Scaling New

POSSIBILITIES

Puma Biotechnology, Inc. | 2025 Annual Report

Puma is scaling new heights with its continued commercial execution of NERLYNX® and with development of its investigational drug alisertib.

PUMA BIOTECHNOLOGY, INC. is a biopharmaceutical company with a focus on the development and commercialization of innovative products to enhance cancer care. Puma in-licensed the global development and commercialization rights to PB272 (neratinib, oral) in 2011. In 2022, Puma in-licensed global research and development and commercial rights to alisertib, a selective, small molecule, orally administered inhibitor of aurora kinase A.

Neratinib is a potent irreversible tyrosine kinase inhibitor that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Puma has focused on developing the oral version of neratinib, and its primary drug candidate was directed at the treatment of HER2-positive breast cancer.

Neratinib, oral was approved by the U.S. Food and Drug Administration (FDA) in 2017 for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, following adjuvant trastuzumab-based therapy. Puma commenced commercial sales of the drug in 2017, and it is marketed in the United States as NERLYNX® tablets. In February 2020, NERLYNX was also approved by the FDA in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. NERLYNX was granted marketing authorization by the European Commission in 2018 for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who are less than one year from completion of prior adjuvant trastuzumab-based therapy. Commercial sales commenced in the European Union in 2019.

Puma has entered into additional exclusive license agreements with various parties to commercialize NERLYNX in regions outside the United States, including the European Union, Canada, Latin America, Greater China, Israel, Southeast Asia, Australia, New Zealand, South Korea, the Middle East, and parts of Africa. Puma also has an exclusive distribution agreement to support access to NERLYNX in Russia and the Commonwealth of Independent States (CIS). Puma plans to continue to pursue the commercialization of NERLYNX outside the United States.

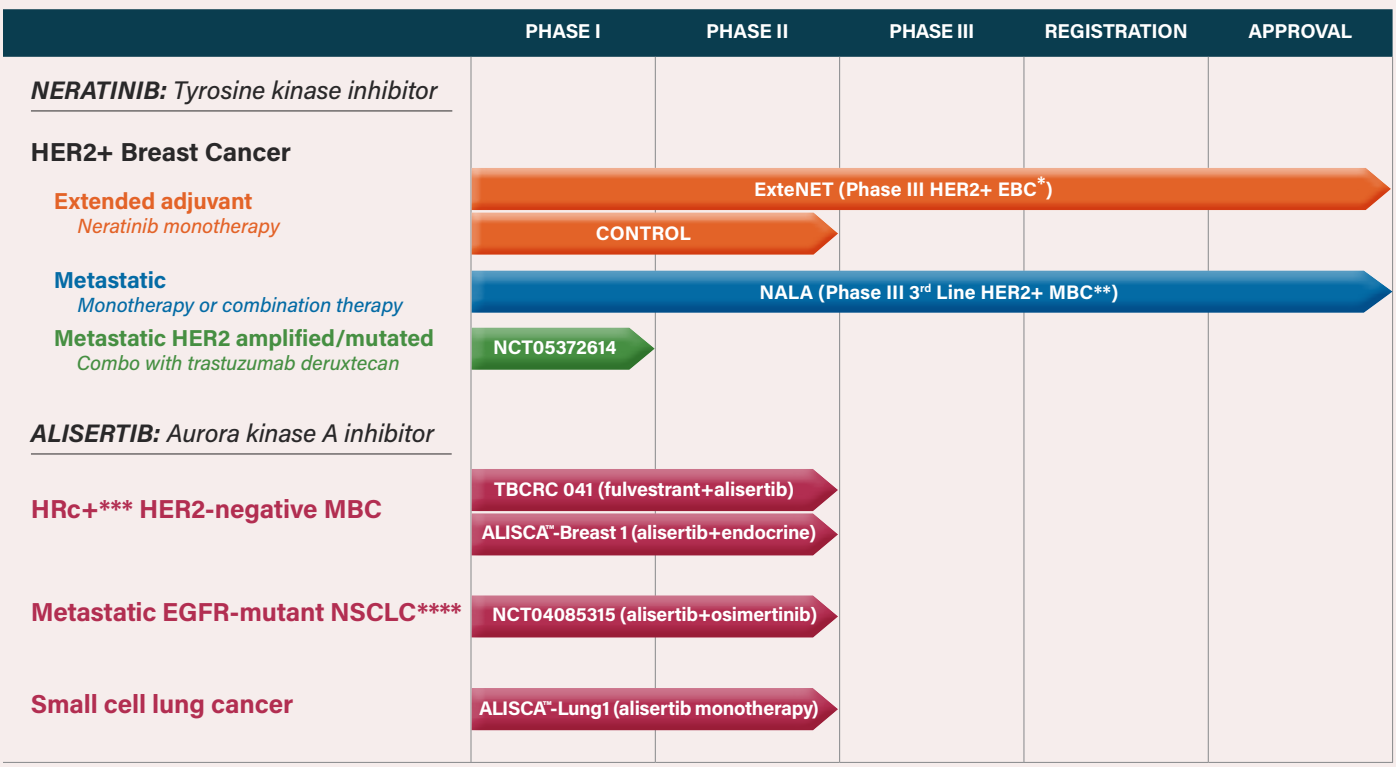
NERLYNX® is a registered trademark of Puma Biotechnology, Inc.

Alisertib is an adenosine triphosphate–competitive and reversible inhibitor of aurora kinase A and results in disruption of mitosis leading to apoptosis of rapidly proliferating tumor cells that are dependent on aurora kinase A. Alisertib has been tested in clinical trials in patients with metastatic cancers including breast cancer, small cell lung cancer, head and neck cancer, ovarian cancer, peripheral T cell lymphoma and acute myeloid leukemia. Puma is currently focusing on the development of alisertib on the treatment of patients with small cell lung cancer, metastatic estrogen receptor-positive (ER-positive) HER2-negative breast cancer and triple-negative breast cancer.

Small cell lung cancer is an aggressive form of lung cancer with a poor prognosis, and with limited treatment options for patients whose cancer has progressed on or after platinum-based chemotherapy. In September 2023, the FDA granted Orphan Drug Designation to alisertib, a selective, small-molecule, orally administered inhibitor of aurora kinase A, for the treatment of patients with small cell lung cancer. In February 2024, Puma initiated ALISCA™-Lung 1, a Phase II clinical trial of alisertib monotherapy for the treatment of patients with extensive-stage small cell lung cancer.

Hormone receptor-positive (HR-positive), human epidermal growth factor receptor 2-negative (HER2-negative) breast cancer is the most prevalent type of breast cancer, in which endocrine therapy resistance and distant relapse remain unmet challenges. In November 2024, Puma initiated ALISCA™-Breast1, a Phase II clinical trial of alisertib in combination with endocrine therapy for the treatment of patients with chemotherapy-naïve HR-positive, HER2-negative recurrent or metastatic breast cancer who have been previously treated with a CDK4/6 inhibitor and received at least two prior lines of endocrine therapy in the recurrent or metastatic setting.

Product Pipeline



** EBC: Early breast cancer* *** MBC: Metastatic breast cancer* **** HRc+: Hormone receptor-positive* ***** NSCLC: Non-small cell lung cancer*

To Our Stockholders

At Puma Biotechnology, we are united by one mission—to develop and deliver innovative therapies to help cancer patients. In 2025, we explored new possibilities in that effort with meaningful progress in our commercial and clinical-stage programs for NERLYNX® and alisertib. Our work across clinical development, commercialization, and patient access reflects a shared commitment to turning scientific progress into real impact for the people we serve. This is what motivates us every day.

Throughout the year, we drove commercial momentum for NERLYNX. For the first time since 2018, patient demand for NERLYNX in the United States increased year over year. This milestone highlights the focus and dedication of our commercial team and the confidence that physicians and patients place in our therapy. At the same time, our alisertib clinical program moved forward, with both Phase II trials progressing toward important interim data readouts expected in 2026.

NERLYNX®

NERLYNX is our anchor commercial product, playing an important role as a therapy for patients with HER2-positive breast cancer. Since its initial approval by the U.S. Food and Drug Administration in 2017, NERLYNX has been an important addition to the physician's armamentarium and is the only FDA approved extended adjuvant treatment for patients with early stage HER2-overexpressed/amplified breast cancer following trastuzumab based therapy. In 2020, we obtained the additional approval of the treatment for use in the United States in combination with capecitabine in patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 treatments. NERLYNX was granted marketing authorization by the European Commission in 2018 for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who are less than one year from completion of prior adjuvant trastuzumab-based therapy and also received marketing approval in mainland China from the National Medical Products Administration (NMPA) of China in 2020. In addition, NERLYNX is approved in more than 60 countries outside the United States, demonstrating our commitment to help cancer patients worldwide. We have extended the reach of this important medicine to cancer patients globally, and we remain committed to continuing to do so.

Commercial Performance

In 2025, we accomplished an important milestone with our first year-over-year increase in NERLYNX demand in the United States since 2018. This renewed momentum reflects the strength of our commercial strategy, including our extensive efforts to increase patient awareness and broaden access. We are very pleased with this performance. We remain concentrated on expanding demand and use of NERLYNX in 2026 with the goal of further increasing market penetration.

Exploring New Combinations

At the American Association for Cancer Research Annual Meeting in April 2025, data was presented from a Phase I trial that evaluated neratinib in combination with trastuzumab deruxtecan in patients with solid tumors harboring HER2 alterations. This study, sponsored by the National Cancer Institute, established a recommended Phase II dose and showed a manageable safety profile for the combination. We were encouraged by early signs of activity across a range

Alan H. Auerbach
Chairman, Chief Executive Officer, President and Founder

of HER2-altered tumors, including promising results in cancers that are often difficult to treat, such as pancreatic cancer. The Phase II portion of the study opened enrollment in March 2025, and we look forward to its continued progress.

NERLYNX was also added to the NCCN Clinical Practice Guidelines in Oncology for Breast Cancer as a treatment option for patients with HER2 mutated metastatic breast cancer in April 2025. In addition, it was included in the NCCN Clinical Practice Guidelines in Oncology for Cervical Cancer as a treatment option for patients with recurrent or metastatic cervical cancer with HER2 mutated tumors in December 2025.

ALISERTIB

Alisertib represents an important addition to our pipeline and reflects our focus on advancing targeted therapies across multiple tumor types. Through our exclusive license agreement established in 2022, we have continued to build momentum in the development of this selective, small molecule, orally administered aurora kinase A inhibitor. Our development efforts have expanded across multiple indications, including hormone receptor-positive, HER2-negative breast cancer and small cell lung cancer. In 2025, both of our Phase II clinical trials continued to progress, positioning us for important data readouts that we believe will help inform the next stage of development for this program.

Alisertib in Breast Cancer

Advancing alisertib in hormone receptor-positive, HER2-negative breast cancer remains a key priority for Puma. Our ALISCA™-Breast1 Phase II trial, which we initiated in November 2024, is evaluating alisertib in combination with endocrine therapy in patients with metastatic disease who have progressed on CDK 4/6 inhibitors and received at least two prior lines of endocrine therapy. The study was originally designed to enroll up to 150 patients who were randomized to receive alisertib at doses of 30 mg, 40 mg, or 50 mg twice daily alongside the investigator's choice of endocrine therapy. The study also includes comprehensive biomarker analysis to help identify patient populations that may benefit most from treatment.

We are very pleased with the faster than expected enrollment in the ALISCA™-Breast1 trial, which resulted in an overenrollment. We are encouraged by the potential for alisertib to address the ongoing unmet need in patients whose disease has progressed following CDK 4/6 inhibitor therapy and where treatment options remain limited. We look forward to sharing interim data from the ALISCA™-Breast1 trial in the first half of 2026, which we expect will provide important insights to guide future development.

Alisertib in Lung Cancer

Alisertib is also being evaluated in small cell lung cancer, where there continues to be a significant need for new treatment options. Our ALISCA™-Lung1 Phase II trial, which we initiated in February 2024, is studying alisertib as a monotherapy in patients with extensive stage disease who have progressed after first-line platinum-based chemotherapy and immunotherapy. This aggressive form of lung cancer presents ongoing challenges, particularly for patients whose disease has advanced.

The trial is expected to enroll up to 120 patients and includes biomarker analysis to better understand which molecular subgroups may respond most favorably to alisertib. We anticipate presenting interim data from the ALISCA™-Lung1 trial in the first half of 2026 and believe these findings will help shape future development strategies.

FINANCIALS

In 2025, we executed on our strategic priorities focused on advancing treatments for our patients while exercising disciplined financial management. We reported NERLYNX product revenue, net of $204.1 million, and royalty revenue from our global licensing partners of $24.3 million. We are delighted to report positive net income for our fourth consecutive year, highlighting our continued fiscal discipline and operational efficiency.

We remain steadfast in our efforts to continue to report positive net income in 2026 through prioritizing treatment access for our patients, enhancing global partnerships, and driving commercial excellence—while continuing to invest in the clinical development of alisertib.

SCALING NEW POSSIBILITIES: LOOKING AHEAD

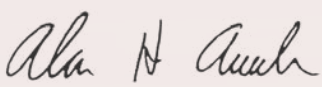
In 2025, driven by our commitment to innovation and our unwavering focus on addressing unmet medical needs, we scaled new possibilities with both NERLYNX and alisertib, a testament to the dedication of our team, the support of our partners, and the trust of our shareholders.

We are excited about the opportunities that lie before us. In 2026, we will continue to advance the development of alisertib, with a focus on presenting interim data from both the ALISCA™-Breast1 and ALISCA™-Lung1 trials. We are also focused on continuing to drive NERLYNX demand and look forward to the further advancement of alisertib in further clinical trials. By leveraging cutting-edge science and collaborating with leading researchers and clinicians, we aim to bring new treatment options to patients.

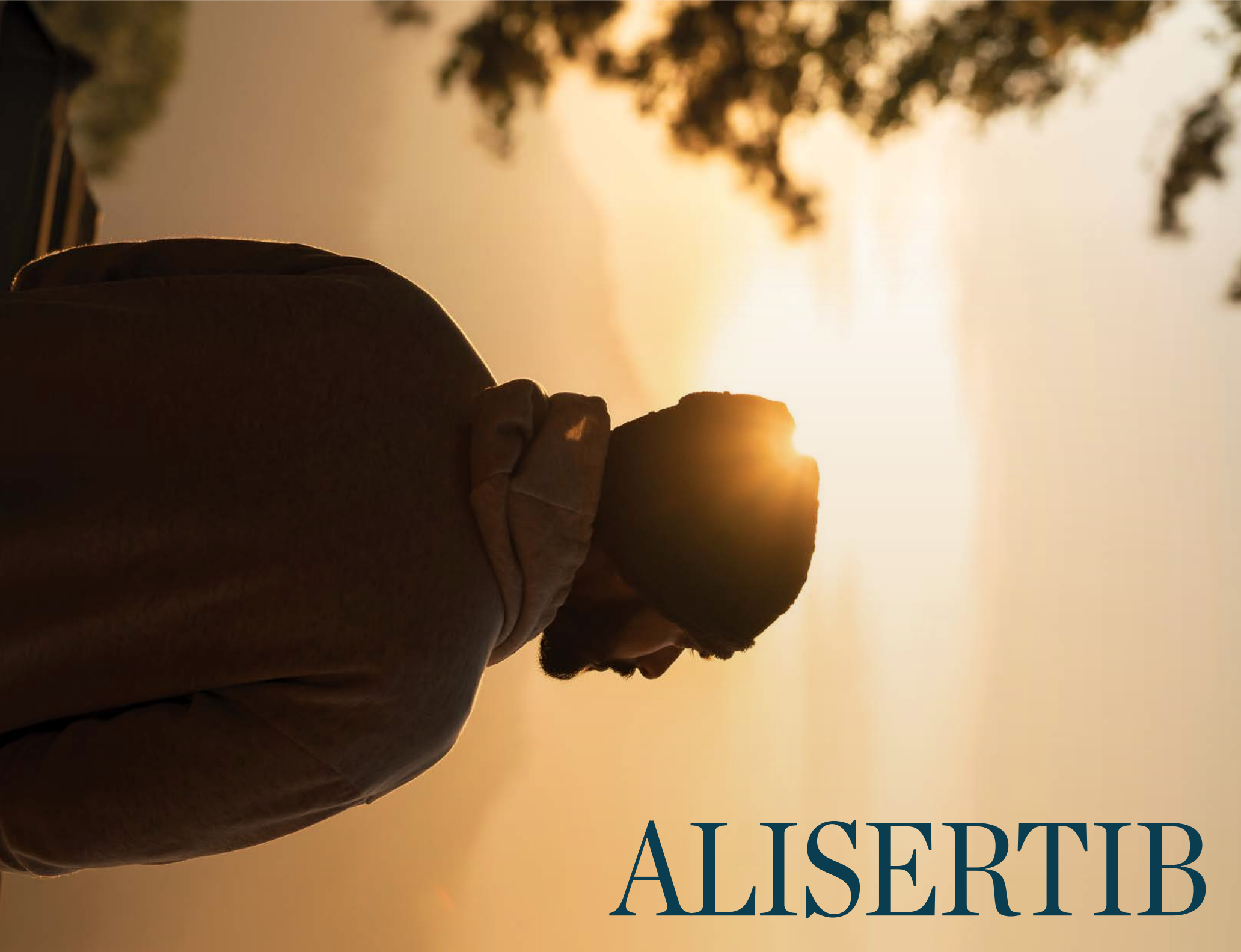
At the heart of everything we do are the patients who inspire us. We are deeply grateful for the opportunity to make a difference in their lives and remain committed to delivering therapies that offer hope and improved outcomes. None of our achievements would be possible without the support of our shareholders, employees, partners, and the broader Puma community. Your belief in our mission and your commitment to our success have been instrumental in our progress. As we move forward, we will continue to prioritize transparency, accountability, and value creation for all stakeholders.

On behalf of the Board of Directors, I would like to thank our stockholders for their continued support and partnership as we work toward our shared mission, scaling new possibilities together in pursuit of a future where cancer patients have access to more treatments to enable longer, healthier lives.

Sincerely,



Alan H. Auerbach
Chairman, Chief Executive Officer, President and Founder



ALISERTIB

“Although we are seeing advances in the treatment of small cell lung cancer, there remains an unmet need for treatment options for patients with small cell lung cancer that has progressed on or after platinum-based chemotherapy. Puma’s ongoing studies of alisertib monotherapy and in combination with paclitaxel and the focus on molecular selection of patients who are likely to respond to alisertib could help define a new approach in this disease.”

TAOFEEK K. OWONIKOKO, M.D., Ph.D., Executive Director, University of Maryland Comprehensive Cancer Center, Senior Associate Dean of Cancer Programs, University of Maryland School of Medicine, Vice President of Cancer Programs, University of Maryland Baltimore.

Small Cell Lung Cancer

ALISCA™-Lung1 | A Phase II Study of Alisertib, an Investigational Drug, in Patients with Extensive Stage Small Cell Lung Cancer

ABOUT THIS CLINICAL TRIAL

This is a multi-center Phase II study (PUMA-ALI-4201) investigating alisertib monotherapy in patients with small cell lung cancer (SCLC). The objectives of the study are to determine whether biomarkers correlate with alisertib response, as well as determine the safety and efficacy in the patient population.

WHO IS ELIGIBLE?

The ALISCA™-Lung1 clinical trial is open to patients 18 years of age or older with pathologically confirmed SCLC following progression on or after first-line treatment with one platinum-based chemotherapy and an anti-programmed death-ligand (PD-L1) immunotherapy agent. Up to one additional systemic anti-cancer therapy for SCLC is allowed, for a total of up to two prior lines of therapy.

NOW ENROLLING

The study is being conducted at approximately 28 sites within the United States. Puma is pleased with the current rate of enrollment and is preparing for formal analysis.

For more information on this clinical trial, location of trial sites, and how to enroll
Go to: https://clinicaltrials.gov ID NCT06095505 or
Email: clinicaltrials@pumabiotechnology.com

ALISCA™-Lung2 | A Phase II Study of Alisertib in Combination with Paclitaxel in Patients with Small Cell Lung Cancer

ABOUT THIS CLINICAL TRIAL

This is a multi-center Phase II open label study (PUMA-ALI-4202) evaluating increasing doses of alisertib administered in combination with paclitaxel in patients with small cell lung cancer (SCLC). The objectives of the study are to assess the safety and tolerability of various doses of alisertib in combination with paclitaxel as well as evaluate clinical effectiveness. Exploratory objectives include evaluating biomarkers of interest in both tumor and liquid biopsies.

WHO IS ELIGIBLE?

The ALISCA™-Lung2 clinical trial is open to patients 18 years of age or older. Patients must have pathologically confirmed SCLC and progressed on or after treatment with two prior treatment regimens. Patients must have received treatment with platinum-based chemotherapy and an anti-programmed death receptor 1 (PD-1) or PD-L1 immunotherapy agent.

OPENING IN 3Q-2026

The study will be conducted at 30 sites in the United States and Europe. Puma is pleased with the current rate of enrollment and is preparing for formal analysis.

For more information on this clinical trial, location of trial sites, and how to enroll
Go to: https://clinicaltrials.gov ID NCT07465757 or
Email: clinicaltrials@pumabiotechnology.com

Metastatic Breast Cancer

ALISCA™-Breast1 | A Phase II Study of Alisertib, an Investigational Drug, in Combination with Endocrine Therapy in Patients with HR-Positive, HER2-Negative Recurrent or Metastatic Breast Cancer

ABOUT THIS CLINICAL TRIAL

This is a randomized, dose optimization, multi-center Phase II study (PUMA-ALI-1201) of alisertib administered in combination with endocrine therapy in patients with hormone receptor-positive (HR+), human epidermal growth factor 2-negative (HER2-negative) metastatic breast cancer (MBC). The objectives of the study are to determine the optimal alisertib dose in combination with selected endocrine therapy based on safety and efficacy, as well as whether biomarkers correlate with alisertib response.

PATIENT POPULATION

The ALISCA™-Breast1 clinical trial enrolled patients 18 years of age or older with pathologically confirmed HR+/HER2-negative MBC following progression on or after at least two prior lines of endocrine therapy in the recurrent or metastatic setting. Prior treatment with a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) in combination with endocrine therapy in the recurrent or metastatic setting was required. Treatment with chemotherapy in the recurrent or metastatic setting was not allowed.

ENROLLMENT COMPLETE

Puma is pleased to announce that enrollment is complete, and the study remains ongoing at sites within the United States, Spain and Portugal, while preparing for formal analysis.

For more information on this clinical trial,
Go to: https://clinicaltrials.gov ID NCT06369285 or
Email: clinicaltrials@pumabiotechnology.com

“The results of study ALI-1201 will help define the future development of alisertib in metastatic ER-positive, HER2-negative breast cancer. With its novel mechanism, alisertib may be able to provide a clinical benefit in patients who have developed resistance to other treatment modalities and where treatment options are limited.”

JOYCE A. O’SHAUGHNESSY, M.D., Chair of Breast Cancer Research for the Sarah Cannon Research Institute in Dallas, Texas

ALISERTIB

NERLYNX®

Breast Cancer

NERLYNX *(neratinib)* | NERLYNX is a once-a-day oral treatment for adults with HER2-positive breast cancer, taken after trastuzumab-based therapy. NERLYNX can help further reduce the risk of recurrence. It is also approved for patients with HER2-positive breast cancer in the metastatic setting.

Despite advances in HER2-positive Breast Cancer, the risk of recurrence and progression remains a significant concern for many patients and physicians. NERLYNX can play an important role in helping HER2-positive breast cancer patients reduce their overall risk and give hope to patients and their families. Currently, NERLYNX is the only drug approved for the extended adjuvant treatment of HER2-positive early stage breast cancer.

We at Puma know, all too well, the impact that HER2-positive breast cancer can have on patients and their families. We are committed and passionate about helping more patients reduce their risk of recurrence or progression.

PUMA OFFERS A WIDE VARIETY OF PATIENT SUPPORT SERVICES:

- Education materials
- Nurse call center
- Co-pay support
- Patient mentor program
- Supportive care voucher

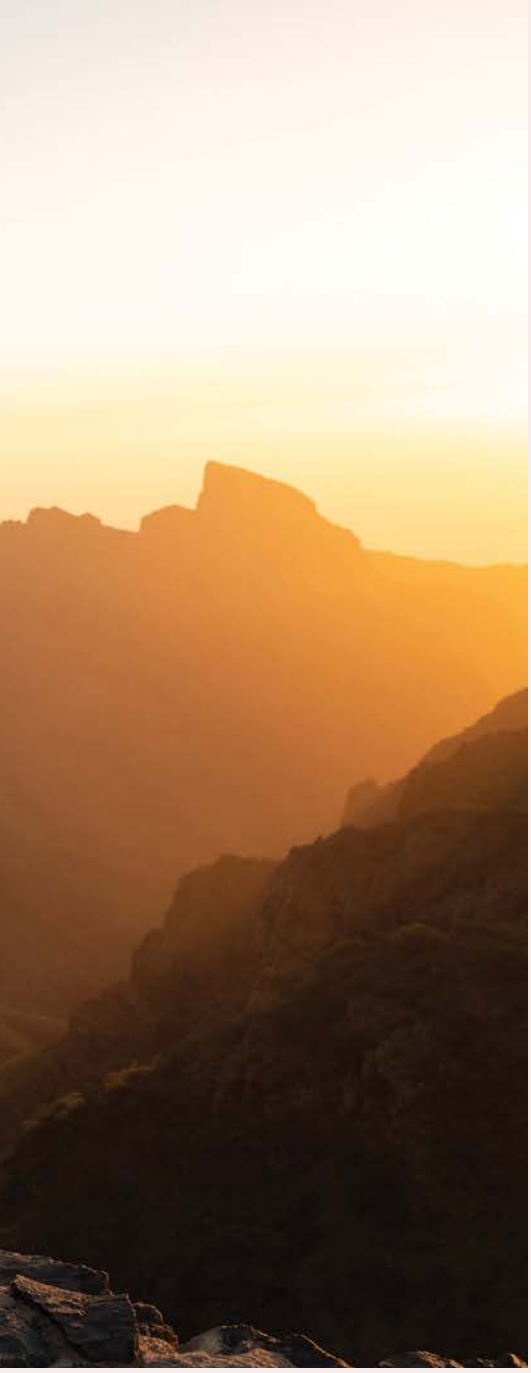
"I wanted to do everything possible to reduce the risk of recurrence."

EDWINA, a former NERLYNX patient

In February 2026, the World Health Organization reported the following statistics for 2022:

Breast cancer is the leading cause of cancer death among women worldwide, with approximately 2.3 million new cases reported each year and more than 670,000 deaths globally per year.

- NERLYNX was approved for HER2-positive early stage breast cancer in July 2017 and for HER2-positive metastatic breast cancer in February 2020
- NERLYNX is now approved in over 60 countries around the world
- NERLYNX is included on key oncology clinical pathways in the United States
- Dose escalation was added to the NERLYNX label in June 2021, helping to improve patient tolerability
- NERLYNX has been utilized by over 5,000 oncologists in the United States since initial launch in 2017



INDICATIONS

NERLYNX® (neratinib) tablets, for oral use, is a kinase inhibitor indicated:

- As a single agent, for the extended adjuvant treatment of adult patients with early-stage HER2-positive breast cancer to follow adjuvant trastuzumab-based therapy.
- In combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Important Safety Information Regarding NERLYNX® (neratinib) U.S. Indication

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS:

- **Diarrhea:** Manage diarrhea through either NERLYNX dose escalation or loperamide prophylaxis. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold NERLYNX in patients experiencing severe and/or persistent diarrhea. Permanently discontinue NERLYNX in patients experiencing Grade 4 diarrhea or Grade ≥ 2 diarrhea that occurs after maximal dose reduction.
- **Hepatotoxicity:** Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated. Withhold NERLYNX in patients experiencing Grade 3 liver abnormalities and permanently discontinue NERLYNX in patients experiencing Grade 4 liver abnormalities.
- **Embryo-Fetal Toxicity:** NERLYNX can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS: The most common adverse reactions (reported in ≥ 5% of patients) were:

- NERLYNX as a single agent: diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increased, nail disorder, dry skin, abdominal distention, epistaxis, weight decreased, and urinary tract infection.
- NERLYNX in combination with capecitabine: diarrhea, nausea, vomiting, decreased appetite, constipation, fatigue/asthenia, weight decreased, dizziness, back pain, arthralgia, urinary tract infection, upper respiratory tract infection, abdominal distention, renal impairment, and muscle spasms.

