive high teens- to thirty percent, tiered, escalated net-sales based royalty payments for products sold in Dr. Reddy's territory, subject to certain standard reductions and offsets. Dr. Reddy's is responsible for performing and funding all development activities necessary to obtain regulatory approval and commercialize olutasidenib in the Dr. Reddy's territory. We are responsible for the exclusive manufacture and supply of olutasidenib for all future development and commercialization activities under the agreement.

We accounted for this agreement following ASC 606 and concluded at the inception of the agreement, the upfront cash payment of $4.0 million was the consideration for granting the license right to Dr. Reddy's, and there are no other material deliverables associated with the upfront payment. Accordingly, we recognized the upfront payment as revenue during the year ended December 31, 2024. The variable considerations related to future development, regulatory and commercial milestones were fully constrained because it was probable that a significant reversal of cumulative

revenue would occur, given the inherent uncertainty of success with these future milestones. We will re-evaluate the transaction price in each reporting period as uncertain events are resolved or other changes in circumstances occur. We will recognize revenues related to the supply of olutasidenib upon delivery and when we are entitled to receive the product transfer price payments.

Under the license and services agreement with Forma as discussed in "Note 5 – In-Licensing and Acquisition", Forma is entitled to a certain portion of sublicensing revenue from olutasidenib. During the year ended December 31, 2024, we recorded $0.9 million sublicense revenue fee which we recorded within cost of product sales, associated with the upfront payment from Dr. Reddy's.

Government Contracts

DOD

In January 2021, we were awarded by the DOD to support our Phase 3 clinical trial to evaluate the safety and efficacy of fostamatinib for the treatment of hospitalized high-risk patients with COVID-19. No revenue was recognized related to this grant for the year ended December 31, 2024. For the years ended December 31, 2023 and 2022, $1.0 million and $4.5 million, respectively, of revenue was recognized related to this grant.

BARDA

In August 2023, we were awarded up to $0.8 million by BARDA for our evaluation of fostamatinib in mitigating the impact of long-term respiratory distress. No revenue was recognized related to this grant for the year ended December 31, 2024. For the year ended December 31, 2023, we recognized $0.1 million of revenue related to this grant.

Strategic Development Collaborations with MD Anderson and CONNECT

In December 2023, we entered into a Strategic Collaboration Agreement with MDACC, a comprehensive cancer research, treatment, and prevention center. The collaboration will expand our evaluation of REZLIDHIA (olutasidenib) in AML and other hematologic cancers. Under the collaboration, we will provide MDACC the study materials and $15.0 million in time-based milestone payments as compensation for services to be provided for the studies, over the five-year collaboration term, unless terminated earlier as provided for in the agreement. Through December 31, 2024, we provided $2.0 million funding to MDACC.

In January 2024, we announced our collaboration with CONNECT, an international collaborative network of pediatric cancer centers, to conduct a Phase 2 clinical trial to evaluate REZLIDHIA (olutasidenib) in glioma. Under the collaboration, we will provide funding up to $3.0 million and study material over the four-year collaboration.

We account for the funding we provide under the above research collaboration agreements as prepaid research and development in the balance sheet to the extent the payment is made in advance of services being rendered, and recognize such amount as research and development expense within the statements of operations as the collaborative partners render the services under the respective agreement.

5. IN-LICENSING AND ACQUISITION

Asset Purchase Agreement with Blueprint

On February 22, 2024, we acquired the US rights to research, develop, manufacture and commercialize GAVRETO (pralsetinib) from Blueprint pursuant to an Asset Purchase Agreement. The acquired assets include, among other things, applicable intellectual property related to pralsetinib in the US, including patents, copyrights and trademarks, as well as clinical regulatory and commercial data and records. Pursuant to the Asset Purchase Agreement, we agreed to pay a purchase price of $15.0 million, $10.0 million of which is payable upon our first commercial sale of GAVRETO (pralsetinib) and an additional $5.0 million of which is payable on the first anniversary of the closing date of

the agreement, subject to certain conditions. Blueprint is also eligible to receive up to $97.5 million in future commercial milestone payments and up to $5.0 million in future regulatory milestone payments. The potential regulatory milestones include full regulatory approval of pralsetinib (or related compounds) for the treatment of adult RET-fusion positive thyroid cancer, and maintenance of the current regulatory approval of pralsetinib for the treatment of adult RET-fusion positive thyroid cancer during the period beginning on February 22, 2024 and ending on the third anniversary of the first commercial sale of pralsetinib subject to certain conditions. Subject to the terms and conditions of the Asset Purchase Agreement, Blueprint would be entitled to tiered royalty payments on net sales of products containing pralsetinib (or related compounds) ranging from 10% to 30%, subject to certain reductions and offsets.