To report SUSPECTED ADVERSE REACTIONS, contact Puma Biotechnology, Inc. at 1-844-NERLYNX (1-844-637-5969) or FDA at 1-800-332-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS:

- Gastric acid reducing agents: Avoid concomitant use with proton pump inhibitors. Separate NERLYNX by at least 2 hours before or 10 hours after H2-receptor antagonists. Or separate NERLYNX by at least 3 hours after antacids.
- Strong CYP3A4 inhibitors: Avoid concomitant use.
- P-gp and moderate CYP3A4 dual inhibitors: Avoid concomitant use.
- Strong or moderate CYP3A4 inducers: Avoid concomitant use.
- Certain P-gp substrates: Monitor for adverse reactions of P-gp substrates for which minimal concentration change may lead to serious adverse reactions when used concomitantly with NERLYNX.

USE IN SPECIFIC POPULATIONS:

- **Lactation:** Advise women not to breastfeed.

Please see Full Prescribing Information for additional safety information.

Form 10-K

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, 2025

or

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

For the transition period from to

Commission File Number: 001-35703

PUMA BIOTECHNOLOGY, INC.

(Exact name of registrant as specified in its charter)

Delaware	**77-0683487**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

10880 Wilshire Boulevard, Suite 1700
Los Angeles, CA 90024
(424) 248-6500
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	PBYI	The NASDAQ Stock Market LLC (NASDAQ Global Select Market)

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit 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 emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

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

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

The aggregate market value of voting stock held by non-affiliates of the registrant was approximately $145.2 million as of June 30, 2025, based upon the closing price of $3.43 per share of the registrant's common stock on the NASDAQ Global Select Market on Monday, June 30, 2025, the last business day of the registrant's most recently completed second fiscal quarter. Shares of common stock held by each executive officer, director and holder of 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. As of February 23, 2026, there were 50,876,487 shares of the registrant's common stock outstanding.

Documents Incorporated by Reference:

Portions of the proxy statement for the registrant's 2026 Annual Meeting of Stockholders (the "2026 Proxy Statement"), are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Any statements about our expectations, beliefs, plans, objectives, assumptions, future events or performance are not historical facts and may be forward looking. These forward-looking statements include, but are not limited to, statements about:

- the commercialization of NERLYNX® (neratinib) tablets ("NERLYNX");
- the development of our drug candidates, including when we expect to undertake, initiate and complete clinical trials of our drug candidates;
- the anticipated timing of regulatory filings;
- the regulatory approval of our drug candidates;
- our use of clinical research organizations ("CRO") and other contractors;
- our ability to find collaborative partners for research, development and commercialization of potential products;
- efforts of our sub-licensees to obtain regulatory approval and commercialize NERLYNX in areas outside the United States;
- our ability to market any of our products;
- our expectations regarding our costs and expenses;
- our anticipated capital requirements and estimates regarding our needs for additional financing;
- our ability to compete against other companies and research institutions;
- our ability to secure adequate protection for our intellectual property;
- our intention and ability to vigorously defend against any litigation to which we are or may become party;
- our ability to in-license additional drugs;
- our ability to attract and retain key personnel; and
- our ability to obtain adequate financing on favorable terms or at all.

These statements are often, but not always, made through the use of words or phrases such as "anticipate," "estimate," "plan," "project," "continuing," "ongoing," "expect," "believe," "intend" and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Discussions containing these forward-looking statements may be found throughout this Annual Report, including the sections entitled "Item 1. Business" in Part I and "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II of this Annual Report. These forward-looking statements involve risks and uncertainties, including the risks discussed in the section entitled "Item 1A. Risk Factors" in Part I of this Annual Report that could cause our actual results to differ materially from those in the forward-looking statements. We undertake no obligation to update the forward-looking statements or to reflect events or circumstances after the date of this document, except as required by law. The risks discussed in this Annual Report should be considered in evaluating our prospects and future financial performance.

SUMMARY OF RISK FACTORS

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock, including those described in the section entitled "Item 1A. Risk Factors" in Part I of this Annual Report. These risks include, among others, the following:

- While we have reported net income in recent years, we cannot assure that we will continue to do so and may not be able to maintain profitability.
- We are currently a single product company with limited commercial sales experience.
- We may not be able to successfully commercialize NERLYNX in the future.
- We may not be able to secure additional financing on favorable terms, or at all, to meet our future capital needs and our failure to obtain additional financing when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or commercialization efforts or other operations.
- The terms of our Note Purchase Agreement place restrictions on our ability to operate our business and on our financial flexibility, and we may be unable to achieve the revenue necessary for us to incur additional borrowings under the Note Purchase Agreement or to satisfy the minimum revenue and cash balance covenants.
- We have in-licensed alisertib, a drug candidate for which we have assumed all responsibility for global development and commercialization. Our development of alisertib will be expensive, lengthy and unpredictable, and any failure to successfully develop alisertib will have a material adverse effect on our business and financial position.
- Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- NERLYNX, alisertib or other drug candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any, as applicable.
- We are in the early stages of development of alisertib, and we cannot be certain that we will be successful if we seek regulatory approvals for our drug candidates.
- We have limited experience as a company in marketing or distributing pharmaceutical products. If we are unable to expand our marketing and sales capabilities in the commercialization of NERLYNX, our business, results of operations and financial condition may be materially adversely affected.
- We are exposed to the risks associated with reliance on a direct sales force to commercialize NERLYNX in the United States.
- Our NERLYNX commercialization efforts may fail to achieve the degree of market acceptance by patients and physicians necessary for commercial success.
- We depend on a limited number of customers for a significant amount of our total revenue, and if we lose any of our significant customers, our business could be harmed.
- Even though the U.S. Food and Drug Administration ("FDA") and the European Commission ("EC") have granted approval of NERLYNX for the extended adjuvant treatment of certain patients with early stage, HER2-positive breast cancer and the FDA has granted approval for NERLYNX for the treatment of certain patients with metastatic HER2-positive breast cancer, the terms of the approvals may limit its commercial potential.

- We are dependent on international third-party sub-licensees for the development and commercialization of NERLYNX in several countries outside the United States. The failure of these sub-licensees to meet their contractual, regulatory or other obligations could adversely affect our business.

- We have no experience in drug formulation or manufacturing and rely exclusively on third parties to formulate and manufacture NERLYNX, alisertib and our other drug candidates, and any disruption or loss of these relationships could delay our development and commercialization efforts.

- Our business, financial condition, results of operations and ongoing clinical trials have been, and could continue to be, harmed by the effects of public health emergencies or outbreaks of epidemics, pandemics or contagious diseases.

- We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm us.

- We depend significantly on in-licensed intellectual property, and the termination of these licenses would significantly harm our business and future prospects.

- Our proprietary rights may not adequately protect our intellectual property and potential products, and if we cannot obtain adequate protection of our intellectual property and potential products, we may not be able to successfully market our potential products.

PART I

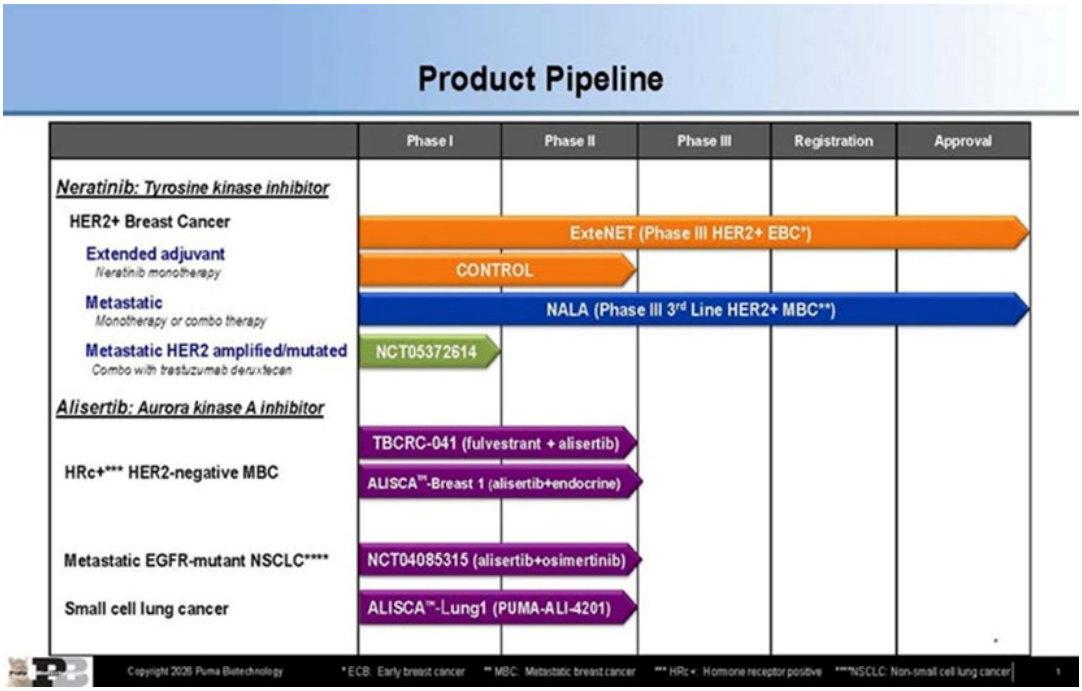
ITEM 1. BUSINESS

Company Overview

Unless otherwise provided in this Annual Report, references to the "Company," "we," "us," and "our" refer to Puma Biotechnology, Inc. and our wholly owned subsidiary.

We are a biopharmaceutical company that develops and commercializes innovative products to enhance cancer care and improve treatment outcomes for patients. We are currently commercializing NERLYNX, an oral version of neratinib, for the treatment of certain HER2-positive breast cancers. Additionally, we have in-licensed, and are responsible for global development and commercialization of, alisertib. Alisertib is a selective, small-molecule inhibitor of Aurora Kinase A that is designed to disrupt mitosis leading to apoptosis of rapidly proliferating tumor cells that are dependent on Aurora Kinase A. Prior to our licensing alisertib from a subsidiary of Takeda Pharmaceutical Company Limited ("Takeda"), alisertib was tested in over 1,300 patients who were treated across 22 company-sponsored trials resulting in a large, well-characterized clinical safety database. Based on information in this database, we believe alisertib has potential application in the treatment of a range of different cancer types, including hormone receptor-positive breast cancer, triple negative breast cancer and small cell lung cancer. We intend to pursue development of alisertib initially in small cell lung cancer and hormone receptor-positive breast cancer.

The following figure provides an overview of our commercial product and drug candidates.



* EBC: Early breast cancer
** MBC: Metastatic breast cancer
*** HRc+: Hormone receptor-positive
**** NSCLC: Non-small cell lung cancer

Neratinib

Breast cancer is the leading cause of cancer death among women worldwide, with approximately 2.3 million new cases reported each year and more than 670,000 deaths globally per year. Up to 20% of breast cancer tumors show over-expression of the HER2 protein. Women with breast cancer that over-expresses HER2, referred to as HER2-positive breast cancer, are at greater risk for disease progression and death than women whose tumors do not over-express HER2. Therapeutic strategies have been developed to block HER2 in order to improve the treatment of this type of breast cancer. Trastuzumab, pertuzumab, lapatinib, T-DM1, fam-trastuzumab deruxtecan and tucatinib are all drugs that are used as single agents, in combination with other drugs and in combination with chemotherapy to treat patients with HER2-positive breast cancer at various stages.

Neratinib is a potent irreversible tyrosine kinase inhibitor ("TKI") that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Based on pre-clinical studies and clinical trials to date, we believe that neratinib may offer an advantage over existing treatments that are used in the treatment of patients with HER2-positive breast cancer. We believe that by more potently inhibiting HER2 at a different site and acting via a mechanism different from other agents, neratinib may have therapeutic benefits in breast cancer patients who have been previously treated with these existing treatments, most notably due to its irreversible inhibition of the HER2 target enzyme.

NERLYNX, the commercial name for neratinib, is currently approved in the United States for two indications: the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy and for use in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. We also believe neratinib has potential clinical application in the treatment of several other cancers as well, including other tumor types that over-express or have a mutation in HER2 or epidermal growth factor receptor ("EGFR"), such as cervical cancer, lung cancer or other solid tumors.

We currently market NERLYNX in the United States using our direct specialty sales force consisting of approximately 35 sales specialists as of December 31, 2025. Our sales specialists are supported by an experienced sales leadership team consisting of regional managers and directors, as well as a commercial team of experienced professionals in marketing, access and reimbursement, managed markets, marketing research, commercial operations and sales force planning and management. Outside the United States, we have entered into exclusive sub-license agreements with third parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved. As of December 31, 2025, NERLYNX has received approval for the treatment of certain patients with extended adjuvant and/or metastatic HER2-positive breast cancer in more than 40 countries outside the United States, including the European Union ("EU"), China, Latin America, Australia, Canada, and Hong Kong. We are currently party to several sub-licenses in various regions outside the United States, including Europe (excluding Ukraine), Australia, Canada, China, Southeast Asia, Israel, South Korea, Russia and various countries and territories in Central America, South America, Africa and the Middle East.

Alisertib

In September 2022, we entered into an exclusive license agreement with Takeda to license the worldwide research and development and commercial rights to alisertib. Alisertib is an investigational, reversible, ATP-competitive inhibitor that is designed to be highly selective for Aurora Kinase A. Inhibition of Aurora Kinase A leads to disruption of mitotic spindle apparatus assembly, disruption of chromosome segregation, and inhibition of cell proliferation. In clinical trials to date, alisertib had shown single agent activity and activity in combination with other cancer drugs in the treatment of many different types of cancers, including hormone receptor-positive breast cancer, triple negative breast cancer, small cell lung cancer and head and neck cancer. Alisertib has also shown activity in previous clinical trials in peripheral T cell lymphoma and non-Hodgkin's lymphoma. Prior to our licensing alisertib from Takeda, the drug was tested in over 1,300 patients who were treated across 22 company-sponsored trials resulting in a large well-characterized clinical safety database.

Strategy

Our goal is to become a leading provider of advanced therapies for the treatment of various forms of cancer. The following elements comprise our strategy to achieve this objective:

- Successfully execute our NERLYNX commercial plan. An important near-term objective is to continue to execute our NERLYNX commercial plan by driving market penetration and duration of therapy consistent with the current NERLYNX label. We continue to focus our efforts on commercializing NERLYNX in the United States. In addition, we have entered into exclusive sub-license agreements with various parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved, in additional countries worldwide.

- Advance the development of alisertib. We intend to pursue the development of alisertib in hormone receptor-positive breast cancer, as well as small cell lung cancer based on the prior clinical data that has been generated. We also plan to evaluate alisertib in biomarker focused populations where it has shown a higher degree of activity, such as patients with c-Myc amplification and RB1 loss/RB1 mutations, as we believe that this may provide a point of differentiation from the other drugs being developed in the treatment of these diseases.

- Maximize the value of our programs by maintaining the flexibility to commercialize our drug candidates independently or through collaborative relationships with third parties. We are currently commercializing NERLYNX using a direct sales force in the United States and using sub-licensees in certain countries outside the United States. As we move additional drug candidates through development toward regulatory approval, we plan to evaluate several options for each drug candidate's commercialization strategy. These options include building upon or leveraging our own internal sales force; entering into a joint marketing partnership with another pharmaceutical or biotechnology company, whereby we jointly sell and market the product; and out-licensing our product, whereby another pharmaceutical or biotechnology company sells and markets our product and pays us a royalty on sales. Our decision may be different for each product that reaches commercialization and will be based on a number of factors including capital necessary to execute on each option, size of the market to be addressed and terms of potential offers from other pharmaceutical and biotechnology companies.

- In-license or acquire additional commercial drugs and/or drug candidates and technologies in order to build a sustainable product pipeline by employing multiple therapeutic approaches and disciplined decision criteria based on clearly defined proof of principal goals. We seek to build a sustainable portfolio including commercial drugs where we can successfully leverage our existing commercial infrastructure and a product pipeline by employing multiple therapeutic approaches and by acquiring drug candidates belonging to known drug classes. In addition, we employ disciplined decision criteria to assess drug candidates. A decision by us to license a drug candidate will depend on a variety of factors, including the scientific merits of the technology; the costs of the transaction and other economic terms of the proposed license; the amount of capital required to develop the technology; and the economic potential of the drug candidate, should it be commercialized. We believe this strategy minimizes our clinical development risk and allows us to accelerate the development and potential commercialization of current and future drug candidates.

Neratinib

HER2-Positive Breast Cancer Overview

Breast cancer is the leading cause of cancer death among women worldwide. In 2022, an estimated 2.3 million new cases and 670,000 breast cancer-related deaths occurred. Up to 20% of breast cancer tumors show over-expression of the HER2 protein and HER2 status is an important prognostic and predictive factor of breast cancer. Therapeutic strategies have been developed to block HER2 in order to improve the treatment of this type of breast cancer.

Trastuzumab, pertuzumab, lapatinib, T-DM1, fam-trastuzumab deruxtecan and tucatinib are all drugs that are used as single agents, in combination with other drugs and in combination with chemotherapy to treat patients with HER2-positive breast cancer at various stages.

Currently, the only treatment approved by the FDA for the treatment of neoadjuvant (newly diagnosed) HER2-positive breast cancer is the combination of pertuzumab plus trastuzumab and taxane chemotherapy. The FDA-approved treatments for the adjuvant treatment of HER2-positive early stage breast cancer are the combination of trastuzumab and chemotherapy, the combination of pertuzumab plus trastuzumab and chemotherapy, or KADCYLA®, which is approved specifically in patients with HER2-positive early stage breast cancer with residual disease after neoadjuvant treatment. In addition, we are aware of numerous additional ongoing clinical trials involving other drug candidates used alone or in combination with existing drugs to treat patients with breast cancer. In addition, we are also aware of a Phase III trial in patients with high risk HER2-positive early stage breast cancer with residual disease after neoadjuvant treatment that is testing the combination of KADCYLA plus tucatinib versus KADCYLA alone (the "CompassHER2 RD Trial"), and the data from the completed Phase III trial in patients with high risk HER2-positive early stage breast cancer with residual disease after neoadjuvant treatment that evaluated fam-trastuzumab deruxtecan versus KADCYLA alone (the "DESTINY-Breast05 Trial").

We believe that there are approximately 30,000 patients in the United States and 37,000 patients in the EU with early stage HER2-positive breast cancer who are treated with adjuvant therapy. We also believe that there are approximately 6,400 patients in the United States with third-line HER2-positive metastatic breast cancer. The number of patients with third-line or later HER2-positive metastatic breast cancer may decrease in future years as the introduction of new neoadjuvant, adjuvant and extended adjuvant treatments may reduce the number of patients with recurrence of HER2-positive breast cancer and therefore reduce the number of patients with HER2-positive metastatic breast cancer.

Background on Neratinib

Neratinib is a potent irreversible TKI that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Based on pre-clinical studies and clinical trials to date, we believe that neratinib may offer an advantage over existing treatments that are used in the treatment of patients with HER2-positive breast cancer. We believe that by more potently inhibiting HER2 at a different site and acting via a mechanism different from other agents, neratinib may have therapeutic benefits in patients who have been previously treated with these existing treatments, most notably due to its irreversible inhibition of the HER2 target enzyme.

In addition, we believe neratinib has clinical application in the treatment of several other cancers as well, including other tumor types that over-express or have a mutation in HER2 or EGFR, such as breast cancer, cervical cancer, lung cancer or other solid tumors.

Neratinib—Early Stage Breast Cancer

Extended Adjuvant Breast Cancer

In 2017, the FDA approved NERLYNX (neratinib) for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. In 2018, the EC granted marketing authorization for NERLYNX in the EU for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who are less than one year from the completion of prior adjuvant trastuzumab-based therapy. These approvals were obtained based on the two-year data obtained in our ExteNET trial.

Two-Year ExteNET Data. In July 2014, we announced top line results from our ExteNET trial, a Phase III clinical trial of neratinib for the extended adjuvant treatment of early stage HER2-positive breast cancer. The data from this trial were presented in an oral presentation at the American Society of Clinical Oncology ("ASCO") Annual Meeting in June 2015 and were published online in *The Lancet Oncology* in February 2016. The ExteNET trial was a double-blind, placebo-controlled, Phase III trial of neratinib versus placebo after adjuvant treatment with Herceptin in women with early stage HER2-positive breast cancer. More specifically, the ExteNET trial enrolled 2,840 patients in 41 countries with early stage HER2-positive breast cancer who had undergone surgery and adjuvant treatment with trastuzumab. After completion of adjuvant treatment with trastuzumab, patients were randomized to receive extended adjuvant treatment with either neratinib or placebo for a period of one year. Patients were then followed for recurrent disease, ductal carcinoma in situ ("DCIS"), or death for a period of two years after randomization in the trial.

The safety results of the study showed that the most frequently observed adverse event for the neratinib-treated patients was diarrhea, with approximately 39.9% of the neratinib-treated patients experiencing grade 3 or higher diarrhea (one patient, 0.1%, had grade 4 diarrhea). Patients who received neratinib in this trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-related diarrhea.

The primary endpoint of the ExteNET trial was invasive disease-free survival ("DFS"). The results of the trial demonstrated that treatment with neratinib resulted in a 33% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.67, $p = 0.009$). The two-year DFS rate for the neratinib arm was 93.9% and the two-year DFS rate for the placebo arm was 91.6%. The secondary endpoint of the trial was disease-free survival including ductal carcinoma in situ ("DFS-DCIS"). The results of the trial demonstrated that treatment with neratinib resulted in a 37% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.63, $p = 0.002$). The two-year DFS-DCIS rate for the neratinib arm was 93.9% and the two-year DFS-DCIS rate for the placebo arm was 91.0%.

As an inclusion criteria for the ExteNET trial, patients needed to have tumors that were HER2-positive using local assessment. In addition, as a pre-defined subgroup in the trial, patients had centralized HER2 testing performed on their tumor as well. At the time the two-year data was compiled, centralized HER2 testing had been performed on 1,704 (60%) of the patients in the ExteNET trial and further central testing on available samples was ongoing. For the 1,463 patients whose tumors were HER2-positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 49% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.51, $p = 0.002$). The two-year DFS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the 2-year DFS rate for the centrally confirmed patients in the placebo arm was 90.6%. For the patients in the trial whose tumors were HER2-positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 51% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.49, $p < 0.001$). The two-year DFS-DCIS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the two-year DFS rate for centrally confirmed patients in the placebo arm was 90.2%.

For the pre-defined subgroup of patients with hormone receptor-positive disease, the results of the trial demonstrated that treatment with neratinib resulted in a 49% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.51, p = 0.001). The two-year DFS rate for the neratinib arm was 95.4% and the two-year DFS rate for the placebo arm was 91.2%. For the patients in the trial whose tumors were HER2-positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 75% reduction of risk of invasive disease recurrence or death (hazard ratio = 0.25, p < 0.001). The two-year DFS rate for the centrally confirmed patients in the neratinib arm was 97.0% and the two-year DFS rate for centrally confirmed patients in the placebo arm was 88.4%.

Five-Year ExteNET Data. In September 2017, we presented updated data from the ExteNET trial at the European Society of Medical Oncology ("ESMO") 2017 Congress in Madrid, Spain. The data represented a predefined five-year invasive disease-free survival ("iDFS") analysis as a follow-up to the primary two-year iDFS analysis of the Phase III ExteNET trial. The results of the trial demonstrated that after a median follow up of 5.2 years, treatment with neratinib resulted in a 27% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.73, p = 0.008). The five-year iDFS rate for the neratinib arm was 90.2% and the 5-year iDFS rate for the placebo arm was 87.7%. The secondary endpoint of the trial was invasive disease-free survival including ductal carcinoma in situ ("iDFS-DCIS"). The results of the trial demonstrated that treatment with neratinib resulted in a 29% reduction of risk of disease recurrence, including DCIS or death versus placebo (hazard ratio = 0.71, p = 0.004). The five-year iDFS-DCIS rate for the neratinib arm was 89.7% and the five-year iDFS-DCIS rate for the placebo arm was 86.8%.

For the pre-defined subgroup of patients with hormone receptor-positive disease, the results of the trial demonstrated that treatment with neratinib resulted in a 40% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.60, p = 0.002). The five-year iDFS rate for the neratinib arm was 91.2% and the five-year iDFS rate for the placebo arm was 86.8%. For the pre-defined subgroup of patients with hormone receptor-negative disease, the results of the trial demonstrated that treatment with neratinib resulted in a hazard ratio of 0.95 (p = 0.762).

The results of the ExteNET trial showed that after two years of follow-up, for patients with hormone receptor-positive, HER2-positive early stage breast cancer who were treated within one year after the completion of trastuzumab based adjuvant therapy, iDFS was 95.3% in the patients treated with neratinib compared with 90.8% in those receiving placebo (hazard ratio = 0.49; 95% CI: (0.30, 0.78); p=0.002).

The safety results were unchanged from the primary two-year iDFS analysis of the study that showed the most frequently observed adverse event for the neratinib-treated patients was diarrhea, with approximately 39.9% of the neratinib-treated patients experiencing grade 3 or higher diarrhea (one patient, or 0.1%, had grade 4 diarrhea). Patients who received neratinib in this trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-related diarrhea.

In October 2020, we announced that efficacy results of neratinib in HER2-positive, hormone receptor-positive ("HR+"), early stage breast cancer from the Phase III ExteNET trial were published in *Clinical Breast Cancer*. The manuscript presented data focusing on hormone receptor-positive patients who initiated treatment within a year of completing an adjuvant trastuzumab containing treatment (HR+ /< 1 yr) and subgroups of clinical interest including patients who did not achieve a pathological complete response (no pCR) after neoadjuvant treatment and therefore were at a high risk of disease recurrence (HR+/ <1 yr, no pCR). In the HR+ /< 1 yr patient population, the absolute 5-year invasive disease-free survival benefit versus placebo was 5.1% (HR=0.58, 95% CI 0.41–0.82) and absolute 8-year overall survival benefit was 2.1%. (HR=0.79, 95% CI 0.55–1.13). The 5-year cumulative incidence of central nervous system ("CNS") metastases was 0.7% in the neratinib arm and 2.1% in the placebo arm.

In the HR+/ <1 yr, no pCR subgroup of patients that were at a high risk of disease recurrence the absolute 5-year iDFS benefit in the neratinib arm versus placebo was 7.4% (HR=0.60; 95% CI 0.33–1.07) and the 8-year overall survival benefit was 9.1% (HR=0.47; 95% CI 0.23– 0.92).

NERLYNX is included in the body of the National Comprehensive Cancer Network ("NCCN") Practice Guidelines for Breast Cancer for the treatment of adjuvant HER2-positive Breast Cancer (BINV-16 & BINV-L) under the heading Useful in Certain Circumstances, with a recommendation for considering extended adjuvant neratinib for patients with HR-positive, HER2-positive disease with a perceived high risk of recurrence. Dose escalation of neratinib is included as an approach to improve the tolerability of neratinib in the treatment of adjuvant HER2-positive breast cancer.

CONTROL. In February 2015, we initiated the CONTROL trial, which is an international, open-label, Phase II study investigating the use of antidiarrheal prophylaxis or dose escalation in the prevention and reduction of neratinib-associated diarrhea and, more specifically, grade 3 diarrhea. In the CONTROL trial, patients with HER2-positive early stage breast cancer who had completed trastuzumab-based adjuvant therapy received neratinib daily for a period of one year.

In December 2021, final results from the CONTROL trial were presented at the CTRC-AACR San Antonio Breast Cancer Symposium.