In accordance with ASC 805 *Business Combinations* (ASC 805), the transaction was accounted for as an asset acquisition, because substantially all of the fair value of the gross assets acquired is concentrated in a single asset, which is the GAVRETO product rights. The GAVRETO product rights comprised developed technology, customers, trademarks and trade name, and are considered a single asset as they are inextricably linked. ASC 805 provides for a screen test, wherein if substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets, the assets acquired are not considered to be a business.

The following table summarizes the total purchase consideration in connection with the asset acquisition (in thousands):

Closing purchase price	$	15,000
Transaction costs		360
Total purchase consideration	$	15,360

Of the total closing purchase price, $10.0 million was paid in July 2024. The remaining $5.0 million was outstanding and presented as acquisition-related liabilities in the balance sheet as of December 31, 2024. We classified the outstanding acquisition-related liabilities as non-current considering the amount is expected to be payable in a period longer than one year. In accordance with the guidance, we classify the payments of the closing purchase price under financing activity in the statements of cash flows, considering that the payment was not made soon after the acquisition date.

The contingent considerations relating to future commercial and regulatory milestones were not included in the total purchase price consideration, and will be accounted for when the contingency is resolved and the consideration becomes payable. Royalties are recognized within cost of product sales, as revenue from GAVRETO product sales is recognized.

In an asset acquisition, the acquiring entity should recognize the assets acquired at cost to the acquiring entity which includes transaction costs and consideration given, allocated based on a relative fair value of the assets acquired measured at acquisition date. The fair value of the developed technology, customers, trademarks and trade name was estimated using a multi-period excess earnings income approach that discounts expected cash flows to present value by applying discount rate that represents the estimated rate that market participants would use to value such assets. The relative fair value is based on estimates that required judgement and certain assumptions, categorized as Level 3 in the fair value hierarchy. Since we acquired a single asset, the total purchase consideration was recorded as intangible assets. The related intangible assets are being amortized on a straight-line basis over the estimated useful life of 12 years, and the related amortization is recorded within cost of product sales.

Simultaneously and in connection with entering into the Asset Purchase Agreement, we also entered into certain supporting agreements, including a customary transition agreement, pursuant to which, during the transition period, Blueprint will transition regulatory and distribution responsibility for GAVRETO to us. We also agreed to purchase certain drug product inventories from Blueprint under a Material Transfer Agreement, and received such inventories amounting to approximately $6.5 million during the year ended December 31, 2024.

License and Transition Services Agreement with Forma

We have a license and transition services agreement with Forma entered in July 2022, for an exclusive license to develop, manufacture and commercialize olutasidenib, a proprietary inhibitor of mutated IDH1 (mIDH1), for any uses worldwide, including for the treatment of AML and other malignancies. Forma became a wholly owned subsidiary of Novo Nordisk following the closing of its acquisition in October 2022. Pursuant to the terms of the license and transition services agreement, we paid an upfront fee of $2.0 million, with the potential to pay up to $67.5 million of additional payments upon achievement of specified development and regulatory milestones and up to $165.5 million of additional payments upon achievement of certain commercial milestones. In addition, subject to the terms and conditions of the license and transition services agreement, Forma would be entitled to tiered royalty payments on net sales of licensed products at percentages ranging from low-teens to mid-thirties, as well as certain portion of our sublicensing revenue, subject to certain standard reductions and offsets.

The transaction was accounted for as an acquisition of asset under ASC 730, *Research and Development*. In accordance with the guidance, in a transaction accounted for as an asset acquisition, any acquired IPR&D that does not have alternative future use is charged to expense at the acquisition date. At the acquisition date, we accounted for the upfront fee of $2.0 million as IPR&D and recorded such cost within research and development expenses in the statements of operations for the year ended December 31, 2022.

Under the accounting guidance, we account for contingent cash payments when it is probable that a liability is incurred and the amount can be reasonably estimated. We account for milestone payment obligations incurred at development stage and prior to a regulatory approval of an indication associated with the acquired licensed asset as research and development expense when the event requiring payment of the milestone occurs. Milestone payment obligations incurred upon and after a regulatory approval of an indication associated with the acquired licensed asset, and at the commercial stage, are recorded as intangible asset when the event requiring payment of the milestones occurs. Prior to the FDA approval of REZLIDHIA in December 2022, we achieved certain regulatory milestone which entitled Forma to receive a $2.5 million milestone payment. Because such milestone payment obligation was incurred prior to a regulatory approval of an indication associated with the acquired licensed asset, we recorded such amount as IPR&D and recorded such cost within research and development expense during the year ended December 31, 2022. On December 1, 2022, the FDA approved REZLIDHIA capsules for the treatment of adult patients with R/R AML with susceptible IDH1 mutations as detected by an FDA-approved test. Following the FDA approval, we launched REZLIDHIA and made first shipments of the product to our customers in December 2022. With this FDA approval and first commercial sale of the product, Forma was entitled to receive a total of $15.0 million in milestone payments. Since such milestone payment obligations were incurred upon and after regulatory approval of the product, we recorded such amount as intangible asset on our balance sheet. No new milestone was met in 2023 and 2024.

The amount recorded as intangible assets are being amortized on a straight-line basis over the estimated useful life of 14 years, and the related amortization is recorded within cost of product sales. Royalties are recognized within cost of product sales, as revenue from REZLIDHIA product sales is recognized.

6. 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,		
	2024	2023	2022
Selling, general and administrative	$ 10,879	$ 6,712	$ 10,217
Research and development	1,514	2,094	2,168
Total stock-based compensation expense	$ 12,393	$ 8,806	$ 12,385

Equity Incentive Plans

On May 16, 2018, our stockholders approved the adoption of our 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 RSUs under our Equity Incentive Plans.

During the year ended December 31, 2024, our Board of Directors approved additional 240,197 shares of common stock reserved for issuance under our Inducement Plan. In May 2024, our stockholders approved an amendment to our 2018 Plan, to, among other items, add an additional 650,000 shares to the number of shares of common stock authorized for issuance under our 2018 Plan.

Stock Options and RSUs

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

		Stock Options			RSUs	
	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, 2023	1,387,129	3,411,632	$ 25.62		185,938	$ 19.82
Authorized for grant	890,197					
Granted	(1,155,881)	717,106	$ 12.68		304,705	$ 12.81
Exercised/Released	—	(93,386)	$ 16.08		(68,908)	$ 18.52
Cancelled and forfeited	476,776	(470,634)	$ 27.65		(34,453)	$ 15.26
Outstanding as of December 31, 2024	1,598,221	3,564,718	$ 23.00	$ 4,528	387,282	$ 14.94
Vested and expected to vest as of December 31, 2024		3,454,968	$ 22.80	$ 4,510		
Exercisable as of December 31, 2024		2,652,876	$ 24.87	$ 1,761		

Of the total stock options outstanding as of December 31, 2024, 109,750 shares outstanding are performance-based stock options wherein the achievements of the corresponding corporate-based milestones were not probable. Accordingly, the related grant date fair value for these performance-based stock options of $2.1 million has not been recognized as stock-based compensation expense as of December 31, 2024.

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, 2024. For the years ended December 31, 2024, 2023 and 2022, the aggregate intrinsic values of stock option exercises were approximately $0.6 million, $0.02 million and $0.2 million, respectively, representing the difference between the fair value of our common stock at the date of exercise and the exercise price paid.

Stock option grants generally vest over 3 to 4 years, and are exercisable for a period of 10 years. For the years ended December 31, 2024, 2023 and 2022, we granted options to purchase 717,106 shares, 367,180 shares and 817,911 shares, respectively, of common stock, with weighted-average grant date fair value of $9.71 per share, $12.80 per share and $12.90 per share, respectively.

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

	Year Ended December 31,		
	2024	2023	2022
Risk-free interest rate	4.1 %	3.9 %	2.6 %
Expected term (in years)	6.1	6.8	6.3
Dividend yield	0.0 %	0.0 %	0.0 %
Expected volatility	87.7 %	84.0 %	74.8 %

As of December 31, 2024, there was approximately $10.6 million of unrecognized stock-based compensation cost which is expected to be recognized over the remaining weighted-average period of 2.04 years, related to time-based stock options, performance-based stock options wherein achievement of the corresponding corporate-based milestones were considered as probable, and RSUs.

Outstanding stock options and stock options exercisable information by range of exercises prices as of December 31, 2024 was as follows:

	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
$9.0 - $18.7	1,259,434	8.50	$ 13.66	586,971	$ 14.54
$19.6 - $21.1	464,302	3.61	$ 20.34	464,302	$ 20.34
$21.4 - $24.0	294,257	2.49	$ 22.59	283,257	$ 22.59
$24.2 - $24.2	538,753	6.13	$ 24.20	462,020	$ 24.20
$24.4 - $35.4	600,872	4.63	$ 31.58	453,338	$ 30.69
$35.9 - $39.80	221,918	4.33	$ 37.63	218,731	$ 37.64
$40.7 - $45.0	185,182	3.19	$ 44.90	184,257	$ 44.90
$9.0 - $45.0	3,564,718	5.82	$ 23.00	2,652,876	$ 24.87

Employee Stock Purchase Plan

Our Purchase Plan permits eligible employees to purchase common stock at a discount through payroll deductions during defined offering periods. Our Purchase Plan provides for a 24-month offering period comprised 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.