Final results showed the incidence of grade 3 diarrhea for the 137 patients who received the loperamide prophylaxis was 31%, the incidence of grade 3 diarrhea for the 64 patients who received the combination of loperamide plus budesonide was 28%, the incidence of grade 3 diarrhea for the 136 patients who received the combination of loperamide plus colestipol was 21%, the incidence of grade 3 diarrhea for the 104 patients who received colestipol alone with loperamide as needed was 33%, the incidence of grade 3 diarrhea for the 60 patients who used the dose escalation 1 regimen (DE 1) was 13%, and the incidence of grade 3 diarrhea for the 62 patients who used dose escalation regimen 2 (DE 2) was 27%. Further information is provided in Table 1 below:

Table 1: Incidence of Treatment-Emergent Diarrhea

	Loperamide (N=137)	**Budesonide (N=64)**	**Colestipol (N=136)**	**Colestipol + Loperamide Loperamide PRN (N=104)**	**Neratinib Dose Escalation Scheme 1 (N=60)**	**Neratinib Dose Escalation Scheme 2 (N=62)**
Patient incidence of diarrhea by worst grade - n (%)						
Any grade	109 (80)	55 (86)	113 (83)	99 (95)	59 (98)	61 (98)
Grade 1	33 (24)	15 (23)	38 (28)	34 (33)	24 (40)	23 (37)
Grade 2	34 (25)	22 (34)	47 (35)	31 (30)	27 (45)	21 (34)
Grade 3	42 (31)	18 (28)	28 (21)	34 (33)	8 (13)	17 (27)
Grade 4	0	0	0	0	0	0
Diarrhea leading to discontinuation	28 (20)	7 (11)	5 (4)	8 (8)	2 (3)	4 (6)
Hospitalization (due to diarrhea)	2 (1)	0	0	0	0	0

Adoption of neratinib dose escalation at the initiation of treatment, particularly the 2-week DE schedule ("DE1"), most markedly reduced the incidence, severity, and duration of neratinib-associated grade 3 diarrhea in CONTROL compared to other treatment cohorts. Both DE strategies showed a lower incidence of grade 3 diarrhea (DE1 13%; DE2 27%) compared with that observed in the ExteNET trial (historical control: 39.8%). No grade 4 diarrhea was reported in any cohort. The median cumulative duration of grade 3 diarrhea ranged from 2 – 2.5 days across the CONTROL DE study cohorts for the entire 12-month treatment period (compared with 5.0 days for ExteNET). The proportion of patients discontinuing neratinib because of diarrhea was lower in both DE cohorts (DE1 3%; DE2 6%) compared with ExteNET (17%). The adoption of neratinib DE + loperamide PRN during the first 2 weeks of treatment (DE1 cohort) was associated with the lowest rate of grade 3 diarrhea during the trial compared with all other anti-diarrheal strategies investigated in CONTROL. These final findings from the CONTROL study showed improved tolerability of neratinib with all diarrhea prophylaxis strategies and suggest that neratinib DE1 with loperamide PRN may allow patients to stay on treatment longer and receive the full benefit of neratinib therapy. This study is complete, and the results have been submitted to multiple global Health Authorities to support the addition of a dose escalation regimen to approved package inserts.

Dose escalation as an approach to improve the tolerability of neratinib in the treatment of adjuvant HER2-positive Breast Cancer (BINV-L) is included in the NCCN treatment guidelines. This inclusion aligns with the labeling supplement to the U.S. Prescribing Information approved by the FDA in June 2021, which incorporated the use of NERLYNX dose escalation as evaluated in the Phase II CONTROL study.

Neratinib—Metastatic Breast Cancer

In February 2020, the FDA approved our supplemental New Drug Application ("NDA") for the use of neratinib in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. This approval was based on the results from our NALA trial.

NALA. In February 2013, we reached agreement with the FDA under a Special Protocol Assessment ("SPA") for our Phase III clinical trial (PUMA-NER-1301 or the NALA trial) of neratinib in patients with HER2-positive metastatic breast cancer who have failed two or more prior treatments (third-line disease). An SPA is a written agreement between the trial's sponsor and the FDA regarding the design, endpoints, and planned statistical analysis of the Phase III trial with respect to the effectiveness of neratinib for the indication to be studied to support an NDA. The European Medicines Agency ("EMA") also provided follow-on Scientific Advice ("SA") consistent with that of the FDA regarding our Phase III trial design and endpoints used for such design to support the submission of a marketing authorization application ("MAA") in the EU.

Pursuant to the SPA and SA, the Phase III NALA trial was designed as a randomized controlled trial of neratinib plus capecitabine versus Tykerb® (lapatinib) plus capecitabine in patients with third-line HER2-positive metastatic breast cancer. The trial enrolled 621 patients who were randomized (1:1) to receive either neratinib plus capecitabine or lapatinib plus capecitabine. The trial was conducted globally at sites in North America, Europe, Asia-Pacific and South America. The co-primary endpoints of the trial were centrally confirmed PFS and overall survival ("OS"). An alpha level of 1% was allocated to the PFS and 4% allocated to OS.

In June 2019, we announced that results from the Phase III NALA trial were presented at the ASCO 2019 Annual Meeting in Chicago. For the primary analysis of centrally confirmed PFS, treatment with neratinib plus capecitabine resulted in a statistically significant improvement in centrally confirmed PFS (hazard ratio=0.76, p=0.0059) compared to treatment with lapatinib plus capecitabine. Because the hazard ratio was found to not be constant over time (i.e., the proportional hazard assumption did not hold), the statistical analysis plan for the NALA trial prespecified that a restricted means survival analysis at 24 months would be performed. In this prespecified analysis, the mean PFS for the patients treated with neratinib plus capecitabine was 8.8 months and the mean PFS for the patients treated with lapatinib plus capecitabine was 6.6 months.

For the primary analyses of OS, neratinib plus capecitabine resulted in an improvement in OS that, although not statistically significant, trended numerically in favor of the neratinib plus capecitabine arm of the study (hazard ratio = 0.88, p=0.21). The median OS for the patients treated with neratinib plus capecitabine was 21.0 months and the median OS for the patients treated with lapatinib plus capecitabine was 18.7 months. In the prespecified restricted means analysis, the mean OS at 48 months for the patients treated with neratinib plus capecitabine was 24.0 months and the mean OS for the patients treated with lapatinib plus capecitabine was 22.2 months.

For the secondary endpoint of time to intervention for symptomatic central nervous system disease (also referred to as brain metastases), the results of the trial showed that treatment with neratinib plus capecitabine led to an improvement over the combination of lapatinib plus capecitabine. The overall cumulative incidence of CNS metastases was 22.8% for the neratinib plus capecitabine arm and 29.2% for the lapatinib plus capecitabine arm (p=0.043). For the secondary endpoint of duration of response, neratinib plus capecitabine treatment resulted in a longer duration of response compared to lapatinib and capecitabine treatment, with a median response of 8.54 months compared to a median response of 5.55 months (HR = 0.495, p = 0.0004).

Treatment-emergent adverse events ("TEAEs") were similar between arms: TEAEs leading to neratinib/lapatinib discontinuation were lower with neratinib (10.9%) than with lapatinib (14.5%). There was a higher rate of grade 3 diarrhea with neratinib plus capecitabine compared to lapatinib plus capecitabine (24.4% vs 12.5%); however, the discontinuations due to diarrhea (neratinib plus capecitabine: 2.6%, lapatinib plus capecitabine: 2.3%) were similar in both arms.

NERLYNX plus capecitabine is included in the body of the NCCN Practice Guidelines for Breast Cancer for the treatment of recurrent unresectable (local or regional) or stage IV (M1) HER2-positive Breast Cancer (BINV-Q), with a recommendation for Fourth Line and Beyond (optimal sequence is not known). Dose escalation of neratinib is included as an approach to improve the tolerability of neratinib in the treatment of metastatic HER2-positive breast cancer.

Metastatic Breast Cancer with Brain Metastases

Approximately one-half of the patients with HER2-positive metastatic breast cancer develop metastases that spread to their brain. The current antibody-based treatments, including trastuzumab and pertuzumab, do not enter the brain and therefore are not believed to be effective in treating these patients.

Neratinib was evaluated in a clinical trial with the Translational Breast Cancer Research Consortium, referred to as TBCRC 022. The purpose of the study was to determine how well neratinib worked in treating breast cancer that had spread to the brain. In this research study, the investigators looked to see how well neratinib worked to decrease the size of or stabilize breast cancer that had metastasized to the brain.

In June 2017, we presented interim data from TBCRC 022 at the ASCO 2017 Annual Meeting. The multicenter Phase II clinical trial enrolled patients with HER2-positive metastatic breast cancer who had brain metastases. The trial initially enrolled three cohorts of patients. Patients in the second cohort (n=5) represent patients who had brain metastases that were amenable to surgery and who were administered neratinib monotherapy prior to and after surgical resection. The third cohort (target enrollment=60) enrolled two sub-groups of patients (prior lapatinib-treated and no prior lapatinib) with progressive brain metastases who were administered neratinib in combination with the chemotherapy drug capecitabine. The oral presentation reflected only the patients in the third cohort of patients without prior lapatinib exposure (cohort 3A, n=37), who all had progressive brain metastases at the time of enrollment and who received the combination of capecitabine plus neratinib.

In cohort 3A, 30% of the patients had received prior craniotomy, 65% of the patients had received prior whole brain radiotherapy, and 35% had received prior stereotactic radiosurgery to the brain. No patients had received prior treatment with lapatinib.

The primary endpoint of the trial was CNS Objective Response Rate according to composite criteria that included volumetric brain MRI measurements, steroid use, neurological signs and symptoms, and Response Evaluation Criteria in Solid Tumors ("RECIST") evaluation for non-CNS sites. The secondary endpoint of the trial was CNS response by Response Assessment in Neuro-Oncology-Brain Metastases ("RANO-BM") criteria. The efficacy results from the trial showed that 49% of patients experienced a CNS Objective Response by the composite criteria. The results also showed that the CNS response rate using the RANO-BM criteria was 24%. The median time to CNS progression was 5.5 months and the median overall survival was 13.5 months, though 49% of patients remain alive and survival data are immature.

The results for cohort 3A showed that the most frequently observed severe adverse event for the 37 patients evaluable for safety was diarrhea. Patients received antidiarrheal prophylaxis consisting of high dose loperamide, given together with the combination of capecitabine plus neratinib for the first cycle of treatment in order to try to reduce the neratinib-related diarrhea. Among the 37 patients evaluable for safety, 32% of the patients had grade 3 diarrhea and 41% had grade 2 diarrhea.

Updated results from an additional TBCRC 022 cohort were presented in December 2022 at the 2022 San Antonio Breast Cancer Symposium. This presentation outlined updates from three sub-cohorts of cohort 4: 4A – patients with previously untreated Breast Cancer Brain Metastases ("BCBM"); 4B – patients with BCBM progressing after prior local CNS-directed therapy without prior T-DM1 exposure; and 4C – patients with BCBM progressing after prior local CNS-directed therapy with previous T-DM1 exposure. Patients with measurable HER2-positive BCBM received neratinib 160 mg orally once daily plus T-DM1 3.6 mg/kg intravenously every 21 days in the three parallel-enrolling cohorts. Diarrhea prophylaxis with colestipol and loperamide was required during cycle 1. All enrolled patients underwent a brain MRI plus CT scan of the chest/abdomen/pelvis every six weeks for 18 weeks, followed by every nine weeks thereafter.

The primary endpoint, Response Assessment in Neuro-Oncology-Brain Metastases ("RANO-BM"), was evaluated in each cohort separately. The efficacy results from the trial showed that CNS Objective Response Rate by RANO-BM was 33.3% of patients in cohort 4A, 29.4% in cohort 4B, and 28.6% in cohort 4C. Rates of response + stable disease greater than or equal to six months were 50% in cohort 4A, 35.3% in cohort 4B, and 33.3% in cohort 4C.

Intracranial activity was observed for the combination of neratinib plus T-DM1 in all three cohorts, including in patients with prior T-DM1 exposure, suggesting a reversal of resistance to T-DM1. Overall, the most frequently observed adverse event was diarrhea, grade 2 (32%) and grade 3 (23%).

In April 2018, we announced that NERLYNX has been included as a recommended treatment option in the latest NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers ("CNS Guidelines") for patients with breast cancer and brain metastases. The NCCN designated NERLYNX in combination with capecitabine as a category 2A treatment option and NERLYNX in combination with paclitaxel as a category 2B treatment option. Use of NERLYNX for breast cancer patients with brain metastases is outside the FDA-approved indication for NERLYNX and considered investigational, and we do not market or promote NERLYNX for these uses.

Based upon data from the TBCRC_022 study, NERLYNX plus KADCYLA (T-DM1) was added in June 2025 to the NCCN CNS Guidelines for patients with HER2-positive breast cancer with brain metastases as a category 2A recommendation.

Neratinib—Other Potential Applications

While we believe neratinib has potential applications in other diseases, such as *HER2*-mutated solid tumors, as well as *EGFR* exon 18-mutated non-small cell lung cancer, we are not currently pursuing additional development in these indications at this time.

NERLYNX combinations are included in the body of the NCCN Practice Guidelines for Breast Cancer for patients with HER2-negative metastatic (stage IV) breast cancer and activating mutations in the *HER2* gene as detected by next generation sequencing of tumor tissue or ctDNA under the heading Useful in Certain Circumstances (BINV-Q). NERLYNX is included (i) with or without fulvestrant and (ii) with or without trastuzumab/fulvestrant. This inclusion is described in a table entitled, "Emerging Biomarkers to Identify Novel Therapies for Patients with Stage IV (M1) Disease," within the NCCN Practice Guidelines for Breast Cancer. Dose escalation of neratinib is included as an approach to improve the tolerability of neratinib in the treatment of metastatic HER2-positive breast cancer.

NERLYNX monotherapy is also included in the body of the NCCN Practice Guidelines for Cervical Cancer for use as a second-line or subsequent therapy for patients with recurrent or metastatic cervical cancer and a mutation in the *HER2* gene. NERLYNX is included in CERV-F under the heading Useful in Certain Circumstances and designated as a category 2A treatment option. Use of NERLYNX in cervical cancer patients is outside the FDA-approved indication for NERLYNX and considered investigational, and we may not market or promote NERLYNX for these uses.

Neratinib is also being investigated in an ongoing Phase 1 trial (NCT05372614) that is sponsored by the National Cancer Institute to evaluate the combination of neratinib and fam-trastuzumab deruxtecan (ENHERTU®) in patients with metastatic solid tumors. The Phase 1 trial includes patients with metastatic solid tumors harboring HER2-overexpression (immunohistochemistry 3+), ERBB2 amplifications, or activating HER2 mutations. The primary objectives are to assess safety and tolerability of the combination, and the secondary objectives include evaluating pharmacokinetics, preliminary efficacy, and potential biomarkers of response.

Alisertib

Alisertib is an investigational reversible, ATP-competitive inhibitor that is designed to be highly selective for Aurora Kinase A. Inhibition of Aurora Kinase A leads to disruption of mitotic spindle apparatus assembly, disruption of chromosome segregation, and inhibition of cell proliferation. In clinical trials to date, alisertib had shown single agent activity and activity in combination with other cancer drugs in the treatment of many different types of cancers, including hormone receptor-positive breast cancer, triple negative breast cancer, small cell lung cancer and head and neck cancer. The drug has also shown activity in previous clinical trials in peripheral T cell lymphoma and non-Hodgkin's lymphoma. Prior to our licensing alisertib from Takeda the drug was tested in over 1,300 patients who were treated across 22 company sponsored trials resulting in a large well characterized clinical safety database.

We intend to pursue the development of alisertib in hormone receptor-positive. HER2-negative, breast cancer as well as small cell lung cancer based on the prior clinical data that has been generated. We also plan to evaluate alisertib in biomarker focused populations where it has shown a higher degree of activity, such as patients with c-Myc amplification and RB1 loss/RB1 mutations, as we believe that this may provide a point of differentiation from the other drugs being developed in the treatment of these diseases. During 2023, we met with the FDA to discuss our alisertib clinical development plan in both proposed indications and discussed potential dosing schedules for alisertib. Following comments from the FDA on the proposed clinical development plans, we initiated clinical trials for both small cell lung cancer and breast cancer in 2024 and completed enrollment in the breast cancer clinical trial in February 2026.

Alisertib in Small Cell Lung Cancer

In a Phase II trial that was published in *Lancet Oncology* in 2015, alisertib was tested as a single agent in several cohorts of patients with solid tumors. These included small cell lung cancer as well as breast cancer. In small cell lung cancer, the study design involved the administration of alisertib to patients who had previously received up to two prior cytotoxic regimens in the metastatic setting. Patients were administered alisertib monotherapy at a dose of 50 mg twice a day ("BID") for seven days followed by a 14-day break.

In patients with chemotherapy sensitive disease, alisertib resulted in a response rate of 19% and a duration of response of 3.1 months. For the patients with chemotherapy refractory disease or chemotherapy resistant disease, alisertib resulted in a response rate of 25% and a duration of response of 4.3 months. The main grade 3 or higher adverse events ("AEs") seen in the trial were neutropenia, anemia, leukopenia and thrombocytopenia.

Alisertib was also tested in a randomized Phase II trial of paclitaxel plus alisertib versus paclitaxel plus placebo in patients with second line small cell lung cancer, the results of which were published in the *Journal of Thoracic Oncology* in 2020. In the trial, alisertib was dosed at 40 mg BID for 3 weeks on days 1–3, 8–10, and 15–17 plus paclitaxel (60 mg/m2 intravenously on days 1, 8, and 15) whereas the comparator arm received placebo plus paclitaxel (80 mg/m2 intravenously on days 1, 8, and 15) in 28-day cycles.

Randomization was stratified by type of relapse after primary treatment, based on the common definition for each type (with sensitive defined as relapsed greater than 90 but less than 180 days after primary treatment and resistant or refractory defined as relapsed less than or equal to 90 days after primary treatment). The protocol was initially written by the sponsor to record relapse type as the time from initial response. The protocol was corrected approximately midway through the trial to correct the stratification definition of relapse type after primary treatment so that relapses were recorded "from last administration of platinum-based chemotherapy," which is in line with the NCCN treatment guidelines and clinical treatment practice rather than "from initial response." To maintain balance, the primary end point of PFS was analyzed by using the original stratification definition of relapse type. However, a sensitivity analysis that used the corrected stratification definition was also performed. The trial also incorporated an extensive biomarker analysis with a prespecified analysis of c-Myc expression and an exploratory, retrospective analysis of genetic alterations in circulating tumor DNA ("ctDNA") with clinical outcome.

The primary endpoint in the trial was PFS. For the intent to treat ("ITT") population the hazard ratio using the original definition was 0.77 with a p value of 0.113. Using the corrected definition of relapse type, the hazard ratio was 0.71 with a p value of 0.038. For the patients with chemotherapy resistant or refractory relapse the hazard ratio was 0.66 with a p value of 0.037. For the ITT population the OS data showed a hazard ratio of 0.87 with a p value of 0.714 and using the corrected definition the hazard ratio was 0.79 with a p value of 0.209. Higher rates of grade 3 or higher AEs were seen in the alisertib arm for neutropenia, anemia and decreased neutrophil count.

For the patients in the trial who were found to be positive for c-Myc expression by immunohistochemistry the hazard ratio in the trial was 0.29 with a median PFS for the paclitaxel plus alisertib arm of 4.64 months and a median PFS for the placebo plus paclitaxel arm of 2.27 months. The trial also incorporated an analysis of patients with alterations in cell cycle genes including cyclin-dependent kinase 6 gene (CDK6), retinoblastoma-like 1 gene (RBL1), retinoblastoma-like 2 gene (RBL2), and retinoblastoma 1 gene (RB1). Of note RB1 mutations were the most frequent mutation with approximately 60% of the patients having RB1 mutations while CDK6, RBL1 and RBL2 mutations were found with very low frequency. For patients with cell cycles mutations (RB1, CDK6, RBL1 and RBL2), the PFS in the paclitaxel plus alisertib arm was 3.68 months while the placebo plus paclitaxel arm was 1.8 months and the hazard ratio was 0.395 with a p value of 0.003. The overall survival in this subgroup of patients was 7.2 months for the alisertib arm and 4.47 months for the placebo arm with a hazard ratio of 0.427 and a p value of 0.00085.

Development plan. In the United States, approximately 31,000 to 33,000 individuals are newly diagnosed with small cell lung cancer each year and approximately 16,000 to 17,000 patients die from the disease annually. There are two biomarkers of interest, c-Myc expression and RB1 mutations, that we intend to study with alisertib based on prior clinical trial results which may provide differentiation from other drugs in development. According to published biomarker data from an alisertib clinical trial, approximately 72% of samples from patients with small cell lung cancer had c-Myc expression and approximately 60-80% had RB1 mutations.

In August 2023, we announced that we had been notified by the FDA that we can proceed under our Investigational New Drug application ("IND") with the clinical development of alisertib monotherapy for the treatment of patients with extensive stage small cell lung cancer. Our Phase II trial ALISertib in CAncer (ALISCA™-Lung1) Phase II trial (PUMA-ALI-4201)) will enroll up to 60 patients with extensive stage small cell lung cancer who have progressed after first-line platinum-based chemotherapy and immunotherapy. Patients must provide tissue-based biopsies so that biomarkers can be analyzed. Alisertib will be dosed at 50 mg BID on days 1-7 of every 21-day cycle. In February 2024 we announced that we initiated the Phase II ALISCA™-Lung1 trial. This trial was amended in August 2025 to evaluate a higher dose of 60mg BID. This study is ongoing and actively recruiting patients.

The primary endpoint of the trial is objective response rate with secondary endpoints of duration of response, disease control rate, PFS and overall survival. We will look at each of these endpoints within selected pre-specified biomarker subgroups to assess whether there is enhanced efficacy in any biomarker subgroup. We will perform a biomarker analysis of the ALI-4201 trial in parallel with the execution of the clinical trial. We plan to perform an initial interim analysis for the evaluation of the biomarkers as well as an evaluation of the efficacy. Based upon the outcomes of the study, we anticipate meeting with the FDA to explore the potential for an accelerated approval pathway for alisertib in small cell lung cancer.

Alisertib in Breast Cancer

In the same Phase II trial of alisertib monotherapy that was published in *Lancet Oncology* in 2015, alisertib was also tested in patients with HER2-negative, hormone receptor-positive breast cancer, HER2-positive breast cancer and triple negative breast cancer. Patients were administered alisertib monotherapy at a dose of 50 mg BID for seven days followed by a 14-day break. In the cohort of patients with HER2-negative, hormone receptor-positive breast cancer, treatment with alisertib resulted in a response rate of 23% with a PFS of 7.9 months. The main grade 3/4 AEs seen were neutropenia, leukopenia, stomatitis and fatigue.

Alisertib was also tested in a randomized Phase II trial in hormone receptor-positive, HER2-negative metastatic breast cancer patients that was presented at the San Antonio Breast Cancer Symposium in 2020 and published in *JAMA Oncology* in March 2023. In this trial alisertib was dosed at 50 mg BID on days 1-3, 8-10 and 15-17 on a 28 day cycle while fulvestrant was dosed at its approved dose of 500 mg IM on days 1 and 15. The baseline characteristics from the trial were well balanced although a higher percentage of patients with prior chemotherapy given in the metastatic setting were present in the alisertib plus fulvestrant arm. Of note, patients were required to have been treated with prior fulvestrant as an inclusion criteria for the trial.

The results from the trial showed a response rate of 19.6% in the alisertib alone arm and 20.0% in the alisertib plus fulvestrant arm. The median duration of response was 15.1 months for the alisertib alone arm and 8.5 months for the alisertib plus fulvestrant arm. The PFS was 5.6 months in the alisertib alone arm and 5.4 months in the alisertib plus fulvestrant arm. The main AEs seen in the trial were similar to the prior monotherapy trial with incidences of neutropenia, anemia, and decreases in white blood cells and lymphocytes seen.

Alisertib was also tested in a randomized Phase II trial in hormone receptor-positive, HER2-negative metastatic breast cancer and triple negative breast cancer patients, which was published in *JAMA Network Open* in 2021, in which patients were randomized to receive either paclitaxel plus alisertib or paclitaxel alone. In this trial alisertib was dosed at 40 mg BID on days 1-3, 8-10 and 15-17 on a 28-day cycle while paclitaxel was dosed at 60 mg/m2 on days 1, 8 and 15 of a 28-day cycle. In the control arm paclitaxel was dosed at 90 mg/m2 on days 1, 8 and 15 of a 28-day cycle.

The combination of paclitaxel plus alisertib resulted in a statistically significant improvement in PFS with a hazard ratio of 0.56 and a p value of 0.005. The median PFS in the paclitaxel plus alisertib arm was 10.2 months and the median PFS in the paclitaxel alone arm was 7.1 months. Treatment with paclitaxel plus alisertib resulted in a numerically higher but not statistically significant improvement in overall survival where the median OS for the paclitaxel plus alisertib arm was 26.3 months versus 25.1 months for the single agent paclitaxel arm of the trial, which resulted in a hazard ratio of 0.89 and a p value of 0.61.

The standard of care for the first line treatment of hormone receptor-positive, HER2-negative metastatic breast cancer in the United States is treatment with Cyclin-dependent kinases (CDK) 4/6 inhibitors (CDK 4/6 inhibitors). In the cohort of patients in the trial who were treated with CDK 4/6 inhibitors, the combination of paclitaxel plus alisertib resulted in a median PFS of 13.9 months while paclitaxel alone resulted in a median PFS of 5.6 months. The hazard ratio was 0.59 with a p value of 0.19.

In the cohort of patients with triple negative breast cancer, the combination of paclitaxel plus alisertib resulted in an improvement in PFS with a hazard ratio of 0.35 and a p value of 0.022. The median PFS in the paclitaxel plus alisertib arm was 9.6 months and the median PFS in the paclitaxel plus placebo arm was 5.7 months. Treatment with paclitaxel plus alisertib resulted in a higher but not statistically significant improvement in overall survival where the median OS for the paclitaxel plus alisertib arm was 16 months versus 12.7 months for the paclitaxel alone arm of the trial, which resulted in a hazard ratio of 0.51 and a p value of 0.09.

Higher rates of grade 3 or higher AEs were seen in the paclitaxel plus alisertib arm for neutropenia, leukopenia, diarrhea, mucositis and stomatitis.

Archival tissue samples from patients enrolled in the clinical study were analyzed as part of a biomarker evaluation strategy. Of the 140 patients enrolled in the trial, 45 from the alisertib plus paclitaxel arm and 51 from the paclitaxel arm had sufficient tissue available for next generation sequencing, and 31 from the alisertib plus paclitaxel arm and 35 from the paclitaxel arm had enough for RNA sequencing/gene set enrichment analysis. The most frequently mutated genes were PIK3CA (45%) and TP53 (44%). No mutations were significantly associated with response or resistance to alisertib plus paclitaxel, including those in PIK3CA, TP53, AKT1, HER2, and CDH1.

Increased MYC RNA expression was observed in tumors from patients who did not derive clinical benefit from paclitaxel alone (defined as PFS less than six months) compared to those with benefit from paclitaxel alone (defined as PFS greater than or equal to six months). Increased MYC RNA expression was not observed in patients who did not appear to benefit from alisertib plus paclitaxel. Elevated expression of genes involved in MYC activation and in unfolded protein response (a pro- survival mechanism) were enriched in alisertib plus paclitaxel responders compared to paclitaxel responders and were associated with poor response to paclitaxel alone. In 12 patients with exceptional response to alisertib plus paclitaxel (defined as PFS greater than or equal to 12 months), increased expression of genes involved in MYC activation and in epithelial to mesenchymal transition (a hallmark of cancer progression and metastasis) was observed in comparison to cancers from patients whose disease progressed within six months of initiating alisertib + paclitaxel (n=11) or those with exceptional response to paclitaxel alone (n=4).

Development plan. In the United States the incidence of hormone receptor-positive HER2-negative breast cancer is 40,000 patients per year with 29,700 deaths per year. There are two biomarkers of interest that we intend to study with alisertib, c-Myc amplifications and RB1 mutations/deletions. According to biomarker analyses from clinical trials, approximately 50% of hormone receptor-positive breast cancer tumors may have c-Myc amplifications and approximately 2-9% of hormone receptor-positive HER2-negative breast cancer samples have RB1 mutations detected at the time of resistance to CDK 4/6 inhibitors.

Based on our interactions with the FDA, we initiated a Phase II trial of alisertib in combination with endocrine treatment (consisting of either anastrozole, exemestane, letrozole, fulvestrant or tamoxifen) in patients with chemotherapy-naïve HER2-negative, hormone receptor-positive metastatic breast cancer (ALISCA™-Breast1). Patients must have been previously treated with CDK 4/6 inhibitors and received at least two prior lines of endocrine therapy in the recurrent or metastatic setting to be eligible for the trial. In November 2024, we announced that we initiated the Phase II ALISCA™-Breast1 trial, and the study is actively enrolling patients.

The ALISCA™-Breast1 trial is designed to dose patients with alisertib given at either 30 mg, 40 mg or 50 mg twice daily (BID) on days 1-3, 8-10 and 15-17 on a 28-day cycle in combination with the endocrine therapy of the investigator's choice. Patients must not have been previously treated with the endocrine treatment that will be given in combination with alisertib in the trial. Each dose level is expected to enroll up to 50 patients. Patients must provide blood samples and tissue-based biopsies so that biomarkers can be evaluated. The primary objective is to determine the optimal alisertib dose level administered in combination with selected endocrine therapy to be used in future studies. The primary efficacy end points include objective response rate, duration of response, disease control rate and PFS. As a secondary objective, we will evaluate each of these efficacy endpoints within biomarker subgroups in order to determine whether any biomarker subgroup correlates with more favorable efficacy results, such as those observed in preclinical and clinical studies in other cancers including breast cancer and small cell lung cancer. Pending the outcome of this study, we may then look to focus the future clinical development of alisertib in combination with endocrine therapy for patients with HER2-negative, hormone receptor-positive breast cancer in patients with any potential biomarkers. The trial was designed to enroll a total of 150 patients, which was achieved in February 2026. Due to the larger number of patients in screening, we anticipate that the trial will enroll more than 150 patients.