Our previous 24-month offering period under our Purchase Plan ended on June 30, 2024, and a new 24-month offering period started on July 1, 2024. The fair value of awards under our Purchase Plan is estimated on the date of our new offering period using the Black-Scholes option pricing model, which is being amortized over the requisite service periods. As of December 31, 2024, there was approximately $0.3 million, which is expected to be recognized over the remaining weighted average period of 1.12 years, related to our Purchase Plan.

For the years ended December 31, 2024, 2023 and 2022, there were 65,409 shares, 94,179 shares and 114,685 shares, respectively, of common stock purchased under the Purchase Plan, at an average price of $7.06 per share, $10.60 per share and $10.10 per share, respectively. As of December 31, 2024, there were 184,174 shares reserved for future issuance under the Purchase Plan.

7. INVENTORIES

The following table summarizes inventories, net (in thousands):

	As of December 31,	
	2024	2023
Raw materials	$ 1,077	$ 4,609
Work in process	1,226	1,876
Finished goods	5,014	1,508
Total	$ 7,317	$ 7,993
Reported as:		
Inventories	$ 6,002	$ 5,522
Other assets	1,315	2,471
Total	$ 7,317	$ 7,993

Inventories as of December 31, 2024 and 2023 include inventories acquired from Forma pursuant to the license and transition agreement. Inventories as of December 31, 2024 also include inventories acquired from Blueprint pursuant to a Material Transfer Agreement as discussed in Note 5 – In-Licencing and Acquisition. As of December 31, 2024, advance payments to the manufacturer of our raw materials were included within prepaid and other current assets in the balance sheet amounted to $3.8 million. No such advance payment was included within prepaid and other current assets as of December 31, 2023.

Non-current inventories consists of active pharmaceutical ingredient classified as raw materials which have multi-year shelf life, as well as certain work in process and finished goods inventories that are not expected to be consumed beyond our normal operating cycle.

8. CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS

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

	As of December 31,	
	2024	2023
Cash	$ 20,135	$ 8,247
Money market funds	16,386	9,685
US treasury bills	7,263	12,594
Government-sponsored enterprise securities	23,177	11,233
Corporate bonds and commercial paper	10,360	15,174
	$ 77,321	$ 56,933
Reported as:		
Cash and cash equivalents	$ 56,746	$ 32,786
Short-term investments	20,575	24,147
	$ 77,321	$ 56,933

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

As of December 31, 2024	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
US treasury bills	$ 7,260	$ 3	$ —	$ 7,263
Government-sponsored enterprise securities	23,174	3	—	23,177
Corporate bonds and commercial paper	10,356	4	—	10,360
Total	$ 40,790	$ 10	$ —	$ 40,800

As of December 31, 2023	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
US treasury bills	$ 12,591	$ 3	$ —	$ 12,594
Government-sponsored enterprise securities	11,230	7	(4)	11,233
Corporate bonds and commercial paper	15,172	5	(3)	15,174
Total	$ 38,993	$ 15	$ (7)	$ 39,001

As of December 31, 2024 and 2023, our cash equivalents and short-term investments had a weighted-average time to maturity of approximately 69 days and 82 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, 2024, there were no individual securities that were in a significant unrealized loss position, and no individual securities have been in a loss position for more than one year. We regularly review the securities in an unrealized loss position and evaluate the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. We have not recognized any credit losses on these securities as of December 31, 2024 and 2023.

9. 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, 2024			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 16,386	$ —	$ —	$ 16,386
US treasury bills	—	7,263	—	7,263
Government-sponsored enterprise securities	—	23,177	—	23,177
Corporate bonds and commercial paper	—	10,360	—	10,360
Total	$ 16,386	$ 40,800	$ —	$ 57,186

	Assets at Fair Value as of December 31, 2023			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 9,685	$ —	$ —	$ 9,685
US treasury bills	—	12,594	—	12,594
Government-sponsored enterprise securities	—	11,233	—	11,233
Corporate bonds and commercial paper	—	15,174	—	15,174
Total	$ 9,685	$ 39,001	$ —	$ 48,686

10. OTHER BALANCE SHEET COMPONENTS

Property and equipment

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

	As of December 31,	
	2024	2023
Laboratory equipment	$ 129	$ 1,470
Computer and software	153	363
Others	71	36
Total property and equipment	353	1,869
Less accumulated depreciation and amortization	(261)	(1,704)
Property and equipment, net	$ 92	$ 165

Depreciation and amortization expense was $0.1 million, $0.2 million and $0.9 million for the years ended December 31, 2024, 2023 and 2022, respectively. Certain property and equipment were either sold, retired or disposed of, which related costs and accumulated depreciation were removed from the balance sheet, and any resulting gain or loss were reflected in statements of operations in the period realized.