Clinical Testing of Our Drug Candidates

Any drug candidates we seek to develop will require extensive pre-clinical and clinical testing to determine its safety and efficacy in the potential applications before seeking and obtaining regulatory approval. This process is expensive and time consuming. In completing these trials, we are dependent upon third-party consultants, consisting mainly of investigators and collaborators, who will conduct such trials.

We and our third-party consultants conduct pre-clinical testing in accordance with Good Laboratory Practices ("GLP") and clinical testing in accordance with Good Clinical Practice standards ("GCP"), which are international ethical and scientific quality standards utilized for pre-clinical and clinical testing, respectively. GCP is the standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials and the FDA requires compliance with GCP regulations in the conduct of clinical trials. Additionally, our pre-clinical and clinical testing completed in the EU is conducted in accordance with applicable EU standards, such as the EU Clinical Trials Regulation (Regulation (EU) No 536/2014 of April 16, 2014), and applicable national laws of the 27 EU member states.

We have entered into, and may enter into in the future, master service agreements with CROs with respect to initiating, managing and conducting the clinical trials of our products. These contracts contain standard terms for the type of services provided that contain cancellation clauses requiring between 30 and 45 days written notice and that obligate us to pay for any services previously rendered with prepaid, unused funds being returned to us.

Competition

The development and commercialization of new products to treat cancer is highly competitive. Significant financial resources are invested in research, development and commercialization of new cancer products. We have faced and will likely continue to face considerable competition from major pharmaceutical, biotechnology and specialty cancer companies. Our competitors include, but are not limited to, Genentech, Novartis, Roche, Boehringer Ingelheim, Lilly, Merck, AbbVie, Pfizer, Amgen, Daiichi Sankyo, Jazz and Seagen. Merck, AbbVie, Amgen, Daiichi Sankyo and Jazz are developing their drugs for the treatment of small cell lung cancer. All of the other competitors are developing their drugs for the treatment of early stage and/or metastatic HER2-positive breast cancer and/or for cancers that have a HER2 mutation or HER2-negative, hormone receptor-positive metastatic breast cancer. We are aware of the results of the DESTINY-Breast11 neoadjuvant trial, which showed that trastuzumab deruxtecan significantly increased pathologic complete response rates over standard therapy. We are also aware of the results of the DESTINY-Breast05 adjuvant trial of trastuzumab deruxtecan in early stage HER2-positive breast cancer, which showed that trastuzumab deruxtecan reduced the risk of disease recurrence or death in patients with high-risk HER2-positive early breast cancer following neoadjuvant therapy. Lastly, we are aware of the CompassHER2 RD trial of tucatinib in early stage HER2-positive breast cancer. In addition, we are also competing with academic institutions, governmental agencies and private organizations that are conducting research in the field of cancer.

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

We could see a reduction or elimination of our commercial opportunity if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or foreign regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market.

We anticipate that we will continue to face significant competition in the ongoing commercialization of NERLYNX and the commercialization of any of our drug candidates that receive marketing approval. Our competition will be determined by several factors including but not limited to the specific indications approved, the timing of any approvals as well as competitive activity and entrants within this space. We expect that competition among products approved for sale will be based on various factors, including safety, efficacy, pricing and contracting, patient support services, access and reimbursement, formulary and pathway adoption as well as patent position.

Sales and Marketing

United States

We currently have an oncology sales force in the United States comprised of approximately 35 sales specialists, four clinical nurse educators, five strategic account managers and one national strategic account director who are focused on promoting NERLYNX to oncologists and the oncology care team. This sales force is supported by an experienced leadership team consisting of five regional business leaders, a Senior Vice President of Sales and a Senior Vice President of Marketing. In addition, the broader commercial team is comprised of experienced professionals in marketing, training, sales operations, global product strategy as well as access and reimbursement. Our commercial infrastructure includes capabilities in manufacturing, regulatory, quality control, and compliance. It is also supported from a clinical and cancer landscape perspective by our medical affairs group.

We launched NERLYNX in the United States in July 2017 with the goal of establishing NERLYNX as the standard of care for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer to follow adjuvant trastuzumab-based therapy. In February 2020, NERLYNX was also approved in the United States in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

We believe that the key commercial priorities for NERLYNX include:

- educating healthcare providers about the evolving clinical data for NERLYNX and its ability to reduce the risk of recurrence in the extended adjuvant setting for patients battling HER2-positive breast cancer;
- educating HER2-positive breast cancer patients about the risks of recurrence and empowering them to ask their MDs if NERLYNX is an appropriate option for them;
- removing access barriers by ensuring broad insurance coverage; and
- providing patients with appropriate co-pay support as well as tools and resources to better maintain persistency and compliance.

In the United States, we sell our products through a specialty pharmacy network and special distributor network. The specialty pharmacy network sells directly to patients and consists of Accredo, CVS, ONCO 360, Optum and Biologics. Our specialty distributor network sells to hospitals, physician practices and other sites of care and consists of McKesson, ASD/Oncology Supply, Cardinal Health, DMS Pharmaceutical Group and Bio Care.

International

Outside the United States, we seek to enter into exclusive sub-license agreements with third parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved. In 2018, the EC granted a marketing authorization for NERLYNX in the EU for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who completed adjuvant trastuzumab-based therapy less than one year ago. In December 2021, NERLYNX was included in the updated National Reimbursement Drug List ("NRDL") by the China National Healthcare Security Administration for patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer after adjuvant trastuzumab based therapy. The addition of NERLYNX to the China NRDL now enables broad access to neratinib to more women throughout China. We continue to pursue commercialization of NERLYNX in Europe and other countries outside the United States, where approved. The following table shows the HER2-positive breast cancer approvals for NERLYNX by disease and country:

Extended adjuvant		**Metastatic**	
United States	July 2017	United States	February 2020
European Union	August 2018	Argentina	January 2021
Australia	March 2019	Peru	March 2021
Canada	July 2019	Chile	May 2021
Argentina	August 2019	Canada	June 2021
Hong Kong	October 2019	Taiwan	October 2021
Singapore	November 2019	Israel	July 2022
Switzerland	March 2020	Ecuador	August 2022
Brunei	April 2020	Singapore	September 2022
China	April 2020	Colombia	March 2023
Chile	April 2020	Malaysia	September 2023
New Zealand	June 2020	Mexico	October 2023
Taiwan	June 2020	Brazil	May 2024
Ecuador	July 2020	Thailand	December 2024
Malaysia	July 2020		
Peru	March 2021		
Macau	August 2021		
South Korea	October 2021		
Brazil	December 2021		
Mexico	January 2022		
Philippines	June 2022		
Israel	July 2022		
South Africa	January 2023		
Morocco	February 2023		
UAE	September 2023		
Syria	January 2024		
Saudi Arabia	July 2024		
Algeria	July 2024		
Turkey	November 2024		
Thailand	December 2024		
Iran	August 2025		

We currently have sub-licenses in each of these regions with third parties that are commercializing NERLYNX in their respective geography.

Intellectual Property and License Agreements

Neratinib Patent Portfolio

We hold a worldwide exclusive license under our license agreement with Pfizer, as amended (the "Pfizer Agreement") to 21 granted U.S. patents and one pending U.S. patent applications, as well as foreign counterparts thereof, and other patent applications and patents claiming priority therefrom to develop and commercialize certain compounds, including neratinib.

In the United States, we have a license to an issued patent, which is set to expire in 2030, for the composition of matter of neratinib, our lead compound. We also have a license to an issued U.S. patent for the use of neratinib in the extended adjuvant treatment of early stage HER2-positive breast cancer that has previously been treated with a trastuzumab containing regimen that expires in 2030, two issued patents for the use of neratinib in combination with capecitabine, the latter of which is set to expire in 2031, and two issued patents for the formulation of NERLYNX® that are set to expire in 2030; two issued patents for the polymorphic forms of neratinib which are set to expire in 2028; one issued patent for the preparation of the polymorphic forms of neratinib which is set to expire in 2028; and three issued patents for the use of the polymorphic forms of neratinib in the treatment of breast cancer which are set to expire in 2028. In jurisdictions which permit such, we will seek patent term extensions where possible for certain of our patents (discussed further below, including in "Government Regulation"). We plan to pursue additional patents in and outside the United States, based on our existing neratinib patent portfolio, that covers neratinib composition, formulations, and combinations and uses thereof, and additional therapeutic uses of neratinib. In addition, we will pursue patent protection for any new discoveries or inventions made in the course of our development of neratinib.

In the United States, marketing approval for neratinib was obtained on July 17, 2017, which provided five years of regulatory exclusivity. Marketing approval in the United States for neratinib in combination with capecitabine was obtained on February 25, 2020, which provided three years of regulatory exclusivity. Requests for patent term extension under the Hatch-Waxman Act have been filed for two patents in the United States: U.S. Patent No. 7,399,865 and U.S. Patent No. 9,211,291. We elected to apply patent term extension to U.S. Patent No. 7,399,865. The U.S. Patent and Trademark Office ("USPTO") has determined that U.S. Patent No. 7,399,865 is eligible for five years of patent term extension. U.S. Patent No. 7,399,865 Patent Term Extension ("PTE") Certificate was issued on November 19, 2021. U.S. Patent No. 7,399,865 will expire December 29, 2030. See "Government Regulation" below. If we obtain marketing approval in the United States for new uses or combination therapies for neratinib, we may be eligible for additional periods of regulatory exclusivity, such as three-year market exclusivity covering the new use. If we obtain market approval for neratinib or other drug candidates or in certain jurisdictions outside the United States, we may be eligible for regulatory protection, such as eight to eleven years of data and marketing exclusivity potentially available for new drugs in the EU; up to five years of patent extension potentially available in Europe (Supplemental Protection Certificate), and eight years of data exclusivity potentially available in Japan. In Europe, marketing approval for neratinib was obtained on August 31, 2018, which provided 10 years of regulatory exclusivity. Between 2019 and 2024, marketing approval for neratinib was obtained in Argentina, Brazil, Brunei, Canada, Chile, China, Ecuador, Hong Kong, Israel, Malaysia, Mexico, Singapore, Taiwan, Brazil and Thailand. Where available and eligible, regulatory or data exclusivity has been obtained, or is currently being pursued in these jurisdictions outside the United States and Europe. Patent term extension or supplemental protection certificate are being, or will be, pursued in jurisdictions where available and eligible, including Chile, Europe and Taiwan. We are pursuing patent term extension in the form of patent term adjustment ("PTA"), in market approved jurisdictions where PTA is available. Where PTA requests require proceedings in a court setting, there is no guarantee that such PTA requests will be granted. Current market approved jurisdictions where patent term extensions or supplemental protection certificates are not available, not eligible, or not pursued, include Argentina, Brunei, Canada, China, Ecuador, Hong Kong, Israel, Malaysia and Singapore. There can be no assurance that we will qualify for any such regulatory exclusivity, or that any such exclusivity will prevent competitors from seeking approval solely on the basis of their own studies. See "Government Regulation" below.

On November 28, 2011, a Boehringer Ingelheim entity filed an opposition to European Patent No. EP1848414, which was licensed from Pfizer in 2011, and which included specific claims to a pharmaceutical composition for use in treating cancer in a subject with a cancer having a mutation in epidermal growth factor receptor with a T790M mutation. Oral proceedings were held before the Opposition Division of the European Patent Office in Munich, Germany on February 4, 2014. The decision of the Opposition Division was to uphold the granted claims of the European patent that relate to the T790M mutation without any modification. This included specific claims to a pharmaceutical composition comprising an irreversible epidermal growth factor receptor inhibitor for use in treating cancer in a subject having a T790M mutation and claims for the pharmaceutical composition for use in the treatment of numerous cancers, including lung cancer and non-small cell lung cancer. Both parties appealed this decision. The opposition was rejected as inadmissible by the Board of Appeal of the European Patent Office on December 1, 2020, and the EP1848414 patent was upheld as originally granted. We have filed Supplemental Protection Certificate applications in the countries where the EP1848414 patent was validated. Of these Supplemental Protection Certificate applications, seven have been granted, two are undergoing appeal proceedings, ten have been abandoned, two proceedings have been stayed, and the remaining four are in active prosecution.

An opposition was filed by Hexal AG ("Hexal") on August 3, 2016 against European Patent No. EP2416774, which was licensed from Pfizer in 2011, and which claims neratinib for use in a method for treating HER-2/neu overexpressed/amplified cancer and improving IDFS, wherein the method comprises delivering neratinib therapy to HER-2/neu overexpressed/amplified cancer patients following the completion of at least one year of trastuzumab adjuvant therapy, and wherein the neratinib therapy comprises treating the cancer patients with neratinib for at least twelve months. An oral hearing was held on December 8, 2017, wherein the patent was maintained as granted. Following an appeal filed by Hexal, the Board of Appeal of the European Patent Office rejected the claims as granted and all pending auxiliary requests during the oral hearing of September 2, 2021. Before issuance of a decision, we withdrew approval of the text in which the patent was granted and all pending auxiliary requests, thereby revoking the patent and concluding the appeal. One European divisional application, namely EP15188350.1, was granted with the European patent number EP3000467 on March 1, 2023. Oppositions against EP3000467 were filed by Hexal on November 3, 2023, by Alfred E. Tiefenbacher (GmbH & Co. KG) on November 28, 2023 and by Generics (UK) Limited ("Generics") on December 1, 2023. EP3000467 is used as the basic patent for Supplementary Protection Certificate applications for the EMA-approved NERLYNX® product, of which 18 have been granted, three proceedings have been stayed, and 10 are in active prosecution. The patentee response to the notice of opposition was filed on April 15, 2024, following which, all three opponents filed additional arguments in reply to the patentee's submission. On February 6, 2025, we filed our response to the summons to attend oral proceedings, including six auxiliary requests. Alfred E. Tiefenbacher and Hexal AG filed their responses to the summons to oral proceedings on February 6 and 7, 2025, respectively. Hexal filed a further brief on March 19, 2025. Oral proceedings took place on April 9 and 10, 2025. EP3000467 was upheld as amended after the first instance hearing based on Auxiliary Request 1, which covers the EMA approved indication for NERLYNX® as an extended adjuvant therapy for treating early-stage hormone receptor-positive HER-2-overexpressed/amplified breast cancer. The first instance decision may be appealed. Hexal filed an appeal on June 6, 2025, Generics filed an appeal on June 20, 2025 and Wyeth filed an appeal on June 30, 2025. On September 5, 2025, Wyeth filed its grounds of appeal, including nine auxiliary requests. One the same day, Hexal filed its grounds of appeal. Generics filed its grounds of appeal on September 4, 2025, and Alfred E. Tiefenbacher filed its grounds of appeal on September 1, 2025. On December 16, 2025, Alfred E. Tiefenbacher withdrew its appeal. Wyeth responded to the opponents' grounds of appeal on January 12, 2026. One European divisional application is pending in the same family, namely EP 23157078.8. A response to the European Search Opinion ("ESO") for this application was filed February 14, 2024. The first office action was issued on January 28, 2025 with a response to the first office action filed on July 22, 2025.

On October 6, 2017, Hexal also filed an opposition against European Patent No. EP2326329 which was licensed from Pfizer in 2011, and which claims a combination of neratinib and pharmaceutically acceptable salts thereof with capecitabine for use in a method of treating an Erb-2 positive metastatic breast cancer. An oral hearing was held on February 13, 2019, wherein the patent was maintained as granted. Hexal then appealed, the Board of Appeal of the European Patent Office rejected the claims as granted and the pending auxiliary request during the oral hearing of November 16, 2022. Before issuance of a decision, we withdrew approval of the text in which the patent was granted and the pending auxiliary request, thereby revoking the patent and concluding the appeal. A divisional application, EP16203986.1 was granted with the patent number EP3175853 on November 1, 2023. This patent was also opposed by Sandoz AG on July 2, 2024. The patentee's response was filed on December 12, 2024. On December 19, 2024, Sandoz AG requested the opposition division to delay issuance of their preliminary opinion by two months since they intend to respond to the patentee's submission. Oral proceedings are scheduled for April 16, 2026. The patentee filed its written submission on February 16, 2026. A divisional application, EP23206402.2, remains pending in this family. Substantive examination has commenced and a response to the European Search Opinion (ESO) was filed on May 20, 2025.

On May 21, 2020, Dr. Richard Cooke at the firm Elkington and Fife LLP filed an opposition against European Patent No. EP2498756, which was licensed from Pfizer in 2011, and which claims, *inter alia*, tablet formulations of neratinib maleate comprising intragranular and extragranular components. An oral hearing was held on April 6, 2022, wherein the patent has been maintained in amended form. The Interlocutory Decision of the Opposition Division was issued on July 25, 2022. Hexal, has not appealed the decision within the prescribed time and the Interlocutory Decision became final. A divisional application for EP19154710.8 has been granted as EP3566697, and EP22169771.7 has received a decision to grant, taking effect on March 5, 2025.

An opposition was filed by Generics on September 3, 2015 against European Patent No. EP2656844, which was licensed from Pfizer in 2011, and which claims, *inter alia*, a pharmaceutical pack containing 50 to 300 mg of neratinib and pharmaceutically acceptable salts thereof and vinorelbine for use in a method of treating a neoplasm. An oral hearing was held July 3, 2017, wherein the patent was maintained as granted. Generics then appealed. The appeal was dismissed by the Board of Appeal of the European Patent Office on August 11, 2020, and the EP2656844 patent was upheld as originally granted.

Unipharm filed a pre-grant opposition to Israeli Patent Application No. IL210616 on January 31, 2016. This application was licensed from Pfizer in 2011. An oral hearing was held in Jerusalem before the Israeli Patent Office on January 22, 2018. The patent was granted by the Israeli Patent Office upon filing of amendments to the claims. No opposition to the patent has been filed within the allowed opposition period. The granted claims are directed to use of a combination of neratinib and capecitabine in the manufacture of a medicament for treating a neoplasm.

Alisertib Patent Portfolio

We hold a worldwide exclusive license under our license agreement with Takeda (the "Takeda Agreement"), to 22 granted U.S. patents and five pending U.S. patent applications, as well as foreign counterparts thereof, and other patent applications and patents claiming priority thereof for a total of approximately 368 foreign patents and patent applications to develop and commercialize alisertib.

We have a license to issued U.S. patents that include species claims and genus claims to the composition of matter of alisertib which are set to expire in 2029 and 2027, respectively, not including any extension for Hatch-Waxman exclusivity. We also have issued U.S. patents for the use of alisertib in combination with certain other agents in the treatment of certain proliferative disorders, small-cell lung cancer and breast cancer, which are currently set to expire in 2032, 2033 and 2034, respectively, not including any extension for Hatch-Waxman exclusivity.

We plan to pursue additional patents in and outside the United States, based on our existing alisertib patent portfolio, that covers alisertib composition, formulations, combinations and uses thereof, and additional therapeutic uses of alisertib. In addition, we will pursue patent protection for any new discoveries or inventions made in the course of our development of alisertib.

Our goal is to obtain, maintain and enforce patent protection for our products, formulations, processes, methods and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current drug candidates and any future drug candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the United States and abroad. However, even patent protection may not always provide us with complete protection against competitors who seek to circumvent our patents. See "Risk Factors—*Risks Related to Our Intellectual Property—Our proprietary rights may not adequately protect our intellectual property and potential products, and if we cannot obtain adequate protection of our intellectual property and potential products, we may not be able to successfully market our potential products."*

We depend upon the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors, none of which is patentable. To help protect our proprietary know-how, which is not patentable, and inventions for which patents may be difficult to obtain or enforce, we rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

In-License Agreements

Pfizer License Agreement

We license the worldwide exclusive rights for the development, manufacture and commercialization of neratinib (oral), neratinib (intravenous), PB357, and certain related compounds from Pfizer. Under the Pfizer Agreement, Pfizer was obligated to transfer to us certain information, records, regulatory filings, materials and inventory controlled by Pfizer and relating to or useful for developing these compounds and to continue to conduct certain ongoing clinical studies until a certain time. After that time, we were obligated to continue such studies pursuant to an approved development plan, including after the license agreement terminates for reasons unrelated to Pfizer's breach of the license agreement, subject to certain specified exceptions. We were also obligated to commence a new clinical trial for a product containing one of these compounds within a specified period of time and use commercially reasonable efforts to complete such trial and achieve certain milestones as provided in a development plan. If certain of our out-of-pocket costs in completing such studies exceeded a mutually agreed amount, Pfizer was obligated to pay for certain additional out-of-pocket costs to complete such studies. We must use commercially reasonable efforts to develop and commercialize products containing these compounds in specified major-market countries and other countries in which we believe it is commercially reasonable to develop and commercialize such products. In July 2021, we entered into a confirmatory agreement with Pfizer and Wyeth LLC

("Wyeth"), confirming that the rights granted to us by Pfizer under the Pfizer Agreement included Wyeth's rights in neratinib (oral), neratinib (intravenous), PB357, and certain related compounds.

As consideration for the license, we are required to make payments upon the achievement of certain milestones totaling approximately $187.5 million if all such milestones are achieved. In connection with the FDA approval of NERLYNX in July 2017, we triggered a one-time milestone payment pursuant to the agreement. In June 2020, we entered into a letter agreement (the "Letter Agreement") with Pfizer relating to the method of payment associated with a one-time milestone payment under the license agreement with Pfizer. The Letter Agreement permitted us to make the milestone payment in installments with the remaining amount payable to Pfizer (including interest). The milestone payment accrued interest at 6.25% per annum. The milestone payment including accrued interest of $1.8 million was paid in full in September 2021. In addition, we reached a commercial milestone by achieving aggregate worldwide net sales of $250.0 million in calendar year 2022, resulting in a payment to Pfizer of $12.5 million during the three months ended March 31, 2023. We capitalized the milestones as intangible assets and are amortizing the assets to cost of sales on a straight-line basis over the estimated useful life of the licensed patent through 2030. Should we commercialize additional compounds licensed from Pfizer or any products containing any of these compounds, we will be obligated to pay Pfizer annual royalties at a fixed rate in the low-to-mid teens of net sales of all such products, subject to certain reductions and offsets in some circumstances. Our royalty obligation continues on a product-by-product and country-by-country basis, until the later of (1) the last to expire licensed patent covering the applicable licensed product in such country, or (2) the earlier of generic competition for such licensed product reaching a certain level in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. In the event that we sub-license the rights granted to us under the license agreement with Pfizer to a third party, the same milestone and royalty payments are required. We can terminate the license agreement at will, or for safety concerns, in each case upon specified advance notice.

The Pfizer Agreement originally stipulated that should we commercialize any of the compounds licensed from Pfizer or any products containing any of these compounds, we will be obligated to pay to Pfizer incremental annual royalties between approximately 10% and 20% of net sales of all such products, subject, in some circumstances, to certain reductions.

In July 2014, we signed an amendment to the Pfizer Agreement that, among other things reduced the annual royalties to be paid on net sales of licensed products from a tiered royalty rate structure ranging between 10% to 20% to a fixed rate in the low to mid-teens.

Our royalty obligation continues, on a product-by-product and country-by-country basis, until the later of (i) the last to expire valid claim of a licensed patent covering the applicable licensed product in such country, or (ii) the earlier of generic competition for such licensed product reaching a certain level of sales in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. We can terminate the Pfizer Agreement at will at any time or for safety concerns, in each case upon specified advance notice. Each party may terminate the Pfizer Agreement if the other party fails to cure any breach of a material obligation by such other party within a specified time period. Pfizer may terminate the Pfizer Agreement in the event of our bankruptcy, receivership, insolvency or similar proceeding. The Pfizer Agreement contains other customary clauses and terms as are common in similar agreements in the industry.

Takeda License Agreement

In September 2022, we entered an exclusive license agreement with Takeda to license from Takeda the worldwide right to research, develop, commercialize and otherwise exploit alisertib, also referred to as MLN-8237, a selective, small-molecule, orally administered inhibitor of Aurora Kinase A. Under the terms of the Takeda Agreement, we assumed sole responsibility for the global development and commercialization of alisertib. We paid Takeda an upfront license fee of $7.0 million in October 2022 and Takeda is eligible to receive potential future milestone payments of up to $287.3 million upon our achievement of certain regulatory and commercial milestones during the term of the exclusive license agreement, as well as tiered royalty payments for any net sales of alisertib.

Under the Takeda Agreement, we must use commercially reasonable efforts to develop and commercialize one product containing alisertib in specified major-market countries. We may terminate the Takeda Agreement at will at any time upon specified advance notice. Each party may terminate the Takeda Agreement if the other party fails to cure any material breach of the Takeda Agreement by such other party within a specified time period. In addition, each party may terminate the Takeda Agreement following the other party's bankruptcy, insolvency, reorganization, receivership, dissolution, liquidation or similar events. The Takeda Agreement contains other customary clauses and terms as are common in similar agreements in the industry.

Sub-License Agreements

The following summary describes our material sub-license agreements. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to each of these agreements, copies of which have been filed as exhibits to this Annual Report.

Specialised Therapeutics Agreement

On November 20, 2017, we entered into a sub-license agreement (the "Specialised Therapeutics Agreement") with Specialised Therapeutics Asia Pte Ltd. ("STA"). Pursuant to the Specialised Therapeutics Agreement, we granted to STA, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license to commercialize any pharmaceutical product containing neratinib in finished form for the extended adjuvant treatment of patients with early stage HER2-positive breast cancer and HER2-positive metastatic breast cancer in Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Papua New Guinea, Philippines, Singapore, Thailand, Timor-Leste and Vietnam (the "STA Territory").

The Specialised Therapeutics Agreement sets forth the parties' respective obligations with respect to the development, commercialization, and supply of the licensed product. Within the STA Territory, STA will be generally responsible for regulatory and commercialization activities, and we will be solely responsible for the manufacturing and supply of the licensed product under a supply agreement entered into between the parties.

Pursuant to the Specialised Therapeutics Agreement, we received an upfront payment and will potentially receive additional regulatory milestone payments. In addition, we will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the STA Territory.

The term of the Specialised Therapeutics Agreement continues, on a country-by-country basis, until the later of (i) the expiration or abandonment of the last patent covering the licensed product or (ii) the earlier of (a) the date upon which sales of generic versions of licensed product reach a specified level in such country, or (b) the tenth anniversary of the first commercial sale of the licensed product in such country. The Specialised Therapeutics Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent. The Specialised Therapeutics Agreement will also terminate upon the termination of the supply agreement for licensed products between the parties.

Medison Agreement

During the first quarter of 2018, we entered into a sub-license agreement (the "Medison Agreement"), with Medison Pharma Ltd. ("Medison"). Pursuant to the Medison Agreement, we granted to Medison, under certain of our intellectual property rights relating to neratinib, an exclusive license to commercialize neratinib and certain related compounds and participate in the named patient supply in Israel (the "Medison Territory"), subject to the terms of the Medison Agreement and the related supply agreement. Pursuant to the Medison Agreement, we will potentially receive milestone payments due to us upon successful completion of certain separate, distinct performance obligations. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products in the Medison Territory.

Pint Agreement

On March 30, 2018, we entered into a sub-license agreement (the "Pint Agreement"), with Pint Pharma International SA ("Pint"). Pursuant to the Pint Agreement, we granted to Pint, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license to develop and commercialize any product containing neratinib and certain related compounds in Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, Venezuela, French Guiana, the Falkland Islands and Mexico (the "Pint Territory").

The Pint Agreement sets forth the parties' respective obligations with respect to the development, commercialization, and supply of the licensed product. Pint will, at its expense, develop the licensed product for the purpose of obtaining regulatory approval in the Pint Territory, subject to our consent to conduct such development activities and approval of certain aspects of clinical studies conducted by Pint. Within the Pint Territory, Pint will also be responsible for regulatory and commercialization activities. We will be solely responsible for the manufacturing and supply of the licensed product under a supply agreement that will be entered into between the parties, subject to certain exceptions therein.

Pursuant to the Pint Agreement, we received an upfront payment and will potentially receive additional regulatory and sales-based milestone payments. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pint Territory.

The term of the Pint Agreement continues, on a country-by-country basis, until the later of (i) the expiration or abandonment of the last licensed patent covering the licensed product in such country, or (ii) the earlier of (a) the date upon which sales of generic versions of licensed product reach a specified level in such country, or (b) the tenth anniversary of the first commercial sale of the licensed product in such country. The Pint Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent. Pint may also terminate the Pint Agreement at will, for certain safety concerns.

Knight Agreement

On January 9, 2019, we entered into a sub-license agreement (the "Knight Agreement"), with Knight Therapeutics, Inc. ("Knight"). Pursuant to the Knight Agreement, we granted to Knight, under certain of the our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license (i) to commercialize any product containing neratinib and certain related compounds in Canada (the "Knight Territory"), (ii) to seek and maintain regulatory approvals for the licensed products in the Knight Territory and (iii) to manufacture the licensed products anywhere in the world solely for the development and commercialization of the licensed products in the Knight Territory for human use, subject to the terms of the Knight Agreement and a supply agreement to be negotiated and executed by the parties.

Under the terms of the Knight Agreement, we will be solely responsible for the manufacturing and supply of the licensed products to Knight, but under limited circumstances Knight may obtain the right to manufacture the licensed products under the supply agreement.

The Knight Agreement sets forth the parties' respective obligations with respect to the commercialization of the licensed products. Within the Knight Territory, we will be solely responsible for obtaining the regulatory approval for the indication of extended adjuvant treatment of HER2-positive early stage breast cancer (the "Initial Indication"), and Knight will use commercially reasonable efforts to prepare, file and manage regulatory filings for any other indications in the field of human use. Promptly after obtaining the regulatory approval for the Initial Indication in the Knight Territory, we will transfer such regulatory approval to Knight, and Knight will own and hold any regulatory approvals for the licensed products in the Knight Territory in its name.

Pursuant to the Knight Agreement, we received an upfront payment and will potentially receive additional regulatory and commercial milestone payments. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products in the Knight Territory.

The term of the Knight Agreement continues, on a licensed product-by-licensed product basis, until the later of (i) the expiration or abandonment of the last valid claim of the licensed patents that covers such licensed product in the Territory, or (ii) the earlier of (a) the time when generic competitors to such licensed product have achieved a specified level in such country, or (b) ten (10) years following the date of first commercial sale of such licensed product in the Territory. The Knight Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent.

Pierre Fabre Agreement

On March 29, 2019, we entered into a sub-license agreement (the "Pierre Fabre Agreement"), with Pierre Fabre Medicament SAS ("Pierre Fabre"). Pursuant to the Pierre Fabre Agreement, we granted to Pierre Fabre under certain of our intellectual property rights relating to neratinib an exclusive, sub-licensable (under certain circumstances) license to develop, manufacture and commercialize any pharmaceutical product containing neratinib for therapeutic and prophylactic indications for human or veterinary use in European countries (excluding Ukraine), along with countries in North Africa and francophone countries of West Africa (the "Pierre Fabre Territory"). On November 25, 2019, we entered into a license amendment (the "First Pierre Fabre Amendment"), with Pierre Fabre to extend the Pierre Fabre Territory to the Middle East, South Africa, Sudan and Turkey (as extended, the "First Pierre Fabre Territory").

On February 24, 2021, we resolved a dispute with our former partner CANbridge Biomed Limited and terminated our sub-license agreement. Simultaneous to the termination of this agreement, we entered into a third license amendment (the "Third Pierre Fabre Amendment") with Pierre Fabre to further extend Pierre Fabre's licensed territory to Greater China, (the "Third Pierre Fabre Territory") which includes mainland China, Taiwan, Hong Kong and Macao (each a "China Region").

Pursuant to the Pierre Fabre Agreement, we received an upfront payment and will potentially receive additional regulatory and sales-based milestone payments based on regulatory and sales activities in the Licensee Territory (as such term is defined in the Third Pierre Fabre Amendment). Pursuant to the Third Pierre Fabre Amendment, we received an upfront payment of $50.0 million and will potentially receive additional regulatory and sales-based milestone payments up to $240.0 million based solely on regulatory and sales activities in the Third Pierre Fabre Territory. In addition, we will receive double-digit royalties based on net sales of the licensed products in the Licensee Territory, and double-digit royalties based on net sales of the licensed products in the Third Pierre Fabre Territory. For the purposes of calculating royalties, sales of the licensed products in the Third Pierre Fabre Territory will be excluded from the sales of licensed products made in the Licensee Territory.

Under the terms of the Pierre Fabre Agreement, as amended, we are obligated to supply Pierre Fabre with the licensed products in accordance with the related supply agreement. Pierre Fabre will be responsible for conducting additional clinical studies and leading regulatory activities in connection with the EMA, and Greater China.

The term of the Pierre Fabre Agreement, as amended, continues until, on a country-by-country basis, the later of (i) the expiration or abandonment of the last licensed patent covering the licensed product in such country and (ii) the earlier of (a) the date upon which sales of generic versions of the licensed product reach a specified level in such country, or (b) the tenth anniversary of the first commercial sale of a licensed product in such country.

The Pierre Fabre Agreement, as amended, may be terminated by either party, in its entirety, if the other party commits a material breach, subject to a cure period, or if the other party is insolvent, and Pierre Fabre may terminate the Pierre Fabre Agreement, as amended, at its convenience or if there is evidence of safety issues with the licensed product. Pierre Fabre may terminate the Pierre Fabre Agreement, as amended, on a territory-by-territory basis, by terminating only the Licensee Territory or the Third Pierre Fabre Territory, for any of the foregoing reasons. We may terminate the Pierre Fabre Agreement, as amended, on a China Region-by-China Region basis or, under certain circumstances, in the entire Third Pierre Fabre Territory if Pierre Fabre is in material violation of certain anti-corruption laws.

Bixink Agreement

During the second quarter of 2020, we entered into a sub-license agreement (the "Bixink Agreement") with Bixink Therapeutics Co., Ltd. ("Bixink"). The Bixink Agreement granted intellectual property rights and set forth the respective obligations with respect to development, commercialization and supply of NERLYNX in South Korea (the "Bixink Territory"). The Bixink Agreement includes potential milestone payments due to us upon successful completion of certain performance obligations, such as achieving regulatory approvals. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Bixink Territory.

Manufacturing

We do not currently have our own manufacturing facilities. We intend to continue to use our financial resources to support commercialization of NERLYNX and development of our drug candidates, including alisertib, rather than diverting resources to establish our own manufacturing facilities. While our drug candidates were developed by Pfizer and Takeda, both the drug substance and drug product are manufactured by third-party contractors. We are currently using third-party contractors to manufacture, supply, store and distribute our neratinib products (including NERLYNX) in clinical trials and commercial quantities as well as for alisertib in clinical trials.

Should alisertib or any of our other drug candidates obtain marketing approval, we anticipate establishing relationships with third-party manufacturers and other service providers in connection with commercial production of our products. We have some flexibility in securing other manufacturers to produce our drug candidates; however, our alternatives may be limited due to proprietary technologies or methods used in the manufacture of some of our drug candidates.

Government Regulation

United States—FDA Process

The research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing, among other things, of drug products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, warning letters, fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

Drug Approval Process. None of our drug candidates may be marketed in the United States until the drug has received FDA approval. The steps required before a drug may be marketed in the United States generally include the following:

- completion of extensive pre-clinical laboratory tests, animal studies, and formulation studies, certain of which must be conducted in accordance with the FDA's GLP requirements and other applicable regulations;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB") or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and efficacy of the drug for each proposed indication;
- submission to the FDA of an NDA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient ("API") and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices ("cGMPs") and potential inspection of clinical trial sites to assess compliance with GCP; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Pre-clinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the pre-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the conduct of the trial, such as whether human research subjects will be exposed to an unreasonable health risk. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. Therefore, submission of an IND may not necessarily result in the FDA allowing clinical trials to begin.

Clinical trials involve administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be provided to the FDA as part of a separate submission to the IND. Further, an IRB for each medical center proposing to conduct the clinical trial must review and approve the study protocol and informed consent information for study subjects for any clinical trial before it commences at that center, and the IRB must monitor the study until it is completed. There are also requirements governing reporting of ongoing clinical trials and clinical trial results to public registries. Study subjects must sign an informed consent form before participating in a clinical trial.

Clinical trials necessary for product approval typically are conducted in three sequential phases, but the phases may overlap. Phase I usually involves the initial introduction of the investigational drug into a limited population, typically healthy humans, to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase II usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage; (ii) identify possible adverse effects and safety risks; and (iii) evaluate preliminarily the efficacy of the drug for specific targeted indications. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase III clinical trials. Phase III trials are undertaken in an expanded patient population at multiple, geographically dispersed clinical trial centers to further evaluate clinical efficacy and test further for safety by using the drug in its final form in order to establish the risk/benefit profile of the drug and provide an adequate basis for product labeling. Post-approval trials, sometimes referred to as Phase IV studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase IV clinical trials as a condition of approval of an NDA.

Furthermore, the sponsor, the FDA or an IRB may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, such as in the circumstances where the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given an opportunity to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase II clinical testing, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach consensus on the next phase of development. Sponsors typically use the end of a Phase II meeting to discuss their Phase II clinical results and present their plans for the pivotal Phase III clinical trial that they believe will support submission of an NDA.

A sponsor may request an SPA to reach an agreement with the FDA that the protocol design, clinical endpoints, and statistical analyses are acceptable to support regulatory approval of the drug candidate with respect to effectiveness in the indication studied. If such an agreement is reached, it will be documented and made part of the administrative record, and it will be binding on the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining the safety or effectiveness of the product after clinical studies begin, if the relevant data, assumptions, or information provided by the sponsor in a request for SPA change are found to be false statements or misstatements or omit relevant facts, or if the sponsor fails to follow the protocol that was agreed upon with the FDA. A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. There is no guarantee that a study will ultimately be adequate to support an approval, even if the study is subject to an SPA.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. 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.

Assuming successful completion of the required clinical testing, the results of pre-clinical studies and of clinical trials, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. An NDA must be accompanied by a significant user fee, which may be waived in circumstances, such as where the drug is approved for an orphan-designated indication, or for the first NDA submitted by a qualifying small business.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to a filing review before the FDA accepts it for filing and substantive review. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act ("PDUFA") guidelines that are currently in effect, the FDA has a goal of 10 months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted.

The FDA also may refer an application for a novel drug to an advisory committee. 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.

Before approving an NDA, the FDA inspects the facility or the facilities at which the drug and/or its API is manufactured and will not approve the product unless the manufacturing is in compliance with cGMPs 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 GCPs.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data and/or additional clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA could approve the NDA with a Risk Evaluation and Mitigation Strategy to mitigate risks of the drug, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. Once the FDA approves a drug, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing, including Phase IV clinical trials, and surveillance programs to monitor the safety effects of approved products that have been commercialized. The FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs or other information. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

Orphan Drug Designation. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same approved indication or use within such disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity within the relevant indication or inability to manufacture the product in sufficient quantities to meet the needs relating to the approved use or indication of patients with the relevant rare disease or condition. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. However, competitors, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of a competing product for seven years if a competitor obtains approval of the "same drug," as defined by the FDA with respect to the relevant indication or

use, or if a drug candidate is determined to be contained within a competitor's product approved for the same indication or use. In addition, if an orphan designated product receives marketing approval for an disease or condition broader than what is designated, it may not be entitled to orphan exclusivity.

Expedited Review and Approval Programs. The FDA has various programs, including fast track designation, breakthrough therapy designation, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing certain drugs and in the case of accelerated approval, provide for approval on the basis of surrogate or intermediate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening diseases or conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. Fast track designation, breakthrough therapy designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

For example, fast track designation is designed to facilitate the development and expedite the review of drugs designed to treat serious or life-threatening diseases or conditions and which demonstrate the potential to address an unmet medical need for such diseases or conditions. Fast track designation applies to the combination of the drug candidate and the specific indication for which it is being studied. The sponsor of a fast track drug candidate has opportunities for more frequent interactions with the FDA review team during development. With regard to a fast track-designated drug candidate, the FDA may also consider for review sections of the NDA on a rolling basis before the complete application is submitted if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A drug candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A drug candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the drug candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase I and an organizational commitment to expedite the development and review of the drug candidate, including involvement of senior managers.

Any drug candidate submitted to the FDA for approval, including a product with a fast track designation or breakthrough therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review. An NDA is eligible for priority review if the drug candidate is designed to treat a serious condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available products. The FDA will attempt to direct additional resources to the evaluation of an application for a drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to 10 months for review of new molecular entity NDAs under its current PDUFA review goals.

Depending on the design of the applicable clinical studies, drug candidates intended for serious or life threatening conditions may also be eligible for accelerated approval upon a determination that the drug candidate has an effect on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome, or an effect on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled confirmatory clinical trials to verify or characterize the anticipated effect on irreversible morbidity or mortality or other clinical benefit and may require that such confirmatory trials be well underway prior to granting any accelerated approval. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required clinical trials in a timely manner, or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval.

Post-Approval Requirements. After a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. In addition, certain changes to an approved product, such as adding new indications, making certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval. Before a company can market products for additional indications, it must obtain additional approvals from the FDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. A company cannot be sure that any additional approval for new indications for any drug candidate will be approved on a timely basis, or at all.

If post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to (i) report certain adverse reactions to the FDA and maintain pharmacovigilance programs to proactively look for these adverse events; (ii) comply with certain requirements concerning advertising and promotional labeling for their products; and (iii) continue to have quality control and manufacturing procedures conform to cGMPs after approval. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing facilities; this latter effort includes assessment of ongoing compliance with cGMPs. Accordingly, manufacturers and their subcontractors must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drugs. A company can make only those claims relating to safety and efficacy that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Marketing Exclusivity

Data and market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA"), or an NDA submitted under section 505(b)(2) of the FDCA by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the holder of the NDA for the reference drug.

The FDCA also provides three years of non-patent exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active agent or from accepting and reviewing an application referencing the approved drug's application. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be

required to conduct or obtain a right of reference to all of the pre-clinical studies and clinical trials necessary to demonstrate safety and effectiveness.

Foreign Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulations governing, among other things, clinical trials, marketing authorization ("MA"), commercial sales and distribution of our products. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country-specific regulation.

Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials and approval of regulatory authorities of foreign countries before we may market products in those countries. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement also vary greatly from country to country.

Non-Clinical Studies and Clinical Trials

As in the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products, e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use ("ICH") guidelines on GCP as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for EU member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the EU Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each EU member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR transition period ended on January 31, 2025, and all clinical trials (and related applications) are now fully subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our drug candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal drug candidates can only be placed on the market after obtaining an MA. To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit an MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" – are issued by the European Commission ("EC") through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use ("CHMP") of the EMA, and are valid throughout the EU. The centralized procedure is mandatory for certain types of products, such as (i) medicinal products, derived from biotechnology processes, such as genetic engineering, (ii) designated orphan medicinal products, (iii) advanced therapy medicinal products ("ATMPs") such as gene therapy, somatic cell therapy or tissue-engineered medicines, and (iv) medicinal products containing a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU or for drug candidates that constitute a significant therapeutic, scientific or technical innovation, or for which the granting of an MA would be in the interest of public health in the EU.

- "National MAs" – are issued by the competent authorities of the EU member states, and only cover their respective territory and are available for drug candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure, an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state. The competent authority of the reference member state prepares a draft assessment report, a draft summary of the product characteristics ("SmPC"), and a draft of the labeling and package leaflet, which are sent to the other member states (referred to as the member states concerned) for their approval. If the member states concerned raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling or packaging proposed by the reference member state, the product is subsequently granted a national MA in all the member states, i.e., in the reference member state and the member states concerned.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU member states assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment, but this is not guaranteed. The benefits of a PRIME designation include the appointment of a CHMP rapporteur before submission of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

Data and Marketing Exclusivity

As in the United States, it may be possible in foreign countries to obtain a period of market and/or data exclusivity that would have the effect of postponing the entry into the marketplace of a competitor's generic or biosimilar product.

For example, in the EU, new products authorized for marketing ("reference products") generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of 11 years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

In Japan, our products may be eligible for eight years of data exclusivity. There can be no assurance that we will qualify for such regulatory exclusivity, or that such exclusivity will prevent competitors from seeking approval solely on the basis of their own studies.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition (ii) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

Orphan designation must be requested before submitting an MAA. An EU orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of an MA, orphan medicinal products are entitled to 10 years of market exclusivity for the approved indication, which means that the competent authorities cannot accept another MAA, or grant an MA, or accept an application to extend an MA for a similar medicinal product for the same indication for a period of 10 years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period 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 which it received orphan destination, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, MA may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance ("QPPV") who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAA must include a risk management plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

Failure to comply with the aforementioned EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area ("EEA") which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

For other countries outside of the EU and the United States, the requirements governing product development, the conduct of clinical trials, manufacturing, distribution, marketing approval, advertising and promotion, product licensing, pricing and reimbursement vary from country to country. Additionally, clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Further, to the extent that any of our drug candidates, once approved, are sold in a foreign country, we may be subject to applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Brexit and the Regulatory Framework in the United Kingdom

Following the end of the Brexit transition period on January 1, 2021, and the implementation of the Windsor Framework on January 1, 2025, the United Kingdom ("UK") is not generally subject to EU laws in respect of medicines. The EU laws that have been transposed into UK law through secondary legislation remain applicable in the UK; however, new legislation such as the (EU) CTR is not applicable in the UK.

Under the Medicines and Medical Devices Act 2021, the Secretary of State or an 'appropriate authority' has delegated powers to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") is the UK's standalone medicines and medical devices regulator. As a result of the Ireland/Northern Ireland protocol, different rules applied in Northern Ireland than in England, Wales, and Scotland, together, Great Britain ("GB"), which continued to follow the EU regulatory regime. However, on January 1, 2025, a new arrangement called the "Windsor Framework" came into effect and reintegrated Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products. The Windsor Framework removes EU licensing processes and EU labelling and serialization requirements in relation to Northern Ireland and introduces a UK-wide licensing process for medicines.

The UK regulatory framework in relation to clinical trials is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which is derived from existing EU legislation (as implemented into UK law, through secondary legislation). In April 2025, the UK adopted the Medicines for Human Use (Clinical Trials) Amendment Regulations. The amendment, which will take full effect from April 2026, aims to provide a more flexible regime to make it easier to conduct clinical trials in the UK, increase the transparency of clinical trials conducted in the UK and make clinical trials more patient centered.

MAs in the UK are governed by the Human Medicines Regulations (SI 2012/1916), as amended. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder opted-out. Under the terms of the Windsor Framework, these MAs became valid for the whole of the UK from January 1, 2025. In order to use the centralized procedure to obtain an MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore, since Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures. Applications are governed by the Human Medicines Regulations (SI 2012/1916) and are made electronically through the MHRA Submissions Portal. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, a 150-day assessment (subject to clock-stops) and a rolling review procedure. In addition, since January 1, 2024, the MHRA may rely on the International Recognition Procedure ("IRP"), when reviewing certain types of MAAs. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (e.g., the regulatory authorities in Australia, Canada, Switzerland, Singapore, Japan, the United States. and the EU). The MHRA will conduct a targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. The IRP allows medicinal products approved by such trusted regulatory partners that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update an MA in the UK. Applications should be decided within a maximum of 60 days if there are no major objections identified that cannot be resolved within such 60-day period and the approval from the trusted regulatory partner selected has been granted within the previous two years or if there are such major objections identified or such approval hasn't been granted within the previous two years within 110 days. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals. In the UK, the initial duration of an MA is five years and following renewal will be valid for an unlimited period unless the MHRA decides on justified grounds relating to pharmacovigilance to proceed with only one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the market in the UK within three years shall cease to be in force.

There is no pre-MA orphan designation in the UK. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in the UK, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in the UK.

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

Coverage and Reimbursement

In the United States and internationally, sales of NERLYNX and any other products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability of adequate coverage and reimbursement from third-party payors, such as state and federal governments, managed care providers and private insurance plans. Private insurers, such as health maintenance organizations and managed care providers, have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and the out-of-pocket obligations of member patients for such products. We may need to conduct pharmacoeconomic studies to demonstrate the cost-effectiveness of our products for formulary coverage and reimbursement. Even with such studies, our products may be considered less safe, less effective or less cost-effective than existing or future products, and third-party payors may not provide limits or deny coverage and reimbursement for our drug candidates, in whole or in part.

In many countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. In the EU, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the

cost effectiveness of a particular product to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. 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. The downward pressure on healthcare costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower.

In addition, particularly in the United States and increasingly in other countries, we are required to provide discounts and pay rebates under federal programs we participate in. For example, we pay rebates under the Medicaid Drug Rebate Program ("MDRP") and offer discounts under the 340B drug pricing program in order for reimbursement to be available for our products. It is possible that future legislation in the United States and other jurisdictions could be enacted to potentially impact reimbursement rates for the products we are developing and may develop in the future. This legislation could increase the levels of discounts and rebates paid to federal and state government entities and significantly impact our ability to generate revenues.

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our future business. For example, the Affordable Care Act (the "ACA") was enacted in 2010 and substantially changed the way healthcare is financed by both governmental and private insurers. Among other provisions, the ACA included an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents and a new formula that increases the rebates a manufacturer must pay under the MDRP. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, led to reductions of Medicare payments to providers, which will remain in effect through 2032, unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Most significantly, the Inflation Reduction Act ("IRA") was enacted in 2022. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); redesigns the Medicare Part D benefit (beginning in 2024); and replaces the Part D coverage gap discount program with a new manufacturer discount program (which began in 2025). U.S. Centers for Medicare & Medicaid Services ("CMS") has published the negotiated prices for the initial 10 drugs, which went into effect in January 2026, and the subsequent 15 drugs, which will first be effective in 2027. CMS has also published the next set of 15 drugs that will be subject to negotiation. The IRA permits the Secretary of the Department of Health and Human Services ("HHS") to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented, although the Medicare drug price negotiation program is currently subject to legal challenges. The impact of the IRA on us and the pharmaceutical industry cannot yet be fully determined, but is likely to be significant.

Under the IRA manufacturer discount program that replaced the coverage gap discount program as of January 1, 2025, manufacturers must give a 10 percent discount on Part D drugs in the initial coverage phase, and a 20 percent discount on Part D drugs in the so-called "catastrophic phase" (the phase after the patient incurs costs above the initial phase out-of-pocket threshold, which was $2,000 beginning in 2025). The IRA allows the 10 and 20 percent discounts to be phased in over time for certain drugs for "specified manufacturers." In April 2024, CMS informed us that we are deemed a specified small manufacturer and the discount will be phased in over several years and will increase over time. We are continuing to evaluate the potential impact of this status on our future revenues.

NERLYNX is reimbursed under Medicare Part D, and we have incurred IRA inflation rebates. We may incur additional Part D inflation rebates in subsequent periods. Such rebate liability could be significant. The reimbursement amount for NERLYNX under Medicare Part D will be impacted by the 10 and 20 percent discounts under the IRA's new discounting program (as noted above). We anticipate that these increased discounts will impact NERLYNX revenues over time, while also having an industry-wide impact on the patient out of pocket costs of Part D drugs. The impact on NERLYNX revenues could be offset because the IRA's redesign of certain Part D components, some of which went into effect in 2024, resulted in an increase in the number of patients able to afford this therapy. The amount of the offset, if any, is inherently uncertain and difficult to predict.

The IRA manufacturer discount program also increases financial obligations of Part D prescription drug plans with respect to beneficiaries in the catastrophic coverage phase. This may incentivize Part D prescription drug plans to seek greater price concessions from us in order to include NERLYNX on their formularies.

More recently, the One Big Beautiful Bill Act, which was enacted in July 2025, imposes significant reductions in the funding of the Medicaid program. Such reductions are expected to decrease the number of persons enrolled in Medicaid and reduce the services covered by Medicaid, which could adversely affect our sales of NERLYNX and any other product candidate that we commercialize.

The Trump administration is pursuing a two-fold strategy to reduce drug costs in the United States. While it is unclear whether and how the Trump proposals will be implemented, the Trump policies are likely to have a negative impact on the pharmaceutical industry and on our ability to receive adequate revenues for our products. On the one hand, President Trump has threatened to impose significant tariffs on pharmaceutical manufacturers that do not adopt pricing policies such as most favored nation pricing, which would tie the price for drugs in the United States to the lowest price in a group of other countries. In response, multiple manufacturers have entered into confidential pricing agreements with the federal government. On the other hand, the Trump administration is pursuing traditional regulatory pathways to impose drug pricing policies and published two proposed regulations in December 2025, referred to as Globe and Guard. If finalized, these regulations would implement mandatory payment models under which manufacturers of eligible drugs would be required to pay rebates to the federal government on a portion of the units of their drugs that are reimbursed by Medicare, with the rebate amount based on most favored nation pricing. Imposing a rebate in the United States that is based on drug prices outside the United States would mark a drastic and unprecedented shift in the United States pharmaceutical market, and while the impact of the Globe and Guard proposed regulations, if finalized, cannot yet be determined, it is likely to be significant. Even regulatory proposals or executive actions that are ultimately deemed unlawful could negatively impact the U.S. pharmaceutical sector and our business.

The cost of prescription pharmaceuticals in the United States continues to be the subject of considerable discussion. There have been several Congressional inquiries, as well as legislative and regulatory initiatives and executive orders 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 drug products.

In the United States, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing. These actions include but are not limited to price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. In some cases, these actions have been designed to encourage importation from other countries and bulk purchasing. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states, and at least one state board is imposing an upper payment limit. States are also seeking to implement general, across the board price caps for pharmaceuticals, or are seeking to regulate drug distribution.

Similar political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing systems, parallel distribution and parallel trade. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced countries. Reductions in the pricing of our medicinal products in one EU member state could affect the price in other EU member states and, thus, have a negative impact on our financial results.

Health Technology Assessment ("HTA") of medicinal products in the EU is an essential element of the pricing and reimbursement decision-making process in a number of EU member states. The outcome of HTA has a direct impact on the pricing and reimbursement status granted to the medicinal product. A negative HTA by a leading and recognized HTA body concerning a medicinal product could undermine the prospects to obtain reimbursement for such product not only in the EU member state in which the negative assessment was issued, but also in other EU member states.

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive establishes a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states. The network facilitates and supports the exchange of scientific information concerning HTAs. Further to this, in December 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product, i.e. oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology and making decisions on pricing and reimbursement.

In the future, there may continue to be additional proposals relating to the reform of the U.S. and international healthcare systems. Future legislation, or regulatory actions implementing recent or future legislation may have a significant effect on our business. Our ability to successfully commercialize products depends in part on the extent to which reimbursement for the costs of our products and related treatments will be available in the United States and worldwide from government health administration authorities, private health insurers and other organizations. The adoption of certain proposals could limit the prices we are able to charge for our products, the amounts of reimbursement available for our products, and limit the acceptance and availability of our products. Therefore, substantial uncertainty exists as to the reimbursement status of newly approved health care products by third-party payors.

Government Price Reporting

Medicaid is a joint federal and state program for low-income and disabled beneficiaries. Medicare is a federal program covering individuals aged 65 and over as well as those with certain disabilities. As a condition of having federal funds being made available for covered outpatient drugs under Medicaid and Medicare Part B, we have enrolled in the MDRP, which requires us to pay a rebate to state Medicaid programs for each unit of our covered outpatient drugs dispensed to a Medicaid beneficiary and paid for by a state Medicaid program. Medicaid rebates are based on pricing data that we must report on a monthly and quarterly basis to the CMS, the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the average manufacturer price ("AMP") for each drug and, in the case of our innovator products, the best price ("BP"). If we become aware that our MDRP price reporting submission for a prior period was incorrect or has changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. If we fail to provide information timely or are found to have knowingly submitted false information to the government, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP.

Federal law requires that a manufacturer that participates in the MDRP also participate in the Public Health Service's 340B drug pricing program (the "340B program") in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. We participate in the 340B program, which is administered by the Health Resources and Services Administration ("HRSA") that requires us to charge statutorily defined covered entities no more than the 340B "ceiling price" for our covered outpatient drugs used in an outpatient setting. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B

ceiling price calculation and discount requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized a revised regulation implementing an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs.

In order to be eligible to have drug products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we also must participate in the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. Under the VA/FSS program, we must report the Non-Federal Average Manufacturer Price ("Non-FAMP") for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). We must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If we fail to provide timely information or are found to have knowingly submitted false information, we may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency reporting requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states.

Sales and Marketing

The FDA regulates all advertising and promotion activities for products under its jurisdiction prior to and after approval, including standards and regulations for direct-to-consumer advertising, dissemination of off-label information, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to collect additional data or conduct additional pre-clinical studies and clinical trials. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patient. The FDA does not regulate the behavior of physicians in their choice to prescribe treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA and other regulatory agencies, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA. In addition to the FDA, a company can be subject to legal claims from other governmental agencies and private parties relating to marketing practices such as the Federal Trade Commission ("FTC"), competitors, patients, and other third parties.