Intangible assets

Intangible assets consist of the following (in thousands):

	As of December 31,	
	2024	2023
Intangible assets cost	$ 30,360	$ 15,000
Accumulated amortization	(3,260)	(1,122)
Intangible assets, net	$ 27,100	$ 13,878

See “Note 5 – In-Licensing and Acquisition” for related discussions of capitalized intangible assets. For the years ended December 31, 2024, 2023 and 2022, amortization expense recorded within cost of sales in the statements of operations were $2.1 million, $1.1 million and $0.1 million, respectively.

As of December 31, 2024, the weighted average remaining amortization period of outstanding intangible assets was 11.54 years. The following table presents the estimated future amortization expense of intangible assets (in thousands):

For the year ending December 31,	
2025	$ 2,351
2026	2,351
2027	2,351
2028	2,351
2029	2,351
Thereafter	15,345
	$ 27,100

Other accrued liabilities

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

	As of December 31,	
	2024	2023
Accrued commercial expenses	$ 3,661	$ 1,852
Accrued other expenses	6,735	3,482
Total other accrued liabilities	$ 10,396	$ 5,334

11. DEBT

The following table summarizes loans payable, net (in thousands):

	As of December 31,	
	2024	2023
Principal outstanding	$ 60,000	$ 60,000
Unamortized debt issuance costs	(320)	(398)
Principal outstanding, net of unamortized debt issuance costs	$ 59,680	$ 59,602
Reported as:		
Loans payable, net, current portion	$ 7,272	$ 7,229
Long-term portion of loans payable, net	52,408	52,373
	$ 59,680	$ 59,602

We have a Credit Agreement with MidCap entered on September 27, 2019 (Closing Date) and amended on March 29, 2021 (First Amendment), February 11, 2022 (Second Amendment), July 27, 2022 (Third Amendment), and April 11, 2024 (Fourth Amendment). The Credit Agreement provides for a $60.0 million term loan credit facility, which was fully funded as of December 31, 2024 and 2023.

In April 2024, we entered into Fourth Amendment to the Credit Agreement, which among other things, extended the maturity date and interest only period for the term loans, revised the interest rate, reset the prepayment fee, increased the exit fee, and updated certain financial covenants. Under the amended Credit Agreement, the term loans mature on September 1, 2027, and the interest-only period is through October 1, 2025. The interest rate applicable to the term loans under is the sum of one-month SOFR, plus an adjustment of 0.11448%, subject to 4.00% applicable floor, plus applicable margin of 6.50%. A final payment fee of 4.25% of principal is due at maturity date of the term loans. The amendment was accounted for as debt modification. The unamortized debt issuance costs are continuously being amortized as interest expense through maturity using the effective interest rate method.

Prior to the Fourth Amendment to the Credit Agreement, the term loans would mature on September 1, 2026, and the interest-only period was through October 1, 2024. The term loans bore interest rate equal to the sum of one-month SOFR, plus an adjustment of 0.11448%, subject to 1.50% applicable floor, plus applicable margin of 5.65%, and a final payment fee of 2.50% of principal due at maturity date.

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. The obligations under the amended Credit Agreement are secured by a perfected security interest in all of our assets including our intellectual property.

Interest expense, including amortization of the debt discount and accretion of the final fees related to the Credit Agreement for the years ended December 31, 2024, 2023 and 2022 were $7.9 million, $6.8 million and $3.0 million, respectively. Accrued interest of $2.1 million and $1.5 million as of December 31, 2024 and 2023, respectively, was included within other accrued liabilities in the balance sheet.

The following table presents the future minimum principal payments of the outstanding loan as of December 31, 2024 (in thousands):

For the year ending December 31,	
2025	$ 7,500
2026	30,000
2027	22,500
Principal amount (Tranches 1, 2, 3 and 4)	$ 60,000

The amended Credit Agreement contains certain covenants which, among others, require us to deliver financial reports at designated times of the year and maintain minimum unrestricted cash and trailing net revenues. As of December 31, 2024, we were not in violation of any covenants.

12. COMMITMENTS AND CONTINGENCIES

Operating Leases

We have a sublease agreement with Atara entered in October 2022 to sublease an office space currently used as headquarters located in South San Francisco, California. Subject to the terms of the sublease agreement, the lease term commenced in November 2022 and shall expire in May 2025. As of December 31, 2024, the future minimum lease payments related to our sublease agreement with Atara amounted to $0.3 million, and the weighted average remaining term of the lease was 0.42 years.

In February 2025, we entered into a lease agreement with 611 Gateway to lease the same office space currently subleased from Atara. Subject to the terms of the lease agreement, the lease term shall commence following the expiration of the sublease with Atara and shall expire in July 2027. Future minimum lease payments related to such lease amounted to approximately $1.4 million, of which, $0.3 million, $0.7 million and $0.4 million are due for the years ending December 31, 2025, 2026 and 2027, respectively.

We previously leased our prior headquarters office space located in South San Francisco, California with Healthpeak Properties, Inc. (formerly known as HCP BTC, LLC), and had a sublease agreement with an unrelated third-party to sublet a portion of the leased facility. Both the lease and the sublease expired in January 2023.

The components of our operating lease expense were as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Fixed operating lease expense	$ 663	$ 1,109	$ 5,470
Variable operating lease expense	112	134	818
Total operating lease expense	$ 775	$ 1,243	$ 6,288

Supplemental information related to our operating lease expense was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Cash payments included in the measurement of operating lease liabilities	$ 739	$ 1,534	$ 10,485

Supplemental information related to our operating sublease was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Fixed sublease expense	$ —	$ 365	$ 4,381
Variable sublease expense	—	77	911
Sublease income	—	(442)	(5,292)
Net	$ —	$ —	$ —

Purchase Commitments and Obligations

In the ordinary course of business, we enter into agreements with contract manufacturers to manufacture our inventory products. Although the agreements generally provide a termination clause with or without cause, we may still be subjected to payment of cancellation fees. The level of cancellation fees is generally dependent on the timing of the written notice in relation to the commencement of work, with the maximum cancellation fees equal to the full price of the work order. In October 2024, we entered into an agreement with a third-party contract manufacturer to manufacture TAVALISSE that is expected to be delivered starting in 2026 through 2029. As of December 31, 2024, the contractual obligation not included in our financial statements related an agreement that may potentially be subjected to cancellation fees amounted to approximately $24.1 million, with approximately $6.8 million due in one year and $9.3 million due within two to three years. As of December 31, 2024, we have not incurred any cancellation fees under our agreements with contract manufacturers

Legal Contingencies

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any material legal proceedings that, if determined adversely us, would have a material adverse effect on us. For more information, see “Part I, Item 3, Legal Proceedings” of this Annual Report on Form 10-K.

13. STOCKHOLDERS’ EQUITY

Preferred Stock

We are authorized to issue 10,000,000 shares of preferred stock. As of December 31, 2024 and 2023, 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 restated in May 2018, authorizes us to issue 400,000,000 shares of common stock.

Open Market Sale Agreement

In August 2020, we entered into an Open Market Sale Agreement with Jefferies, 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. We have an active Registration Statement filed with the SEC, which registered, among other securities, a base prospectus which covers the offering, issuance, and sale by us of up to $250.0 million in the aggregate of the securities identified from time to time in one or more offerings, which include the $100.0 million of shares of our common stock that may be offered, issued and sold under the Open Market Sale Agreement. As of December 31, 2024, no shares had been sold under the Open Market Sale Agreement.

14. INCOME TAXES

The provision for income tax for the year ended December 31, 2024 of $0.9 million was related to foreign withholding tax and state taxes. We have not recorded 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. For the years ended December 31, 2023 and 2022, there was no foreign withholding tax, and we have not recorded state and federal income taxes due to our pre-tax book losses and a full valuation allowance was recorded against our deferred tax assets.

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):

	As of December 31,	
	2024	2023
Deferred tax assets		
Net operating loss carryforwards	$ 222,744	$ 229,967
Orphan drug and research and development credits	62,314	62,457
Capitalized research and development credits	19,604	21,017
Deferred revenue	10,181	11,223
Deferred compensation	11,701	10,365
Other, net	2,751	3,898
Deferred tax liabilities		
Others	(61)	(296)
Total net deferred tax assets	329,234	338,631
Less: valuation allowance	(329,234)	(338,631)
Deferred tax assets, net of allowance	$ —	$ —

The valuation allowance decreased by approximately $9.4 million, and increased by $1.0 million and $15.3 million for the years ended December 31, 2024, 2023 and 2022, respectively.

The realization of deferred tax assets is dependent if there are sufficient positive evidences that exist to conclude that it is more-likely-than-not that our deferred tax assets will be realized. This assessment requires significant judgment. In making this determination, all available evidence, both positive and negative, shall be considered to determine whether, based on the weight of that evidence, a valuation allowance for deferred tax assets is needed. If sufficient positive evidence may become available to allow us to reach a conclusion that a portion of the valuation allowance against the deferred tax assets may be reversed, the reversal would result in an income tax benefit for the quarterly and annual fiscal period in which we determine to release such valuation allowance.