Outside the United States, our ability to market a product is contingent upon obtaining marketing authorization from the appropriate regulatory authorities and similar requirements to the ones described above may apply in foreign jurisdictions. The requirements governing, among other things, marketing authorization and pricing and reimbursement vary widely from country to country.

Other Healthcare Laws

We are also subject to various federal, state and foreign laws pertaining to health care "fraud and abuse," including anti-kickback laws, false claims laws and transparency laws.

The federal Anti-Kickback Statute ("AKS") prohibits, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution; however, these are drawn narrowly and require strict compliance in order to offer protection. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Federal civil and criminal false claims laws, such as the federal False Claims Act ("FCA") prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented false, fictitious or fraudulent claims for payment or approval by the federal government, including federal health care programs, such as Medicare and Medicaid, and knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. Private individuals can bring "qui tam" actions under the FCA, on behalf of the government and such individuals, commonly known as "whistleblowers," may share in amounts paid by the entity to the government in fines or settlement. Moreover, a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA.

The federal Civil Monetary Penalties law prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal transparency requirements under the Physician Payments Sunshine Act, created under the ACA, requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to annually report to CMS information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, anesthesiology assistants and certified nurse midwives), and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician's immediate family members.

Violations of these laws may be punishable by criminal and/or civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal health care programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also may be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called "responsible corporate officer" doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing. Given the penalties that may be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements.

There are also state and foreign law and regulations equivalents of each of the above federal laws, such as state anti-kickback and false claims laws, that may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by any non-governmental third-party payors, including private insurers. These laws and regulations may differ from one another in significant ways, thus further complicating compliance efforts. For instance, in the EU, many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on pharmaceutical companies. Certain countries also mandate implementation of commercial compliance programs or require disclosure of marketing expenditures and pricing information. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, additional reporting obligations and oversight if a manufacturer becomes subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Data Privacy and Security

Numerous state, federal and foreign laws, regulations, and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Other Laws and Regulatory Processes

We are subject to a variety of financial disclosure and securities trading regulations as a public company in the United States with securities traded on the NASDAQ Global Select Market, including laws relating to the oversight activities of the Securities and Exchange Commission (the "SEC"), and the rules and regulations of The NASDAQ Stock Market LLC. In addition, the Financial Accounting Standards Board ("FASB"), the SEC, and other bodies that have jurisdiction over the form and content of our accounts, our financial statements and other public disclosure are constantly discussing and interpreting proposals and existing pronouncements designed to ensure that companies best display relevant and transparent information relating to their respective businesses.

Our present and future business has been and will continue to be subject to various other laws and regulations. Various laws, regulations and recommendations relating to safe working conditions, laboratory practices, experimental use of animals, and the purchase, storage, movement, import and export, and use and disposal of hazardous or potentially hazardous substances used in connection with our research work are or may be applicable to our activities. Certain agreements entered into by us involving exclusive license rights or acquisitions may be subject to national or supranational antitrust regulatory control, the effect of which cannot be predicted. The extent of government regulation that might result from future legislation or administrative action cannot accurately be predicted.

Human Capital

Employees

As of December 31, 2025, our workforce consisted of 179 full-time employees. Throughout 2025, the size of our employee population was fairly consistent, ending with headcount slightly higher at the end of the year due to additional positions being added in multiple functions and replacement positions which were open at the beginning of 2025 being filled. Our largest employee population is the field-based commercial team, working from home offices and visiting customers in their territories. Our second largest employee population is located in the greater Los Angeles area, aligned with our corporate headquarters in Los Angeles, California. The majority of our non-field sales employees work remotely from home on a consistent basis. We operate in a virtual work environment, allowing functional management and employees to determine when working virtually is more efficient and productive, and when in-office collaboration is beneficial. This work model allows us to attract and hire employees from across the country, which contributes to increased employee engagement, satisfaction and retention. We are an equal opportunity employer and believe strongly in hiring and maintaining a diverse, equitable and inclusive workforce. This is reflected in our numbers with our total workforce being approximately 46% women and 39% ethnically diverse. The following table summarizes our workforce by location for the years ended December 31, 2025 and December 31, 2024:

	December 31, 2025	December 31, 2024
Los Angeles	52	58
South San Francisco	24	26
Field & Remote	103	88
	179	172

We believe that the safety and health of our employees and their families are essential to our business. Our goal is to support the well-being of our employees. We believe that our employees and their families need to be healthy to be the most productive and engaged at work. Our financial, health and wellness benefits are designed to assist employees with financial planning, preventative health care and support when unexpected circumstances arise.

We continue to support employee wellbeing, work flexibility, and work efficiency by offering the following:

- a robust offering of benefit options;
- periodic reminders of our benefit options to our employees;
- a Lifestyle Spending Account to support employee wellness and fitness activities;
- programming, including on-demand and live “Wellness Breaks” facilitated by expert instructors online, and “Walking Challenges” to motivate employees to engage with each other for increased physical fitness opportunities; and
- ergonomic support in the form of training opportunities, 1:1 evaluations and providing ergonomically compatible equipment when necessary.

Compensation & Benefits

We know that attracting, developing and retaining the best employees is a critical part of our competitive edge, future success, and a key component to delivering the best care for patients. We offer a competitive and robust total compensation package to maintain the most qualified employee population.

Our total rewards package consists of competitive salaries benchmarked to market data, cash bonuses and equity grants. Bonus opportunities and equity compensation increase as a percentage of total compensation based on level of responsibility, with actual bonus payout based on performance. In addition to competitive salaries and performance incentives, we offer employees 100% employer-paid premiums for medical, dental, vision, mental health services, and life insurance. In addition, we offer a 401(k) plan with employer match, paid time off, various leave of absence options, fertility benefits, fitness/wellness benefits, volunteer days and more. Our benefit programs are constantly evolving to meet our employees’ needs and are reviewed and modified each year as part of our commitment to employee wellness and success. Total compensation represents a broad spectrum of plans and programs designed to reward and motivate employees throughout their careers at Puma.

Culture and Communication

Our core values are the principles that guide our company strategy and our individual actions. Our positive and supportive culture is continuously referenced by employees as a reason they enjoy working at Puma. We maintain a work environment that is collaborative, friendly, supportive and encourages our employees to focus on patient outcomes as a key motivator. We host employee events with medical and scientific presentations given by experts in the field, patient ambassadors, thought leaders and functional leaders to foster employee education. At all times we strive to distinguish ourselves as a respected biopharmaceutical company that is differentiated by top talent and innovative products to enhance cancer care.

All employees are responsible for upholding our core values, including to be patient-centric, to communicate, collaborate, innovate, and be respectful, as well as for adhering to our Code of Ethics. These values nurture an inclusive workforce striving for excellence that puts the well-being of our patients first. The majority of our employees have obtained advanced degrees in their professions, and we support their continued development with individualized development plans and objectives, mentoring, coaching, training and conference attendance. In addition, we offer an Educational Reimbursement Program to assist employees who want to further their education.

Communication is critical in our ability to continuously enhance our company culture and create a more inclusive environment. We conduct virtual town hall meetings to share information about our business activities, company performance, and other topics of interest to our employees. We continue to publish a quarterly newsletter to share interesting and useful information through our involvement in cancer-related conferences and causes, such as *Breast Cancer Awareness Month.* We also introduce new employees to the organization in our *Welcome to Puma* section, and profile existing employees in our *Get Connected* section, where we share information about their roles, motivations to be with Puma, backgrounds, and interests.

Corporate Information and History

Our principal executive offices are located at 10880 Wilshire Boulevard, Suite 1700, Los Angeles, California 90024 and our telephone number is (424) 248-6500. Our internet address is https://www.pumabiotechnology.com. Our annual, quarterly and current reports, and any amendments to those reports, filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act may be accessed free of charge through our website after we have electronically filed or furnished such material with the SEC. We also make available free of charge on or through our website our Code of Business Conduct and Ethics, Corporate Governance Guidelines, Audit Committee Charter, Compensation Committee Charter, Nominating and Corporate Governance Committee Charter and Research and Development Committee Charter. We will disclose on a current report on Form 8-K or on our website any amendment or waiver of the Code of Business Conduct and Ethics for our executive officers and directors. Any amendment or waiver disclosed on our website will remain available on our website for at least 12 months after the initial disclosure.

The reference to https://www.pumabiotechnology.com (including any other reference to such address in this Annual Report) is an inactive textual reference only, meaning that the information contained on or accessible from the website is not part of this Annual Report and is not incorporated in this report by reference.

We were originally incorporated in the State of Delaware in April 2007 under the name Innovative Acquisitions Corp. We were a “shell” company registered under the Exchange Act with no specific business plan or purpose until we acquired Puma Biotechnology, Inc., a privately held Delaware corporation formed on September 15, 2010 (“Former Puma”), in October 2011. As a result of this transaction, Former Puma became our wholly owned subsidiary and subsequently merged with and into us, at which time we adopted Former Puma’s business plan and changed our name to “Puma Biotechnology, Inc.”

ITEM 1A. RISK FACTORS

In addition to the other information contained in this Annual Report, the following risk factors should be considered carefully in evaluating our company. Our business, financial condition, liquidity and results of operations could be materially adversely affected by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us.

Risks Related to our Financial Condition and Capital Requirements

While we have reported net income in recent years, we cannot assure that we will continue to do so and may not be able to maintain profitability.

We have incurred significant cumulative operating losses since our inception. While we have reported net income in recent years, including the years ended December 31, 2025, 2024 and 2023, we cannot assure that we will continue to do so and will need to continue to generate significant revenue to sustain operations and successfully commercialize neratinib and develop alisertib. As of December 31, 2025, we had an accumulated deficit of approximately $1,283.8 million, outstanding indebtedness of approximately $22.5 million and cash and cash equivalents and marketable securities of approximately $97.5 million.

We expect to continue to incur significant expenses and may incur net losses in the future. Since inception, we have devoted substantially all of our resources to identifying, acquiring and developing NERLYNX and to its commercialization in the indications for which it has received regulatory approval. In September 2022, we in-licensed the development and global commercialization rights to our drug candidate, alisertib. Biopharmaceutical development is a highly speculative undertaking and involves a substantial degree of risk. While we experienced profitability in 2025, 2024 and 2023, we may incur operating losses in the future as we continue our efforts to commercialize NERLYNX in existing indications and to develop neratinib for additional indications, and as we commence development efforts for alisertib and any other drug candidates we may acquire.

In 2017, the FDA approved NERLYNX for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. In February 2020, NERLYNX was also approved by the FDA in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. In 2018, the EC granted a marketing authorization for NERLYNX in the EU for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who completed adjuvant trastuzumab-based therapy less than one year ago. We are also in the early stages of development for alisertib. The successful development and commercialization of any drug candidate will require us to perform a variety of functions, including:

- undertaking pre-clinical development and clinical trials;
- participating in regulatory approval processes;
- formulating and manufacturing products;
- successfully conducting sales and marketing activities; and
- implementing additional internal systems and infrastructure.

We are only in the preliminary stages of most of these activities, particularly as they relate to alisertib. We will need to generate significant revenue in order to offset our expenses and maintain profitability. We may not be able to generate this revenue or maintain profitability in the future. As a result, we expect to incur losses for the foreseeable future. Accordingly, we cannot assure you that we will be able to maintain or increase profitability. Our failure to maintain profitability could negatively impact the value of our common stock.

We are currently a single product company with limited commercial sales experience.

We have invested a significant portion of our efforts and financial resources in the development and commercialization of our lead product, NERLYNX. NERLYNX is the only product for which we currently receive product revenue, and we expect NERLYNX to constitute the vast majority of our product revenue for the foreseeable future. By virtue of being dependent on a single product, we do not have the ability to spread out risk or commercial fluctuations across a portfolio of products. As a result, our success depends entirely on the commercial success of NERLYNX. NERLYNX is the first product that we, as an organization, have launched and commercialized, and there is no guarantee that we will be able to do so successfully. 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 we have.

We may not be able to successfully commercialize NERLYNX in the future.

The future commercial success of NERLYNX depends on the extent to which patients and physicians accept and adopt NERLYNX. For example, if the expected patient population is smaller than we estimate or if physicians are unwilling to prescribe or patients are unwilling to take or continue to take NERLYNX, due to any perceived efficacy limitations or related side effects, including diarrhea, or otherwise, the commercial success of NERLYNX will be limited. Thus, significant uncertainty remains regarding the future commercial potential of NERLYNX. We believe our ability to effectively increase product revenue from NERLYNX depends on our ability to, among other things:

- achieve and maintain compliance with regulatory requirements;
- create and sustain market demand for NERLYNX through our marketing and sales activities and other arrangements established for the promotion of NERLYNX;
- compete with other breast cancer drugs, including clinical trials (either in the present or in the future);
- educate physicians and patients about the benefits, administration and use of NERLYNX;
- train, deploy and support a qualified sales force;
- ensure and maintain appropriate placement on formularies and pathways;
- ensure that our third-party manufacturers manufacture NERLYNX in sufficient quantities, in compliance with requirements of the FDA and similar foreign regulatory agencies where NERLYNX is approved, and at acceptable quality and pricing levels in order to meet commercial demand;
- ensure that our third-party manufacturers develop, validate and maintain commercially viable manufacturing processes that are compliant with current Good Manufacturing Practice ("cGMP") or similar foreign regulations;
- maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- ensure that our entire supply chain efficiently and consistently delivers NERLYNX to our customers;
- maintain broad levels of coverage and reimbursement for NERLYNX from commercial health plans and governmental health programs;
- continue to provide co-pay assistance to help qualified patients with out-of-pocket costs associated with their NERLYNX prescription and/or other programs to ensure patient access to our products;
- maintain acceptance of NERLYNX as safe and effective by patients and the medical community;
- influence the nature and volume of publicity relative to our competitors' products;
- obtain regulatory approvals for additional indications for the use of neratinib; and
- maintain and defend our patent protection and regulatory exclusivity for NERLYNX and to comply with our obligations under, and otherwise maintain, our intellectual property license with Pfizer and our license agreements with third parties.

We cannot assure you that we will successfully address each of these uncertainties or any others we may face in the ongoing commercialization of NERLYNX. In addition, we are dependent on international third-party sub-licensees for the development and commercialization of NERLYNX in several countries outside the United States. The failure of these sub-licensees to meet their contractual, regulatory or other obligations could adversely affect international sales of NERLYNX and hinder our ability to generate revenue. These uncertainties make it difficult to predict our future commercial opportunity and forecast our financial performance.

We may not be able to secure additional financing on favorable terms, or at all, to meet our future capital needs and our failure to obtain additional financing when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or commercialization efforts or other operations.

Our operations have consumed substantial amounts of cash since inception. As we continue to commercialize NERLYNX and as we pursue development of alisertib, our costs and expenses may increase in the future due to, among other things, the cost of a direct sales force and the cost of manufacturing. We will also continue to expend substantial amounts on research and development of our other drug candidates, including conducting clinical trials. Our future capital requirements will depend on many factors, including:

- the costs and expenses of our United States sales and marketing infrastructure, and of manufacturing;
- the degree of success we experience in commercializing NERLYNX;
- the revenue generated by the sale of NERLYNX and any other products that may be approved;
- the costs, timing and outcomes of clinical trials and regulatory reviews associated with developing neratinib for additional indications, alisertib and our other drug candidates;
- the emergence of competing products;
- the extent to which NERLYNX or any other drug candidates we develop are adopted by the physician community and patients;
- the number and types of future drug candidates we develop and commercialize;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the costs of operating as a public company and compliance with existing and future regulations; and
- the extent and scope of our general and administrative expenses.

While our consolidated financial statements have been prepared on a going concern basis, we expect to incur significant losses for the foreseeable future and will continue to remain dependent on our ability to obtain sufficient funding to sustain operations and successfully commercialize NERLYNX and develop alisertib. While we have been successful in raising financing in the past, there can be no assurance that we will be able to do so in the future. Additional financing may not be available on a timely basis on terms acceptable to us, or at all. We may raise funds in equity or debt financings to access funds for our capital needs. If we raise additional funds through further issuances of equity or convertible debt securities, our existing stockholders could suffer significant dilution in their percentage ownership of our company, and any new equity securities we issue could have rights, preferences and privileges senior to those of holders of our common stock. Any debt financing obtained by us in the future would cause us to incur debt service expenses and could include restrictive covenants relating to our capital raising activities and other financial and operational matters, which may make it more difficult for us to obtain additional capital and pursue business opportunities. If we are unable to obtain adequate financing or financing on terms satisfactory to us when we require it, we may terminate or delay the development of one or more of our drug candidates, delay clinical trials necessary to market our products, or delay establishment of sales and marketing capabilities or other activities necessary to commercialize our products. If this were to occur, our ability to continue to grow and support our business and to respond to business challenges could be significantly limited. Furthermore, our ability to obtain funding may be adversely impacted by uncertain market conditions, our success in commercializing NERLYNX, unfavorable decisions of regulatory authorities or adverse clinical trial results. The outcome of these matters cannot be predicted at this time.

The terms of our Note Purchase Agreement place restrictions on our ability to operate our business and on our financial flexibility, and we may be unable to achieve the revenue necessary for us to incur additional borrowings under the Note Purchase Agreement or to satisfy the minimum revenue and cash balance covenants.

We are party to a Note Purchase Agreement with Athyrium Opportunities IV Co-Invest 1 LP ("Athyrium"), providing for potential issuance by us of notes of up to $125.0 million, which mature on July 23, 2026. The terms of our Note Purchase Agreement place restrictions on our ability to operate our business and on our financial flexibility. As of December 31, 2025, the aggregate principal amount outstanding under the notes sold pursuant to the Note Purchase Agreement (collectively, the "Athyrium Notes") was $22.5 million. The Athyrium Notes are secured by collateral which consists of our equity interests in our domestic and foreign subsidiary (including up to 100% of the issued and outstanding equity interests in our subsidiary directly owned by us or the guarantors of the Athyrium Notes) and substantially all of our property. In addition to voluntary prepayments, we may also be required to make mandatory prepayments under the Athyrium Notes in varying amounts within three (3) business days of the occurrence of certain events, including in the event that we receive proceeds from a voluntary or involuntary disposition and such proceeds are not reinvested in eligible assets within 180 days of the date of such disposition, or in the event that we receive extraordinary receipt cash proceeds and such proceeds are not reinvested in eligible assets within 180 days of the date of such extraordinary receipt. The Note Purchase Agreement includes affirmative and negative covenants applicable to us and our subsidiary. The affirmative covenants include, but are not limited to, requirements to (i) maintain our legal existence and take all reasonable actions to maintain our rights, privileges and authorizations (including renewal of permits or licenses) necessary to conduct our business and maintain our intellectual property, (ii) deliver certain financial statements, certificates and other information to Athyrium on a regular basis, (iii) maintain adequate insurance coverage with respect to the properties and business and (iv) cause all of our deposit accounts (other than certain "excluded accounts") to be subject to Deposit Account Control Agreements. The negative covenants include, but are not limited to, restrictions on (i) creating or incurring certain liens on our property, assets or revenues, (ii) making certain investments or incurring additional indebtedness, (iii) engaging in certain business or strategic activities (including transactions with affiliates or insiders) and (iv) paying certain dividends, distributions or other restricted payments. Additionally, pursuant to the Note Purchase Agreement, we must maintain a minimum cash balance in our accounts subject to a deposit account control agreement and must achieve certain levels of product revenue for any four (4) consecutive fiscal quarter periods. These affirmative and negative covenants may make it difficult for us to operate our business. In addition, we cannot assure you that we will be able to achieve the minimum product revenue requirements or minimum cash balance requirements under the Note Purchase Agreement. Our failure to satisfy such requirements, or our direct or indirect breach of certain other covenants, could result in an event of default under the Athyrium Notes. The occurrence and continuation of an event of default could (i) cause interest to accrue at a rate per annum equal to the applicable interest rate under the Note Purchase Agreement *plus* two percent (2.00%) and (ii) cause accrued and unpaid interest on past due amounts (including interest thereon) to be due and payable in cash on demand. Additionally, upon the occurrence or continuation of an event of default, Athyrium, in its capacity as administrative agent, would have the right to exercise remedies against us, including declaring the unpaid principal amount under the Note (and interest thereon) immediately due and payable, and foreclosure against the property securing the Athyrium Notes (including our cash). Other events of default under the Note Purchase Agreement include, but are not limited to, (i) our failure to pay principal or interest due under the Note Purchase Agreement, (ii) our insolvency or related actions (including an assignment for the benefit of creditors), (iii) the existence of material adverse changes in our business or products, (iv) the occurrence of any default under certain other indebtedness in an amount greater than $750,000 or one or more judgments against us in an amount greater than $750,000 individually or in the aggregate that remains unsatisfied, unvacated or unstayed for a period of thirty (30) days after its entry and (v) the delisting of our shares of common stock from the Nasdaq Capital Market.

Risks Related to the Discovery and Development of our Products and Drug Candidates

We have in-licensed alisertib, a drug candidate for which we have assumed all responsibility for global development and commercialization. Our development of alisertib will be expensive, lengthy and unpredictable, and any failure to successfully develop alisertib will have a material adverse effect on our business and financial position.

In September 2022, we in-licensed alisertib from Takeda. Pursuant to our exclusive license agreement with Takeda, we are responsible for global development and commercialization of alisertib. Clinical development of alisertib will be expensive, lengthy and unpredictable. Failure or delay can occur at any time during the development process. There are numerous risks associated with our planned development alisertib, including the following:

- We have limited experience developing alisertib;
- The results of pre-clinical studies and early clinical studies of alisertib may not be predictive of later clinical studies, and success in previous stages cannot ensure positive outcome of future stages of clinical studies;
- Alisertib may fail to show the desired pharmacological properties or safety and efficacy traits despite having progressed through pre-clinical studies and early clinical studies;
- Even if we complete clinical development of alisertib, the results may not be sufficient to obtain regulatory approval in the United States or other countries;
- Our license agreement with Takeda may be terminated by Takeda if we materially breach the agreement, in which case we would lose all rights to develop and commercialize alisertib;
- We plan to rely on third party contractors to formulate and manufacture alisertib for clinical trials and these third-party contractors may be unable to formulate and manufacture alisertib in the volume and quality we require;
- We plan to rely on third-party contractors to conduct our clinical trials of alisertib and if those parties fail to perform their services within expected timelines or fail to comply with regulatory requirements, our development efforts could be delayed;
- Clinical trials are expensive, time-consuming and difficult to design and implement; and
- Development of alisertib could distract management's attention from other important aspects of our business.

Even if we are successful in developing alisertib, we cannot assure you that we will be able to successfully commercialize alisertib. Any delays or failure in our development of alisertib could have material adverse effects on our business, operations and financial condition.

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

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

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

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

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

NERLYNX, alisertib or other drug candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any, as applicable.

Undesirable side effects caused by NERLYNX, alisertib or other drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. To date, subjects treated with NERLYNX have experienced drug-related side effects such as diarrhea. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if we or others later identify undesirable side effects caused by any approved product, including in combination with other approved products or investigational new drugs, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to suspend marketing of a product, or we may decide to remove such product from the marketplace;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

We are in the early stages of development of alisertib, and we cannot be certain that we will be successful if we seek regulatory approvals for our drug candidates.

We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to the development of alisertib. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We cannot predict with any certainty that any NDA or supplemental NDA (or similar foreign applications) to market alisertib or our other drug candidates will be approved by the FDA or foreign regulatory authorities. We are not permitted to market neratinib for other indications or alisertib or any of our other drug candidates in the United States until we receive approval of an NDA from the FDA or until we receive an MA from the EC in the EU, as applicable, for such indications, or, in any foreign countries, until requisite approval from such countries.

Approval of neratinib by the FDA or the EC for any particular indication does not ensure that another foreign jurisdiction will also approve neratinib for such indication, nor does it ensure that neratinib will be approved by the FDA or the EC for any other indications. Similarly, approval of alisertib by the FDA or the EC would not ensure that another jurisdiction will also approve alisertib. Obtaining approval of an NDA or foreign marketing application is an extensive, lengthy, expensive and inherently uncertain process, and the FDA or a foreign regulator may delay, limit or deny approval of a drug candidate for many reasons, including:

- we may not be able to demonstrate that NERLYNX, alisertib or any other drug candidate is safe and effective as a treatment for our targeted indications to the satisfaction of the FDA or other foreign regulator;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or other foreign regulator for marketing approval;
- the FDA or other foreign regulators may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the CRO that we retain to conduct clinical trials or any other third parties involved in the conduct of trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA or other foreign regulators may not find the data from pre-clinical studies and clinical trials sufficient to demonstrate that the clinical and other benefits of NERLYNX, alisertib or any other drug candidate outweigh the safety risks;
- the FDA or other foreign regulators may disagree with our interpretation of data from our pre-clinical studies and clinical trials or may require that we conduct additional studies or trials;
- the FDA or other foreign regulators may not accept data generated at our clinical trial sites;
- the FDA or other foreign regulators may require development of a Risk Evaluation and Mitigation Strategy or similar risk management measures as a condition of approval;
- the FDA or other foreign regulators may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers; or
- the FDA or other foreign regulators may change their approval policies or adopt new regulations.

If we do not obtain regulatory approval of alisertib or our other drug candidates in a particular jurisdiction, we will not be able to market such drug candidate in that jurisdiction. Therefore, failure to obtain regulatory approval of alisertib or our other drug candidates will limit our commercial revenue.

In addition, FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation has been undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. On April 26, 2023, the European Commission published a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation. The proposed changes were since discussed and negotiated by the European Parliament and the Council of the EU as part of the EU ordinary legislative process. A provisional agreement has been reached by the

European Parliament and Council of the EU on the proposed revisions on December 11, 2025. The proposed revisions (affecting the duration of regulatory data protection and market protection, including for orphan medicinal products, revising the eligibility for expedited pathways, etc.) remain to be formally adopted by the two institutions, which is not anticipated before early 2026. The proposed changes are not expected to enter into application before 2028, and may however have a significant impact on the biopharmaceutical industry in the long term.

We are subject to ongoing obligations and continued regulatory review with regard to NERLYNX, alisertib and any other drug candidates that may receive FDA or foreign regulatory approval, which may result in significant expense. Additionally, NERLYNX, alisertib and our other drug candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

The FDA's approval for NERLYNX and any regulatory approvals that we receive for alisertib or our other drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and similar requirements and GCPs for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and foreign regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or outside the United States. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Disruptions at the FDA and other government agencies caused by funding shortages, staffing limitations or policy changes could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's and foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

In addition, the current U.S. Presidential administration has issued certain policies and Executive Orders directed towards reducing the employee headcount and costs associated with U.S. administrative agencies, including the FDA, and it remains unclear the degree to which these efforts may limit or otherwise adversely affect the FDA's ability to conduct routine activities. If a prolonged government shutdown occurs, or if funding shortages, staffing limitations or similar factors hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, such events could significantly impact the ability of the FDA or other such regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Clinical trials are very expensive, time-consuming and difficult to design and implement.

Although NERLYNX has been approved by the FDA for two limited indications, alisertib and our other drug candidates are in development as well, all of which will require extensive clinical testing before we can submit any NDA or similar foreign entities for regulatory approval. We may face significant difficulties during our development of alisertib. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time consuming. We estimate that clinical trials for any of our drug candidates will take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. The results of pre-clinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful.

We do not know whether our future clinical trials will begin on time or enroll patients on time, or whether our ongoing and/or future clinical trials will be completed on schedule or at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval or a positive opinion from one or more institutional review boards ("IRBs") or ethics committees;
- IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- manufacturing sufficient quantities of drug candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post- treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our drug candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;

- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our drug candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice ("cGMP"), regulations or other applicable requirements, or infections or cross-contaminations of drug candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner; or
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other foreign government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications.

Further, we, the FDA, foreign regulatory authorities, or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, that we are exposing participants to unacceptable health risks, or if the FDA or such other foreign regulator finds deficiencies in our IND or comparable submissions supporting the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our drug candidates could be harmed, and our ability to generate revenue from the drug candidates may be delayed. In addition, any delays in our clinical trials could increase our costs, slow down the approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates.

In addition, the FDA's and other foreign regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The CTR which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate CTA to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR transition period ended on January 31, 2025, and all clinical trials (and related applications) are now fully subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and ongoing clinical trials of competing drugs for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the study. Furthermore, any negative results we may report in clinical trials of any of our drug candidates may make it difficult or impossible to recruit and retain patients in other clinical studies of that same drug candidate. Delays or failures in planned patient enrollment and/or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our drug candidates or could render further development impossible. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance.