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

	Year Ended December 31,		
	2024	2023	2022
Federal statutory tax rate	21.0 %	(21.0)%	(21.0)%
State, net of federal benefit	1.5 %	0.1 %	0.0 %
Valuation allowance	(30.3)%	13.9 %	20.2 %
Stock compensation	6.4 %	5.3 %	2.5 %
Orphan drug and research and development credits	3.1 %	0.2 %	(2.6)%
Foreign tax	3.2 %	— %	— %
Other, net	(0.1)%	1.5 %	1.0 %
Effective tax rate	4.8 %	0.0 %	0.1 %

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 NOL carryovers and tax credits to offset future taxable income. Our existing NOL 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 NOL carryforwards to reflect the results of the Section 382 owner shift analysis as of December 31, 2024. We did not experience any significant changes in ownership in the periods presented. 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, 2024, we had NOL carryforwards for federal income tax purposes of approximately $940.9 million. Of the federal NOL carryforward, $801.7 million, which expire beginning in the year 2026 and the remaining NOL carryforwards can be carried forward indefinitely, subject to annual limitation of 80% of taxable income. We also had state NOL carryforwards of approximately $375.1 million, which expire beginning in the year 2028.

We have general business credits of approximately $44.6 million, which will expire beginning in 2025, if not utilized, and is consisted of research and development credits and orphan drug credits. We also have state research and development tax credits of approximately $32.4 million, which have no expiration date.

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

	Year Ended December 31,		
	2024	2023	2022
Balance at the beginning of the year	$ 8,672	$ 9,426	$ 9,186
Decrease related to prior year tax positions	—	(843)	—
Increase related to current year tax positions	108	89	240
Balance at the end of the year	$ 8,780	$ 8,672	$ 9,426

During the years ended December 2024, 2023 and 2022, the amount of unrecognized tax benefits increased due to additional research and development and orphan drug credits generated during those years. In 2023, we engaged our tax consultant to perform an orphan credits study for years 2015 to 2020. The results of the study decreased the unrecognized tax benefits by $4.7 million. The reversal of the uncertain tax benefits did not affect our effective tax rate as 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 NOL 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.

15. SEGMENT INFORMATION

The following table presents segment information for the periods presented:

	Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Total Revenues	$ 179,278	$ 116,882	$ 120,242
Less:			
Employee related expenses	69,807	63,429	69,477
Commercial related expenses	26,996	24,310	23,846
Cost of product sales	18,647	7,110	1,749
Consultants and third-party services	15,532	17,942	22,218
Outside clinical trial related expenses	10,978	9,694	29,981
Other segment items	13,126	14,888	28,521
Interest expense, net	5,826	4,600	3,023
Provision for income taxes	881	—	—
Segment income (loss)	$ 17,485	$ (25,091)	$ (58,573)

There is no reconciling items or adjustments between segment income (loss) presented above and net income (loss) as presented in our statements of operations. The CODM does not review assets in evaluating the segment results and therefore such information is not presented.

For details of revenues disaggregated by category, see “Note 3 – Revenues”.

Employee related expenses primarily comprised salaries, employee benefits, other employee related expenses and stock-based compensation expense. For details of stock-based compensation expense, see “Note 6 – Stock-Based Compensation.”

Other segment items for the periods presented primarily comprised travel related expenses, business insurance, taxes and licenses, and facility related expenses. Other segment items for the year ended December 31, 2022 also include restructuring costs and IPR&D.

16. RESTRUCTURING CHARGES

During the year ended December 31, 2022, we recorded restructuring charges of $1.3 million as a result of workforce reduction, primarily from development and administration group. Restructuring charges comprised cash severance, bonus and related employee benefits and taxes paid to affected employees.

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, 2024.

The effectiveness of our internal control over financial reporting as of December 31, 2024 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 2024 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, 2024, 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, 2024, 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, 2024 and 2023, the related statements of operations, comprehensive income (loss), stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2024, and the related notes and our report dated March 4, 2025 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 4, 2025

Item 9B. Other Information

Securities Trading Plans of Directors and Executive Officers

During the three months ended December 31, 2024, none of our directors or executive officers adopted or terminated any contract, instruction or written plan for the purchase or sale of our securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) or any "non-Rule 10b5-1 trading arrangement" as defined in Item 408 of Regulation S-K under the Securities Exchange Act of 1934, as amended.

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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. Such information, if any, is incorporated herein by reference.

We have insider trading policies and procedures that set forth acceptable transactions involving the purchase, sale and other disposition of our securities by employees and directors, as well as certain designated consultants and contractors. We believe these policies and procedures are reasonably designed to promote compliance with insider trading laws, rules and regulations and listing standards applicable to the Company. A copy of our Insider Trading Policy is filed with this Annual Report on Form 10-K as Exhibit 19.1.

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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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 "Equity Compensation Plan Information" in our Proxy Statement for the 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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 2025 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2024. 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

1.1	Amended and Restated Open Market Sale Agreement, dated August 2, 2024, by and between Rigel Pharmaceuticals, Inc. and Jefferies LLC (filed as an exhibit to Rigel's Registration Statement on Form S-3, dated August 2, 2024 and incorporated herein by reference).
3.1	Amended and Restated Certificate of Incorporation (filed as an exhibit to Rigel's Current Report on Form 8-K dated June 24, 2003 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 November 3, 2022 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 29, 2012 and incorporated herein by reference).
3.4	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 18, 2018 and incorporated herein by reference).
3.5	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 June 27, 2024 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, filed on September 15, 2000, 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).
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+	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).
10.3+	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).
10.4+	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).
10.5+	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).
10.6+	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).
10.7+	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).
10.8+	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, 2024 filed on August 6, 2024 and incorporated herein by reference).
10.9+#	Rigel Pharmaceuticals, Inc. Inducement Plan, as amended.
10.10+	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).

10.11+	Amended and Restated Executive Severance Plan (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed on November 7, 2023 and incorporated herein by reference).
10.12+	Non-Employee Director Compensation Policy, as amended (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2021 filed on March 1, 2022 and incorporated herein by reference).
10.13+ ^	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).
10.14+^	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).
10.15+ ^	Offer Letter from Rigel Pharmaceuticals, Inc. to Raymond Furey, dated November 17, 2022 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2022 filed on March 7, 2023 and incorporated herein by reference).
10.16+ ^#	Offer Letter from Rigel Pharmaceuticals, Inc. to Lisa Rojkjaer, M.D., dated December 20, 2023.
10.17^	License and Transition Services Agreement with Forma Therapeutics, Inc. dated July 27, 2022 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 filed on November 3, 2022 and incorporated herein by reference).
10.18^	Amendments 1, 2 and 3 to License and Transition Services Agreement with Forma Therapeutics, Inc. (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2023 filed on August 1, 2023 and incorporated herein by reference).
10.19^	License and Collaboration Agreement with 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).
10.20^	Amendment 1 to License and Collaboration Agreement with Eli Lilly and Company, dated September 28, 2023 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed on November 7, 2023 and incorporated herein by reference).
10.21^	Amendment No. 2 to the License and Collaboration Agreement with Eli Lilly and Company, dated March 11, 2024 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 filed on May 7, 2024 and incorporated herein by reference).
10.22^	Collaboration and License Agreements with Kissei Pharmaceutical Co., Ltd., dated October 29, 2018 (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).
10.23^	Supply Agreements with Kissei Pharmaceutical Co., Ltd., dated October 29, 2018 (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^	Amendments 1, 2, 3, and 4 to the Collaboration and License Agreement with Kissei Pharmaceutical Co., Ltd., dated October 29, 2018 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed on November 7, 2024 and incorporated herein by reference).
10.25^#	Amendment 5 to the Collaboration and License Agreement with Kissei Pharmaceutical Co., Ltd., dated October 23, 2024.
10.26^	Exclusive Commercialization License Agreement with Grifols Worldwide Operations Limited, dated January 22, 2019 (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^	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).
10.28^	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).
10.29^	First Amendment to the Credit and Security Agreement with MidCap Financial Trust, dated March 29, 2021 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2021 filed on March 1, 2022 and incorporated herein by reference).
10.30^	Second Amendment to the Credit and Security Agreement with MidCap Financial Trust, dated February 11, 2022 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2021 filed on March 1, 2022 and incorporated herein by reference).
10.31^	Third Amendment to the Credit and Security Agreement with MidCap Financial Trust, dated July 27, 2022 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 filed on November 3, 2022 and incorporated herein by reference).
10.32^	Fourth Amendment to the Credit and Security Agreement with MidCap Financial Trust, dated April 11, 2024 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 filed on May 7, 2024 and incorporated herein by reference).
10.33^	Sublease Agreement with Atara Biotherapeutics, Inc., dated October 28, 2022 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the year ended December 31, 2022 filed on March 7, 2023 and incorporated herein by reference).
10.34#	Amendment No. 1 to Sublease Agreement with Atara Biotherapeutics, Inc., dated October 10, 2024.
10.35^#	Lease Agreement with 611 Gateway Center LP, dated February 25, 2025.
10.36^	Asset Purchase Agreement with Blueprint Medicines Corporation, dated February 22, 2024 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 filed on May 7, 2024 and incorporated herein by reference).
10.37^	Collaboration and License Agreement with Kissei Pharmaceutical Co., Ltd., dated September 3, 2024 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed on November 7, 2024 and incorporated herein by reference).
10.38^	Supply Agreement with Kissei Pharmaceutical Co., Ltd., dated September 3, 2024 (filed as an exhibit to Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed on November 7, 2024 and incorporated herein by reference).
19.1#	Rigel Pharmaceuticals, Inc. Insider Trading Policy.
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).
97	Incentive Compensation Recoupment Policy (Clawback Policy), dated August 10, 2023 (filed as an exhibit to Rigel's Annual Report on Form 10-K for the December 31, 2024 filed on March 5, 2024 and incorporated herein by reference).

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.