The results of our clinical trials may not support our drug candidate claims.

Even if our clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our drug candidates for our targeted indications. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and pre-clinical testing. A failure of a clinical trial to meet its predetermined endpoints would likely cause us to abandon a drug candidate and may delay development of other drug candidates.

Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or comparable foreign regulatory authority approval. We cannot guarantee that the FDA or foreign regulatory authorities will interpret trial results as we do, and more trials could be required before we are able to submit applications seeking approval of our drug candidates. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our drug candidates. Even if regulatory approval is secured for any of our drug candidates, the terms of such approval may limit the scope and use of our drug candidate, which may also limit its commercial potential. Furthermore, the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval, which may lead to the FDA or comparable foreign regulatory authorities delaying, limiting or denying approval of our drug candidates.

We may attempt to secure approval from the FDA through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary regulatory approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained.

We may in the future seek accelerated approval for our one or more of our drug candidates, including alisertib. Under the accelerated approval program, the FDA may grant accelerated approval to a drug candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the drug candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit.

The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit or are not completed in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, the Food and Drug Omnibus Reform Act of 2022, among other things, provided the FDA with additional statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval. Under these provisions, the FDA may require a sponsor of a product seeking accelerated approval to have a confirmatory trial underway prior to such approval being granted.

Prior to seeking accelerated approval for any of our drug candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA, or NDA supplement, for accelerated approval or any other form of expedited development, review or approval. Furthermore, if we decide to submit an application for accelerated approval for our drug candidates, there can be no assurance that such application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our drug candidate would result in a longer time period to commercialization of such drug candidate, if any, could increase the cost of development of such drug candidate and could harm our competitive position in the marketplace.

Risks Related to Commercialization of our Drug Candidates

We have limited experience as a company in marketing or distributing pharmaceutical products. If we are unable to expand our marketing and sales capabilities in the commercialization of NERLYNX, our business, results of operations and financial condition may be materially adversely affected.

In the United States, we rely on a direct sales force. NERLYNX is a marketed drug and none of the members of our sales force had ever promoted NERLYNX prior to its commercial launch. There are risks with establishing, growing and maintaining our own sales and marketing capabilities, including:

- the expense and time required to recruit and train a sales force;
- our inability to recruit, retain or motivate adequate numbers of effective and qualified sales and marketing personnel;
- the inability to provide adequate training to sales and marketing personnel;
- the need to train our sales force to ensure that a consistent and appropriate message about NERLYNX is being delivered to our potential customers;
- the inability of sales personnel to obtain access to physicians or convince adequate numbers of physicians to prescribe any product;
- our inability to equip the sales force with effective materials, including medical and sales literature, to help them inform and educate physicians and patients about the benefits of NERLYNX and its proper administration; and
- unforeseen costs and expenses associated with maintaining an independent sales and marketing organization.

If we are unable to effectively address these risks, our efforts to commercialize NERLYNX successfully could be harmed, which would negatively impact our ability to generate product revenue.

Additionally, we will need to maintain and further develop our sales force to achieve commercial success, and we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. In the event we are unable to continue to develop and effectively maintain our commercial team, including our U.S. sales force, our ability to successfully commercialize our products would be limited, and we would not be able to generate product revenue successfully.

Similarly, if we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability associated with any product revenue may be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. Moreover, we may be negatively impacted by other factors outside of our control relating to such third parties, including, but not limited to, their inability to comply with regulatory requirements. If we do not maintain sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products.

We are exposed to the risks associated with reliance on a direct sales force to commercialize NERLYNX in the United States.

In the United States, we rely on a direct sales force to market NERLYNX. Additionally, for any future products that we successfully develop, we will need to establish or maintain effective sales and marketing capabilities or enter into agreements with third parties to sell or market those products. There are risks with maintaining and growing our own sales and marketing capabilities, including:

- the expense and time required to recruit and train a sales force;
- our inability to recruit, retain or motivate adequate numbers of effective and qualified sales and marketing personnel;
- the inability to provide adequate training to sales and marketing personnel;
- the need to train our sales force to ensure that a consistent and appropriate message about NERLYNX is being delivered to our potential customers;
- the inability of sales personnel to obtain access to physicians or convince adequate numbers of physicians to prescribe any product;
- our inability to equip the sales force with effective materials, including medical and sales literature, to help them inform and educate physicians and patients about the benefits of NERLYNX and its proper administration;
- unforeseen costs and expenses associated with creating or maintaining an independent sales and marketing organization; and
- the premature or unnecessary incurrence of significant commercialization expenses if the commercial launch of a product is delayed or does not occur for any reason.

If we are unable to effectively address these risks, our efforts to commercialize NERLYNX, or any additional drug candidates that we develop, could be harmed, which would negatively impact our ability to generate product revenue.

Outside the United States, we rely entirely on third-party sublicenses for the development and commercialization of NERLYNX. For a description of the risks associated with those arrangements see, "*—Risks Related to Third Parties—We are dependent on international third-party sub-licensees for the development and commercialization of NERLYNX in several countries outside the United States. The failure of these sub-licensees to meet their contractual, regulatory or other obligations could adversely affect our business.*"

Our NERLYNX commercialization efforts may fail to achieve the degree of market acceptance by patients and physicians necessary for commercial success.

NERLYNX was approved by the FDA in 2017. We had total revenue for NERLYNX of $228.4 million, $230.5 million and $235.6 million for the years ended December 31, 2025, 2024 and 2023, respectively. We cannot assure you that the sales of NERLYNX will continue at these levels or grow. We may encounter delays or hurdles related to our sales efforts that affect amount of revenue generated and the timing of such revenue. There is no guarantee that the infrastructure, systems, processes, policies, personnel, relationships and materials we have built to commercialize NERLYNX in the United States will be sufficient for us to achieve success at the levels we expect.

Our NERLYNX commercialization efforts may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If NERLYNX does not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not maintain profitability. The degree of market acceptance of NERLYNX and will depend on a number of factors, including:

- the timing of our receipt of any additional marketing approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the efficacy and safety and potential advantages and disadvantages compared to alternative treatments;
- the prevalence and severity of any side effects associated with our products;
- the additional indications for which our products are approved;
- adverse publicity about our products or favorable publicity about competing products;
- the approval of other products for the same indications as our products;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the success of our physician education programs;
- the strength of our marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement, including patient cost-sharing programs such as copays and deductibles; and
- any restrictions on the use of our products together with other medications.

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

We depend on a limited number of customers for a significant amount of our total revenue, and if we lose any of our significant customers, our business could be harmed.

The majority of our revenue comes from a limited number of customers. In 2025, five customers individually comprised approximately 27.3%, 17.0%, 16.4%, 13.1% and 10.6%, respectively, of our total product revenue. We expect that revenue from a limited number of customers will continue to account for a large portion of our revenue in the future. The loss by us of any of these customers, or a material reduction in their purchases or their market pricing, could harm our business, results of operations, financial condition and prospects. In addition, if any of these customers were to fail to pay us in a timely manner, it could harm our cash flow.

Outside the United States we rely primarily on third-parties to pursue regulatory approval, if necessary, and to commercialize NERLYNX and they may not commit sufficient time or resources to marketing NERLYNX.

Outside the United States, we seek to enter into exclusive sub-license agreements with third parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved. As of December 31, 2025, NERLYNX has received approval for the treatment of certain patients with extended adjuvant and/or metastatic HER2-positive breast cancer in more than 40 countries outside the United States, including the EU, Australia, Canada, and Hong Kong. We are currently party to several sub-licenses in various regions outside the United States, including Europe (excluding Ukraine), Australia, Canada, China, Southeast Asia, Israel, South Korea, Russia and various countries and territories in Central

America, South America, Africa and the Middle East. We depend on these third parties for a significant portion of our total revenue. Royalty revenue obtained pursuant to these sub-license agreements was 11% and 15% of total revenue for the years ended December 31, 2025 and 2024, respectively. We have very little control over these third-parties and any of our existing or future licensees may fail to devote the necessary resources and attention to obtain regulatory approval, where needed, and to market and distribute NERLYNX effectively. If these licensees are unsuccessful in receiving regulatory approvals or in commercializing NERLYNX, our business, results of operations and financial condition will be materially adversely affected. Moreover, we intend to seek additional third parties to sub-license NERLYNX in additional geographies, and may pursue a similar strategy for any future drug candidates that we develop. We cannot assure you that we will be able to enter these agreements on commercial terms, or at all, and our failure to do so would have an adverse effect on our continued commercialization efforts for NERLYNX or any future drug candidates.

Even though the FDA and EC have granted approval of NERLYNX for the extended adjuvant treatment of certain patients with early stage, HER2-positive breast cancer and the FDA has granted approval for NERLYNX for the treatment of certain patients with metastatic HER2-positive breast cancer, the terms of the approvals may limit its commercial potential.

Even though the FDA and EC have granted approval of NERLYNX, the scope and terms of the approvals may limit our ability to commercialize NERLYNX and, therefore, our ability to generate substantial sales revenue. The FDA and EC have both approved NERLYNX for the extended adjuvant treatment of certain adult patients with early stage, HER2-positive breast cancer in patients who are less than one year from the completion of prior adjuvant trastuzumab-based therapy. In connection with the FDA and EC approvals, we have committed to conduct certain post-marketing studies. We have completed the post-marketing commitments related to the FDA approval, and the post-marketing studies related to the EC approval are ongoing. If we fail to comply with all of our post-marketing commitments, or if the results of the post-marketing studies, or any other ongoing clinical studies of neratinib, are negative, the FDA or the EC could decide to withdraw its respective approval, add warnings or narrow the approved indication in the product label.

Regulatory approval for any approved product is limited by the FDA and foreign regulatory authorities to those specific indications and conditions for which clinical safety and efficacy have been demonstrated as set forth on the product label. If we market our products for uses beyond such approved indications, we could be subject to enforcement action, which could have a material adverse effect on our business.

The FDA and foreign regulatory authorities strictly regulate marketing, labeling, advertising and promotion of prescription drugs. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet and off-label promotion. Any regulatory approval that the FDA or foreign regulatory authorities grant is limited to those specific diseases and indications for which a product is deemed to be safe and effective by the FDA and foreign regulatory authorities. For example, the FDA-approved label for NERLYNX is limited to the extended adjuvant treatment of adult patients with early stage, HER2-positive breast cancer following adjuvant trastuzumab-based therapy, and in combination with capecitabine, to the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting. In addition to the FDA or foreign regulatory authorities approval required for new formulations, any new indication for an approved product also requires FDA or foreign regulatory authorities' approval. If we are not able to obtain FDA approval for any desired future indications for our drugs and drug candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians in the United States and outside the United States may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote the products is narrowly limited to those indications that are specifically approved by the FDA or foreign regulatory authorities. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. For example, in April 2018, we announced that NERLYNX (neratinib) has been included as a recommended treatment option in the latest NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers for Breast Cancer patients with brain metastases. The NCCN designated NERLYNX in combination with capecitabine as a category 2A treatment option and NERLYNX in combination with paclitaxel as a category 2B treatment option. In addition, in December 2024, we announced that NCCN Clinical Practice Guidelines in Oncology for Cervical Cancer were updated to include an addition involving neratinib. The updated NCCN Practice Guidelines for Cervical Cancer include neratinib monotherapy for use as second-line or subsequent therapy for recurrent or metastatic disease as an option for patients with HER2-mutated tumors with a designation of category 2A. The NCCN Guidelines Category of Preference is designated as "useful in certain circumstances" as a treatment option for patients with HER2-mutated tumors. Use, as designated for breast cancer patients with brain metastases and in Cervical Cancer, is outside the FDA approved indication for NERLYNX and considered investigational, and we do not market or promote NERLYNX for these uses.

Regulatory authorities in the United States and outside the United States 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. Although court decisions in the United States have suggested that certain off-label promotional activities may be protected under the First Amendment, the scope of any such protection is unclear. If our promotional activities fail to comply with the FDA's or other regulatory authorities' regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA or other regulatory authorities rules and guidelines relating to promotion and advertising may cause the FDA or other regulatory authorities to issue warning letters or untitled letters, bring an enforcement action against us, suspend or withdraw an approved product from the market, require a recall or institute fines or civil fines, or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution, any of which could harm our reputation and our business.

We may fail to obtain orphan drug designations from the FDA for our drug candidates, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the U.S., may designate drugs designed to address relatively small patient populations as "orphan drugs." Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug 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 United States, or a patient population greater than 200,000 in the United States, where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States. In the U.S., orphan designation entitles a party to financial incentives such as opportunities for grant funding for clinical trial costs, tax advantages and user-fee waivers. In addition, if a drug candidate that has orphan designation subsequently receives the first FDA approval for the disease or condition 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 an NDA, to market the same drug for the same approved indication or use within the same rare disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in the relevant indication or use or where the manufacturer is unable to assure sufficient product quantity.

We may decide to seek Orphan Drug Designations for alisertib. There can be no assurances that we will be able to obtain such designations. Even if we, or any future collaborators, obtain orphan drug designation for a drug candidate, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that drug candidate. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active ingredients may be approved for the same indication or use within the same rare disease or condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same disease or condition if the FDA concludes that the later drug is clinically superior in the relevant indication, in that it is shown to be safer, more effective or makes a major contribution to patient care, or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity to meet the needs of the approved indication or use for the patients with the relevant disease or condition. Orphan drug designation neither shortens the development or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Health care reform measures may hinder or prevent our products' and drug candidates' commercial success.

The United States and some foreign jurisdictions have enacted or are considering enacting a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to profitably sell our product and drug candidates, if and when they are approved. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

In March 2010, the ACA became law in the United States. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among other provisions, the ACA included an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents and a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, led to reductions to Medicare payments to providers that will remain in effect through 2032. The American Taxpayer Relief Act of 2012, among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The American Rescue Plan Act of 2021 eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price,

The IRA was enacted in 2022. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); redesigns the Medicare Part D benefit (beginning in 2024); and replaces the Part D coverage gap discount program with a new manufacturer discount program (which began in 2025). The Centers for Medicare & Medicaid Services has published the negotiated prices for the initial ten drugs, which went into effect in January 2026, and the subsequent 15 drugs, which will first be effective in 2027. CMS has also published the next set of 15 drugs that will be subject to negotiation. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented, although the Medicare drug price negotiation program is currently subject to legal challenges. The impact of the IRA on us and the pharmaceutical industry cannot yet be fully determined but is likely to be significant.

Under the IRA manufacturer discount program that replaced the coverage gap discount program as of January 1, 2025, manufacturers must give a 10 percent discount on Part D drugs in the initial coverage phase, and a 20 percent discount on Part D drugs in the so-called "catastrophic phase" (the phase after the patient incurs costs above the initial phase out-of-pocket threshold, which will be $2,000 beginning in 2025). The IRA allows the 10 and 20 percent discounts to be phased in over time for certain drugs for manufacturers that CMS deems to meet specific criteria. In April 2024, CMS informed us that we are deemed a specified small manufacturer, and as a result, the discounts will be phased in over several years and will increase over time. We are continuing to evaluate the potential impact of this status on our future revenues.

NERLYNX is reimbursed under Medicare Part D, and the reimbursement amount will be impacted by the 10 and 20 percent discounts under the IRA's new discounting program (as noted above). We anticipate that these increased discounts will impact NERLYNX revenues over time, while also having an industry-wide impact on the cost of Part D drugs. The impact on NERLYNX revenues could be offset because the IRA's redesign of certain Part D components, some of which went into effect in 2024, resulted in an increase in the number of patients able to afford this therapy. The amount of the offset, if any, is inherently uncertain and difficult to predict.

The IRA manufacturer discount program also increases financial obligations of Part D prescription drug plans with respect to beneficiaries in the catastrophic coverage phase. This may incentivize Part D prescription drug plans to seek greater price concessions from us in order to include NERLYNX on their formularies.

More recently, the One Big Beautiful Bill Act, which was enacted in July 2025, imposes significant reductions in the funding of the Medicaid program. Such reductions are expected to decrease the number of persons enrolled in Medicaid and reduce the services covered by Medicaid, which could adversely affect our sales of NERLYNX and any other product candidate that we commercialize.

The Trump administration is pursuing a two-fold strategy to reduce drug costs in the United States. While it is unclear whether and how the Trump proposals will be implemented, the Trump policies are likely to have a negative impact on the pharmaceutical industry and on our ability to receive adequate revenues for our products. On the one hand, President Trump has threatened to impose significant tariffs on pharmaceutical manufacturers that do not adopt pricing policies such as most favored nation pricing, which would tie the price for drugs in the United States to the lowest price in a group of other countries. In response, multiple manufacturers have entered into confidential pricing agreements with the federal government. On the other hand, the Trump administration is pursuing traditional regulatory pathways to impose drug pricing policies and published two proposed regulations in December 2025, referred to as Globe and Guard. If finalized, these regulations would implement mandatory payment models under which manufacturers of eligible drugs would be required to pay rebates to the federal government on a portion of the units of their drugs that are reimbursed by Medicare, with the rebate amount based on most favored nation pricing. Imposing a rebate in the United States that is based on drug prices outside the United States would mark a drastic and unprecedented shift in the U.S. pharmaceutical market, and while the impact of the Globe and Guard proposed regulations, if finalized, cannot yet be determined, it is likely to be significant. Even regulatory proposals or executive actions that are ultimately deemed unlawful could negatively impact the U.S. pharmaceutical sector and our business.

In addition, the cost of prescription pharmaceuticals in the United States has also been the subject of considerable discussion. There have been several Congressional inquiries, as well as legislative and regulatory initiatives and executive orders 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 drug products. We cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

Moreover, individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure, drug price reporting and other transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states, and at least one state board is imposing an upper payment limit. States are also seeking to implement general, across the board price caps for pharmaceuticals, or are seeking to regulate drug distribution. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs.

We anticipate that other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product and drug candidates, if approved.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize NERLYNX and our other drug candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect our ability to commercialize NERLYNX and our other drug candidates, if approved. In other international markets outside the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment ("HTA") amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product, i.e. oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030. This Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or outside the United States. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, NERLYNX or any future approved product may lose any regulatory approval that may have been obtained and we may not sustain profitability.

Failure to obtain or maintain adequate coverage and reimbursement for our products or drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Successful commercial sales of any approved products will depend on the availability of adequate coverage and reimbursement from government health administration authorities, private health insurers and other third-party payors. Each third-party payor separately decides which products it will cover and establishes the reimbursement level, and there is no guarantee that any of our approved products or drug candidates that may be approved for marketing by regulatory authorities will receive adequate coverage or reimbursement levels. Obtaining and maintaining coverage approval for a product is time-consuming, costly and may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of coverage and reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or limited, we may not be able to successfully commercialize any product or drug candidate for which we obtain marketing approval. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs and biologics. Even if we obtain coverage for a given product, the resulting reimbursement rates may be inadequate and may affect the demand for, or the price of, any drug candidate for which we obtain marketing approval.

We expect to experience pricing pressures in connection with the sale of our current or future commercial products, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. There may be additional pressure by payors and healthcare providers to use generic drugs that contain the active ingredients found in neratinib or any other drug candidates that we may develop. If we fail to successfully secure and maintain adequate coverage and reimbursement for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and expected revenue and profitability which would have a material adverse effect on our business, results of operations and financial condition.

We are subject to federal, state and foreign healthcare fraud and abuse laws, false claims laws and physician payment transparency laws. Failure to comply with these laws may subject us to substantial penalties.

We do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors. However, federal, state and foreign healthcare laws and regulations pertaining to fraud and abuse and physician payment transparency laws and regulations apply to us depending on programs we operate and have been asserted by the government and others to apply to companies like us, and our arrangements with healthcare providers, customers and other entities, including our marketing practices, educational programs and pricing policies. These laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation;

- federal false claims laws, including, without limitation, the False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other federal third-party payors that are false or fraudulent, such as engaging in improper promotion of products or submitting inaccurate price reports to the Medicaid Drug Rebate program. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the federal Civil Monetary Penalties law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;

- federal criminal laws that prohibit executing a scheme to defraud any federal healthcare benefit program or making false statements relating to healthcare matters; 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;

- the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS, information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners (manufacturers are required to submit reports to CMS by the 90th day of each calendar year);

- analogous state equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; and

- European and other foreign law equivalents of each of these laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom recommend, purchase and/or prescribe our products, and the manner in which we promote our products, could be subject to challenge under one or more of such laws.

We are also exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, distributors and agents may engage in fraudulent or other illegal activity. While we have policies and procedures in place prohibiting such activity, misconduct by these parties could include, among other infractions or violations, intentional, reckless and/or negligent conduct or unauthorized activity that violates FDA or foreign regulatory authority requirements, including those laws that require the reporting of true, complete and accurate information to the FDA or foreign regulatory authorities, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, laws that require the true, complete and accurate reporting of financial information or data or other commercial or regulatory laws or requirements. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

If our operations are found to violate any of the laws described above or any other laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment of officers involved, any of which could adversely affect our ability to market our current and any future products, once approved, and materially adversely affect our business, results of operations and financial condition. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

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

We participate in the Medicaid Drug Rebate Program ("MDRP") and other federal and state government pricing programs in the United States, 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 in connection with drugs, including NERLYNX, that are dispensed to beneficiaries of these programs. As a condition of having federal funds being made available for our covered outpatient drugs under Medicaid and Medicare Part B, we have enrolled in the MDRP, which requires us to pay a rebate to state Medicaid programs for each unit of our covered outpatient drugs dispensed to a Medicaid beneficiary and paid for by a state Medicaid program. Medicaid drug rebates are based on

pricing data that we must report on a monthly and quarterly basis to the CMS, the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the average manufacturer price ("AMP") for each drug and, in the case of our innovator products, the best price. If we become aware that our MDRP price reporting submission for a prior period was incorrect or has changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. In addition, there is increased focus by the Office of Inspector General within the U.S. Department of Health and Human Services on the methodologies used by manufacturers to calculate AMP, and BP, to assess manufacturer compliance with MDRP reporting requirements. If we fail to provide information timely or are found to have knowingly submitted false information to the government, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP, which would result in payment not being available for our covered outpatient drugs under Medicaid or, if applicable, Medicare Part B. 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.

Federal law requires that a manufacturer that participates in the MDRP also participate in the Public Health Service's 340B drug pricing program (the "340B program") in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. We participate in the 340B program, which is administered by the Health Resources and Services Administration ("HRSA") and requires us to charge statutorily defined covered entities no more than the 340B "ceiling price" for our covered outpatient drugs used in an outpatient setting. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized a revised regulation implementing an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs.

In order to be eligible to have drug products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we also must participate in the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. Under the VA/FSS program, we must report the Non-Federal Average Manufacturer Price ("Non-FAMP") for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). We must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If we fail to provide timely information or are found to have knowingly submitted false information, we may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information. If we are found to have violated state law requirements, we may become subject to penalties or other enforcement mechanisms, which could have a material adverse effect on our business.

Pricing and rebate calculations are complex, vary among products and programs, and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. The terms, scope and complexity of these government pricing programs change frequently, as do interpretations of applicable requirements for pricing and rebate calculations. Responding to current and future changes may increase our costs and the complexity of compliance will be time consuming. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. Price recalculations under the MDRP also may affect the ceiling price at which we are required to offer products under the 340B program. Pursuant to the IRA, the AMP figures we report to the MDRP will also be used to compute rebates under Medicare Part D triggered by price increases that outpace inflation. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. In the event that CMS were to terminate our Medicaid rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs. We cannot assure you that our submissions will not be found to be incomplete or incorrect.

Risks Related to Third Parties

We are dependent on international third-party sub-licensees for the development and commercialization of NERLYNX in several countries outside the United States. The failure of these sub-licensees to meet their contractual, regulatory or other obligations could adversely affect our business.

We have entered into exclusive sub-license agreements with several third parties that provide these sub-licensees exclusive rights to the development and commercialization of NERLYNX in Europe (excluding Ukraine), Australia, Canada, China, Southeast Asia, Israel, South Korea, Russia and various countries and territories in Central America, South America, Africa and the Middle East. As a result, we are entirely dependent on these parties to achieve regulatory approval of NERLYNX for marketing in these countries and for the commercialization of NERLYNX, if approved. For the years ended December 31, 2025, 2024 and 2023, royalty revenue from these sub-licensees was $24.3 million, $35.3 million and $32.5 million, respectively, and represented 11%, 15% and 14% of total revenue, respectively. The timing and amount of any milestone and royalty payments we may receive under these agreements, as well as the commercial success of NERLYNX in those regions outside of the United States, will depend on, among other things, the efforts, allocation of resources and successful commercialization of NERLYNX by the licensees. We also depend on these third parties to comply with all applicable laws relative to the development and commercialization of our products in those countries. We do not control the individual efforts of these licensees and have limited ability to terminate these agreements if the licensees do not perform as anticipated. The failure of these licensees to devote sufficient time and effort to the development and commercialization of NERLYNX; to meet their obligations to us, including for future royalty and milestone payments; to adequately deploy business continuity plans in the event of a crisis; and/or to satisfactorily resolve significant disagreements with us or address other factors could have an adverse impact on our financial results and operations. In addition, if these third parties violate, or are alleged to have violated, any laws or regulations during the performance of their obligations for us, it is possible that we could suffer financial and reputational harm or other negative outcomes, including possible legal consequences.

Any termination, breach or expiration of any of these sub-license agreements could have a material adverse effect on our financial position by reducing or eliminating the potential for us to receive license fees, milestones and royalties. In such an event, we may be required to devote additional efforts and to incur additional costs associated with pursuing regulatory approval and commercialization of the applicable products and drug candidates. Alternatively, we may attempt to identify and transact with a new sub-licensee, but there can be no assurance that we would be able to identify a suitable sub-licensee or transact on terms that are favorable to us.

We have no experience in drug formulation or manufacturing and rely exclusively on third parties to formulate and manufacture NERLYNX, alisertib and our other drug candidates, and any disruption or loss of these relationships could delay our development and commercialization efforts.

We have no experience in drug formulation or manufacturing and do not intend to establish our own manufacturing facilities. We lack the resources and expertise to formulate or manufacture NERLYNX, alisertib and other potential drug candidates. While our drug candidates were developed by Pfizer and Takeda, both the drug substance and drug product are manufactured by third-party contractors. We are using the same third-party contractors to manufacture, supply, store and distribute drug supplies for our clinical trials and the commercialization of NERLYNX and we plan to use third-party contractors to manufacture, supply, store and distribute drug supplies for our clinical trials of alisertib. If we are unable to continue our relationships with one or more of these third-party contractors, we could experience delays in our development or commercialization efforts as we locate and qualify new manufacturers. We intend to rely on one or more third-party

contractors to manufacture the commercial supply of our drugs. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited, and the FDA or foreign regulatory authorities must approve any replacement manufacturer with respect to NERLYNX and any other approved products. This approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA or comparable foreign regulatory authority approval.

- Our third-party manufacturers might be unable to formulate and manufacture our products and drug candidates in the volume and of the quality required to meet our clinical and/or commercial needs.

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

- The facilities used by our contract manufacturers to manufacture NERLYNX, alisertib and our other drug candidates must be approved for the manufacture of such products or candidates by the FDA or foreign regulatory authorities pursuant to inspections that are conducted following submission of an NDA to the FDA or pursuant to similar foreign applications to foreign regulatory authorities. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP or similar foreign regulations for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA and similar non-U.S. regulatory agencies and corresponding state agencies to ensure strict compliance with cGMP regulations and other government regulations and corresponding foreign standards. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for alisertib and our other drug candidates, if approved, or market NERLYNX.

- If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

Each of these risks could delay our clinical trials, the approval, if any, of alisertib or our other drug candidates by the FDA or comparable foreign regulatory authorities or the commercialization of NERLYNX or result in higher costs or deprive us of potential product revenue.

If our third-party manufacturers fail to manufacture NERLYNX in sufficient quantities and at acceptable quality and pricing levels, or fail to fully comply with cGMP or similar foreign regulations, we may face delays in commercialization or be unable to meet market demand, and may lose potential revenues.

The manufacture of NERLYNX requires significant expertise and capital investment, including the development of advanced manufacturing techniques, process controls and the use of specialized processing equipment. Our third-party manufacturers must comply with federal, state and foreign regulations, including the FDA's regulations governing cGMP and similar requirements outside the United States, enforced by the FDA through its facilities inspection program and by similar foreign regulatory authorities in other jurisdictions where we do business. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The FDA or similar foreign regulatory authorities at any time may implement new standards or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of our products. Any failure by us or our third-party manufacturers to comply with applicable regulations may result in fines and civil penalties, suspension of production, product seizure or recall, operating restrictions, imposition of a consent decree, modification or withdrawal of product approval or criminal prosecution and would limit the availability of our product. Any manufacturing defect or error discovered after products have been produced and distributed also could result in significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation and potential for product liability claims.

If our third-party manufacturers are unable to produce the required commercial quantities of NERLYNX to meet market demand for NERLYNX on a timely basis or at all, or if they fail to comply with applicable laws for the manufacturing of NERLYNX, we will suffer damage to our reputation and commercial prospects and we will lose potential revenue.

We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for our drug candidates.

We depend upon independent investigators and collaborators, such as CROs, universities and medical institutions, to conduct our pre-clinical studies and clinical trials, including those involving neratinib and alisertib, under agreements with us. These collaborators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with regulatory requirements, including GCP requirements, and the applicable protocol. If we, or any of our CROs or third party contractors, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current cGMP or similar foreign regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would cause us to incur additional costs and delay the regulatory approval process. Moreover, third party contractors and investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug-development programs, or if their performance is substandard or otherwise fails to satisfy applicable regulatory requirements, the approval of our FDA or foreign applications, if any, and our introduction of new drugs, if any, will be delayed. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators assist our competitors to our detriment, our competitive position would be harmed. If any of our relationships with these third-party collaborators terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding additional third parties to our clinical trial programs can involve substantial costs and require extensive management time and focus.

Risks Related to our Business Operations

Engaging in international business subjects us to additional business and regulatory risks, and there can be no assurance that our products will be accepted in those markets.

We have entered into exclusive sub-license agreements providing for third parties to pursue regulatory approval and commercialize NERLYNX, if approved, in various specified regions outside of the United States. We plan to continue to pursue commercialization of NERLYNX in additional countries outside the United States where it has been approved. Engaging in international business inherently involves a number of difficulties and risks, including:

- competition from established companies, many of which are well-positioned within their local markets with longer operating histories, more recognizable names and better established distribution networks;
- the availability and level of coverage and reimbursement within prevailing foreign healthcare payment systems and the ability of patients to elect to privately pay for NERLYNX and, if approved, alisertib and our other products;
- difficulties in enforcing intellectual property rights;
- pricing pressure;
- required compliance with existing and changing foreign regulatory requirements and laws;
- laws and business practices favoring local companies;
- longer sales and payment cycles;

- difficulties in enforcing agreements and collecting receivables through certain foreign legal systems;
- political and economic instability, including trade wars, the military conflicts between Russia and Ukraine, the conflicts between Israel and Hamas, recent inflation and disruptions in the capital and credit markets that may reduce our ability to raise additional capital when needed on acceptable terms, if at all;
- foreign currency risks that could adversely affect our financial results;
- potentially adverse tax consequences, tariffs and other trade barriers;
- exposure to liabilities under anti-corruption and anti-money laundering laws, including the U.S. Foreign Corrupt Practices Act ("FCPA"), and similar laws and regulations in other jurisdictions;
- international terrorism and anti-American sentiment;
- difficulties and costs associated with staffing and managing foreign operations; and
- export restrictions and controls relating to technology.

If we or our sub-licensees or third-party manufacturers are unable to address these international risks, we may fail to establish and maintain an international presence, and our business, financial condition and results of operations would suffer.

The failure to comply with anti-bribery, anti-corruption, and anti-money laundering laws, including the FCPA and similar laws associated with our activities outside of the United States, could subject us to penalties and other adverse consequences.

We are subject to the FCPA, regulations of the U.S. Office of Foreign Assets Control, the United Kingdom Bribery Act of 2010 and other anti-corruption, anti-bribery and anti-money laundering laws around the world where we conduct activities, including, if approved in such countries, the sale of our products. We face significant risks and liability if we fail to comply with the FCPA and other anti-corruption and anti-bribery laws that prohibit companies and their employees and third-party business partners, such as distributors or resellers, from authorizing, offering or providing, directly or indirectly, improper payments or benefits to foreign government officials, political parties or candidates, employees of public international organizations including healthcare professionals, or private-sector recipients for the corrupt purpose of obtaining or retaining business, directing business to any person, or securing any advantage. We currently rely on various third parties for certain services outside the United States, including continued development of our drug candidates and, if approved, its subsequent commercialization. We may be held liable for the corrupt or other illegal activities of these third parties and intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize such activities.

Any violation of the FCPA, other applicable anti-bribery, anti-corruption laws, and anti-money laundering laws could result in whistleblower, adverse media coverage, investigations, loss of export privileges, severe criminal or civil sanctions and, in the case of the FCPA, suspension or debarment from U.S. government contracts, which could have a material and adverse effect on our reputation, business, operating results and prospects. In addition, responding to any enforcement action or related investigation may result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees.

If we fail to comply with United States export control and economic sanctions or fail to expand and maintain an effective sales force or successfully develop our international distribution network, our business, financial condition and operating results may be adversely affected.

When selling any products outside of the United States, including NERLYNX, we are subject to United States export control and economic sanctions laws, the violation of which could result in substantial penalties being imposed against us. More broadly, if we fail to comply with export control laws, any sales could fail to grow or could decline, and our ability to grow our business could be adversely affected.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm us.

We rely on computer systems, hardware, software, technology infrastructure and online sites and networks for both internal and external operations that are critical to our business. We own and manage some of these information technology systems but also rely on third parties for a range of information technology systems and related products and services. We and certain of our third-party providers collect, maintain and process data about customers, employees, business partners and others, including personally identifiable information, as well as proprietary information belonging to our business such as trade secrets. Our information technology systems and those of third parties with which we contract may be vulnerable to damage from diverse threat vectors, including cyberattacks, "phishing" attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, computer viruses, malware (e.g. ransomware), sophisticated nation-state and nation-state-supported actors, unauthorized access or use by persons inside our organization or persons with access to systems inside our organization, hacking, natural disasters, terrorism, war and telecommunication and electrical failures despite the implementation of security measures. We are also vulnerable to other cybersecurity risks and threats, including malicious code embedded in open-source software, or misconfigurations, "bugs" or other vulnerabilities in commercial software that is integrated into our (or our suppliers' or service providers') information technology systems, products or services. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. We may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques – including artificial intelligence – that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. System failures, accidents or security breaches could cause interruptions in our operations and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, any integration of artificial intelligence in our or any third party's operations, products or services is expected to pose new or unknown cybersecurity risks and challenges. 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 confidential or proprietary information, we could incur liability and our research and development programs, and the development of our drug candidates could be delayed.

If we or our third-party vendors were to experience a significant cybersecurity breach of our or their information systems or data, the costs associated with the investigation, remediation and potential notification of the breach to counterparties and data subjects could be material. In addition, our remediation efforts may not be successful. There can also be no assurance that our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully implemented, complied with or effective in protecting our information technology systems and confidential information. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents that threaten the confidentiality, integrity and availability of our information technology systems and confidential information. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss, corruption or unauthorized disclosure of our trade secrets, personal information or other proprietary or sensitive information or other similar disruptions. It could also expose us to risks, including an inability to provide our services and fulfill contractual demands, and could cause management distraction and the obligation to devote significant financial and other resources to mitigate such problems, which would increase our future information security costs, including through organizational changes, deploying additional personnel, reinforcing administrative, physical and technical safeguards, further training of employees, changing third-party vendor control practices and engaging third-party subject matter experts and consultants and reduce the demand for our technology and services.

If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of personal information, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media and other parties pursuant to privacy and security laws. Any security compromise affecting us, our service providers, strategic partners, other contractors, consultants, or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures and lead to regulatory scrutiny. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary or personal information, we could incur liability, such as litigation exposure (including class actions), penalties and fines, we could become the subject of regulatory action or investigation, our competitive position could be harmed and the further development and commercialization of our products and services could be delayed. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business. Furthermore, federal, state and international laws and regulations can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties, fines and significant legal liability, if our information technology security efforts fail. We may also be exposed to a risk of loss or litigation and potential liability, which could materially and adversely affect our business, results of operations or financial condition. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

Compliance with governmental regulation and other legal obligations related to privacy, data protection and information security could result in additional costs and liabilities to us or inhibit our ability to collect and process data, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

Privacy and data security have become significant issues in the United States, Europe and in many other jurisdictions where we may in the future conduct our operations. As we receive, collect, process, use and store personal and confidential data, we are subject to diverse laws and regulations relating to data privacy and security. In the United States, numerous federal and state laws and regulations could apply to our operations or the operations of our partners, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e.g. Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

A number of U.S. states have also enacted data privacy and security laws and regulations, which govern the privacy, processing and protection of health-related and other personal information. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act (collectively, the "CCPA") requires covered businesses that process the personal information of California residents to, among other things: (i) provide certain disclosures to California residents regarding the business's collection, use, and disclosure of their personal information; (ii) receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information; and (iii) enter into specific contractual provisions with service providers that process California residents` personal information on the business's behalf. Further, Washington State enacted a broadly applicable law to protect the privacy of personal health information known as the "My Health My Data Act," which generally requires affirmative consent for the collection, use, or sharing of any "consumer health data." Consumer health data is defined to include 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 status; consumer health data also includes information that is derived or extrapolated from non-health information, such as algorithms and machine learning. Other states, including Connecticut and Nevada, have also passed consumer health data laws and given the increased focus on the use of health data by entities that are not subject to HIPAA, additional states are expected to pass consumer health privacy laws. Additional compliance investment and potential business process changes may also be required. Similar laws have been passed in other states, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. Compliance with these privacy and data security requirements is rigorous and time-intensive and may increase our cost of doing business; despite those efforts, there is a risk that we may be subject to fines and penalties, litigation and reputational harm, which could materially and adversely affect our business, financial condition and results of operations.

Furthermore, the FTC also has authority to initiate enforcement actions against entities that mislead customers about HIPAA compliance, make deceptive statements about privacy and data sharing in privacy policies, fail to limit third-party use of personal health information, fail to implement policies to protect personal health information or engage in other unfair practices that harm customers or that may violate Section 5 of the FTC Act. Even when HIPAA does not apply, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Additionally, federal and state consumer protection laws are increasingly being applied by the FTC and states' attorneys general to regulate the collection, use, storage, and disclosure of personal or personally identifiable information, through websites or otherwise, and to regulate the presentation of website content.

In addition, the regulatory framework for the receipt, collection, processing, use, safeguarding, sharing and transfer of personal and confidential data is rapidly evolving and is likely to remain uncertain for the foreseeable future as new global privacy rules are being enacted and existing ones are being updated and strengthened. For example, we may be subject to the EU General Data Protection Regulation ("EU GDPR") and to the United Kingdom General Data Protection Regulation and Data Protection Act 2018 (collectively, the "UK GDPR") (the EU GDPR and UK GDPR together referred to as the "GDPR"). The GDPR is directly applicable in each EU and EEA member state and the UK and applies to companies established in the EU and the EEA or UK as well as companies that collect and use personal data to offer goods or services to, or monitor the behavior of, individuals in the EU and the EEA or UK. The GDPR imposes stringent data protection obligations for processors and controllers of personal data, and penalties and fines for failure to comply with GDPR are significant, including fines of up to €20 million / £17.5 million or 4% of total worldwide annual turnover, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EEA and the United States remains uncertain. Case law from the Court of Justice of the European Union ("CJEU") states that reliance on the standard contractual clauses – a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As the regulatory guidance and enforcement landscape in relation to data transfers continue to develop, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we operate our business, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenue and our business will suffer.

The market for our drugs and drug candidates is characterized by intense competition and rapid technological advances. NERLYNX competes, and alisertib and any of our other drug candidates that receives FDA or foreign regulatory approval will compete, with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products or may offer comparable performance at a lower cost. In addition, a large number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. If our products fail to capture and maintain market share, we may not achieve sufficient product revenue and our business will suffer.

We compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have oncology compounds that have already been approved or are in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in the following:

- developing drugs;
- undertaking pre-clinical testing and clinical trials;
- obtaining FDA and other foreign regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

We may be exposed to liability claims associated with the use of hazardous materials and chemicals.

Our research and development activities may involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations.

The loss of one or more key members of our management team could adversely affect our business.

Our success and future growth depend, to a significant degree, on the skills and continued services of our management team, in particular Alan H. Auerbach, our Chief Executive Officer and President. If Mr. Auerbach resigns or becomes unable to continue in his present role and is not adequately replaced, our business operations could be materially adversely affected. We do not maintain "key man" life insurance for Mr. Auerbach.

If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed

As of December 31, 2025, we had 179 employees. Our future success depends on our ability to identify, attract, hire, train, retain and motivate other highly skilled scientific, technical, marketing, managerial and financial personnel. Although we will seek to hire and retain qualified personnel with experience and abilities commensurate with our needs, there is no assurance that we will succeed despite their collective efforts. Competition for personnel is intense, and any failure to attract and retain the necessary technical, marketing, managerial and financial personnel would have a material adverse effect on our business, prospects, financial condition and results of operations.

We may not successfully manage our growth.

Our success will depend upon the expansion of our operations and our ability to successfully manage our growth. Our future growth, if any, may place a significant strain on our management and on our administrative, operational and financial resources. Our ability to manage our growth effectively will require us to implement and improve our operational, financial and management systems and to expand, train, manage and motivate our employees. These demands may require the hiring of additional management personnel and the development of additional expertise by management. Any increase in resources devoted to research and product development without a corresponding increase in our operational, financial and management systems could have a material adverse effect on our business, financial condition and results of operations.

We may be adversely affected by the current economic environment.

Our ability to attract and retain collaborators or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States and inflationary pressures, or the threat or imposition of substantial tariffs on imports from various countries, including China, Canada and Mexico. We cannot anticipate all the ways in which the current economic climate and financial market conditions could adversely impact our business.

We are exposed to risks associated with reduced profitability and the potential financial instability of our collaborators or customers, many of which may be adversely affected by volatile conditions in the financial markets. For example, unemployment and underemployment, and the resultant loss of insurance, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, our collaboration partners or customers may experience reductions in revenues, profitability and/or cash flow that could lead them to modify, delay or cancel orders for our products once commercialized. If collaboration partners or customers are not successful in generating sufficient revenue or are precluded from securing financing, they may not be able to pay, or may delay payment of, accounts receivable that are owed to us. This, in turn, could adversely affect our financial condition and liquidity. In addition, if economic challenges in the United States result in widespread and prolonged unemployment, either regionally or on a national basis, a substantial number of people may become uninsured or underinsured. To the extent economic challenges result in fewer individuals pursuing or being able to afford our products once commercialized, our business, results of operations, financial condition and cash flows could be adversely affected.

We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits and product recalls.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. If we are unable to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, the commercialization of pharmaceutical products we develop, alone or with collaborators, could be prevented or inhibited.

Product recalls may be issued at our discretion, or at the discretion of government agencies and other entities that have regulatory authority for pharmaceutical sales. Any recall of NERLYNX could materially adversely affect our business by rendering us unable to sell NERLYNX for some time and by adversely affecting our reputation.

We may in the future engage in strategic transactions that increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We actively evaluate various strategic transactions on an ongoing basis, including licensing or otherwise acquiring complementary products, technologies or businesses. Any potential future acquisitions or in-licensing transactions entail numerous risks, including but not limited to:

- risks associated with satisfying the closing conditions relating to such transactions and realizing their anticipated benefits;
- increased operating expenses and cash requirements;
- difficulty integrating acquired technologies, products, operations, and personnel with our existing business;
- the potential disruption of our historical core business;
- diversion of management’s attention in connection with both negotiating the acquisition or license and integrating the business, technology or product;
- retention of key employees;

- difficulties in assimilating employees and corporate cultures of any acquired companies;
- uncertainties in our ability to maintain key business relationships of any acquired companies;
- strain on managerial and operational resources;
- difficulty implementing and maintaining effective internal control over financial reporting at businesses that we acquire, particularly if they are not located near our existing operations;
- exposure to unanticipated liabilities of acquired companies or companies in which we invest;
- the potential need to write down assets or recognize impairment charges; and
- potential costly and time-consuming litigation, including stockholder lawsuits.

As a result of these or other problems and risks, businesses, technologies or products we acquire or invest in or obtain licenses to may not produce the revenues, earnings or business synergies that we anticipated, acquired or licensed drug candidates or technologies may not result in regulatory approvals, and acquired or licensed products may not perform as expected. As a result, we may incur higher costs and realize lower revenues than we had anticipated. We cannot assure you that any acquisitions or investments we have made or may make in the future will be completed or that, if completed, the acquired business, licenses, investments, products, or technologies will generate sufficient revenue to offset the negative costs or other negative effects on our business. Failure to effectively manage our growth through acquisition or in-licensing transactions could adversely affect our growth prospects, business, results of operations, financial condition, and cash flow.

In addition, we may spend significant amounts of funds, issue dilutive securities, assume or incur significant debt obligations, incur large one-time expenses and acquire intangible assets or goodwill in connection with acquisitions and in-licensing transactions that could result in significant future amortization expense and write-offs. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business. Other pharmaceutical companies, many of which may have substantially greater financial, marketing and sales resources, compete with us for these opportunities. Even if appropriate opportunities are available, we may not be able to successfully identify them or we may not have the financial resources necessary to pursue them, and if pursued, we may be unable to structure and execute transactions in the anticipated timeframe, or at all.

Risks Related to our Intellectual Property

We depend significantly on in-licensed intellectual property, and the termination of these licenses would significantly harm our business and future prospects.

We depend significantly on our license agreements with Pfizer and Takeda, respectively. Each of these license agreements may be terminated if we materially breach the agreement and fail to cure our breach during an applicable cure period. Our failure to use commercially reasonable efforts to develop and commercialize licensed products in applicable specified major market countries would constitute a material breach of the applicable license agreement. The applicable license agreement may also be terminated if we become involved in bankruptcy, receivership, insolvency or similar proceedings. In the event either license agreement is terminated, we will lose all of our rights to develop and commercialize the drug candidates covered by such license, which would significantly harm our business and future prospects.

Our proprietary rights may not adequately protect our intellectual property and potential products, and if we cannot obtain adequate protection of our intellectual property and potential products, we may not be able to successfully market our potential products.

Our commercial success will depend in part on obtaining and maintaining intellectual property protection for our products, formulations, processes, methods and other technologies. We will only be able to protect these technologies and products from unauthorized use by third parties to the extent that valid and enforceable intellectual property rights, including patents, cover them, or other market exclusionary rights and regulatory exclusivity periods apply. The patent positions of pharmaceutical companies, like ours, can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States. The general environment for pharmaceutical patents

outside the United States also involves significant uncertainty. Accordingly, we cannot predict the breadth of claims that may be allowed (if any are allowed at all) or enforced, or that the scope of these patent rights could provide a sufficient degree of future protection that could permit us to gain or keep our competitive advantage with respect to these products and technology. For example, we cannot predict:

- the degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to make, use, sell, offer to sell or import competitive products without infringing our patents;
- if and when patents will issue;
- whether or not others will obtain patents claiming inventions similar to those covered by our patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings in connection with patent rights, which may be costly whether we win or lose, and the outcome of which is unpredictable.

The patents we have licensed may be challenged by third parties and could be invalidated or rendered unenforceable. There is no guarantee that a court would agree that any of the patents we have licensed, and which are currently in force, are valid or enforceable. Challenges to the breadth or strength of protection provided by any patents we have licensed, or patent applications we may pursue in the future, with respect to any of our current or future drug candidates or products, could threaten our ability to commercialize any of our current or future drug candidates or products. Changes in either the patent laws or in the interpretations of patent laws in the United States or other countries may diminish the value of our intellectual property.

The patents we have licensed may be affected by certain provisions of the America Invents Act ("AIA"), enacted in 2011. For example, under the AIA, members of the public may seek to challenge an issued patent by petitioning the U.S. Patent and Trademark Office ("USPTO") to institute a post grant proceeding, such as a Post Grant Review ("PGR"), or Inter Parties Review ("IPR"). Once a post grant proceeding is instituted, the USPTO may find grounds to revoke the challenged patent or specific claims therein. A similar procedure (known as a patent opposition) has existed in Europe for many years, and we have defended, and continue to defend, our European patents in certain of those proceedings. We cannot predict whether any other licensed patents will become the subject of a post grant proceeding or patent opposition. If a significant product patent is successfully challenged in a post grant proceeding or patent opposition, it may be revoked, which would have a serious negative impact on our ability to maintain exclusivity in the marketplace for our commercial products affected by such revocation and could adversely affect our future revenues and profitability.

In addition, others may independently develop similar or alternative products and technologies that may be outside the scope of our intellectual property. Furthermore, others may have invented technology claimed by our patents before we or our licensors did so, and they may have filed patents claiming such technology before we did so, weakening our ability to obtain and maintain patent protection for such technology. Should third parties obtain patent rights to similar products or technology, this may have an adverse effect on our business.

We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. Trade secrets, however, are difficult to protect. While we believe that we will use reasonable efforts to protect our trade secrets, our own or our strategic partners' employees, consultants, contractors or advisors may unintentionally or willfully disclose our information to competitors. Such disclosure could adversely affect our ability to prevent further disclosures of our trade secrets. We seek to protect this information, in part, through the use of non-disclosure and confidentiality agreements with employees, consultants, advisors and others. These agreements may be breached, and we may not have adequate remedies for a breach. In addition, we cannot ensure that those agreements will be enforceable, provide adequate protection for our trade secrets, know-how or other proprietary information, or prevent their unauthorized use or disclosure.

To the extent that consultants or key employees apply technological information independently developed by them or by others to our potential products, disputes may arise as to the proprietary rights in such information, which may not be resolved in our favor. Consultants and key employees who work with our confidential and proprietary technologies are required to assign all intellectual property rights in their discoveries to us. However, these consultants or key employees may terminate their relationship with us, and we cannot preclude them indefinitely from dealing with our competitors. If our trade secrets become known to competitors with greater experience and financial resources, the competitors may copy or use our trade secrets and other proprietary information in the advancement of their products, methods or technologies. If

we were to prosecute a claim that a third party had illegally obtained and was using our trade secrets, it could be expensive and time consuming and the outcome could be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets than courts in the United States. Moreover, if our competitors independently develop equivalent knowledge, we would lack any legal or contractual claim to prevent them from using such information, and our business could be harmed.

Additionally, our products may face generic or biosimilar competition before patent exclusivity expires in various jurisdictions. To date, we have been involved in litigation in the United States against the one ANDA applicant that submitted a Paragraph IV certification directed to our patents (Sandoz), and also in China against parties that filed applications and/or received approval for generic versions of NERLYNX. In order to eliminate the burden, expense, distraction and uncertainties of litigation, we entered a settlement and license agreement in 2022 that would permit Sandoz to begin selling a generic version of neratinib in the United States on or around December 8, 2030.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending our intellectual property rights in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. For instance, some jurisdictions, such as China and India, do not consider methods of treating the human body as patentable. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our intellectual property rights or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our proprietary rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our proprietary rights at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Certain fees, including maintenance, renewal, annuity, and other governmental fees, on patents and/or applications are periodically due to be paid to the USPTO and various foreign governmental patent agencies at certain stages over the lifetime of the patents and/or applications. We have systems in place and employ third-party firms to monitor due dates and pay these fees. We also employ law firms and other reputable professionals to assist us in the event an inadvertent lapse can be cured by payment of a late fee or by other means according to the applicable jurisdictional laws and rules. Non-compliance, in certain circumstances, can result in abandonment or lapse of the patent (or patent application) and result in a partial or even complete loss of patent rights in the particular jurisdiction. Our competitors might be able to enter the market under such circumstances, resulting in a possible material adverse effect on our business.

Our ability to commercialize our products will depend on our ability to sell such products without infringing the patent or proprietary rights of third parties. If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our ability to commercialize our products will depend on our ability to sell such products without infringing the patents or other proprietary rights of third parties. Third-party intellectual property rights in our field are complicated and continuously evolving. The coverage of patents is subject to interpretation by the courts, and this interpretation is not always consistent.

Other companies may have or may acquire intellectual property rights that could be enforced against us. If they do so, we may be required to alter our products, formulations, processes, methods or other technologies, obtain a license, assuming one can be obtained, or cease our product-related activities. Holders of such intellectual property rights are not required to give us a license if one were required. If our products or technologies infringe the intellectual property rights of others, such parties could bring legal action against us or our licensors or collaborators claiming damages and seeking to enjoin any activities that they believe infringe their intellectual property rights. If we are sued for patent infringement, we would need to demonstrate that our products or methods of use either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving the invalidity of a patent is particularly difficult in the United States, since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third-party patent, we may need to cease the commercial sale of our products.

Because patent applications can take many years to issue, there may be currently pending applications unknown to us or reissue applications that may later result in issued patents upon which our products or technologies may infringe. There could also be existing patents of which we are unaware that our products or technologies may infringe. In addition, if third parties file patent applications or obtain patents claiming products or technologies also claimed by us in pending applications or issued patents, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. If third parties file IPR or PGR petitions in the USPTO to invalidate our issued U.S. patents, we may have to participate in such proceedings to defend such patents. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our filed foreign patent applications. The outcome of such proceedings in the United States and foreign countries is unpredictable. Some of our competitors may be able to sustain the costs of such proceedings and of complex patent litigation more effectively than we can because they have substantially greater resources. Additionally, any uncertainties resulting from the initiation and continuation of any such proceedings or litigation may have a material adverse effect on our ability to raise the funds necessary to continue our operations.

If a third-party claims that we infringe its intellectual property rights, it could cause our business to suffer in a number of ways, including:

- we may become involved in time-consuming and expensive litigation, even if the claim is without merit, the third party's patent is ultimately invalid or unenforceable, or we are ultimately found to have not infringed;
- we may become liable for substantial damages for past infringement if a court decides that our technologies infringe upon a third party's patent;
- we may be ordered by a court to stop making, using, selling, offering for sale, importing or licensing our products or technologies without a license from a patent holder, and such license may not be available on commercially acceptable terms, if at all, or may require us to pay substantial royalties or grant cross-licenses to our patents; and
- we may have to redesign our products so that they do not infringe upon others' patent rights, which may not be possible or could require substantial investment and/or time.

If any of these events occur, our business could suffer, and the market price of our common stock may decline.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other companies in these industries, including our competitors or potential competitors. We may become subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, although no such claims are pending. Litigation may be necessary to defend against these claims. Even if we successfully defend any such claims, we may incur substantial costs in such defense, and our management may be distracted by these claims.

Risks Related to Owning our Common Stock

The price of our common stock could be subject to volatility related or unrelated to our operations.

The trading price of our common stock has been highly volatile and could continue to be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

- the level of sales of NERLYNX;
- the overall demand for NERLYNX, including the customer ordering and discontinuation patterns;
- actual or anticipated quarterly variation in our results of operations or the results of our competitors;
- announcements regarding results of any clinical trials relating to our drug candidates;
- announcements of medical innovations or new products by our competitors;
- developments involving our sublicensees;
- issuance of new or changed securities analyst reports or recommendations for our stock;
- developments or disputes concerning our intellectual property or other proprietary rights;
- commencement of, or developments in, litigation involving us;
- market conditions in the biopharmaceutical industry;
- timing and announcement of regulatory approvals;
- changes in government regulation that affect us or the biopharmaceutical industry more generally;
- any future sales of our common stock or other securities in connection with raising additional capital or otherwise;
- any major change to the composition of our board of directors or management; and
- general economic conditions and slow or negative growth of our markets.

The stock market in general, and market prices for the securities of biotechnology companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance.

We have been subject to securities litigation in the past, and volatility in the price of our common stock may subject us to securities litigation in the future.

In the past, securities class action litigation has often been brought against a company following periods of volatility in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. These types of lawsuits are subject to inherent uncertainties, and are expensive and time-consuming to investigate, defend and resolve, and in the past, we have been a defendant in such lawsuits. Any other litigation to which we are a party may similarly divert our management's attention and financial and other resources or result in an onerous or unfavorable judgment that may not be reversed upon appeal or in payments of substantial monetary damages or fines. Additionally, we may decide to settle such lawsuits on similarly unfavorable terms, which could adversely affect our business, financial condition, results of operations or stock price.

Issuance of stock to fund our operations may dilute your investment and reduce your equity interest.

We may need to raise capital in the future to fund the development of our drug candidates or for other purposes. Any equity financing may have a significant dilutive effect to stockholders and a material decrease in our existing stockholders' equity interest in us. In November 2021, we also entered into an Open Market Sales Agreement[SM] with Jefferies LLC pursuant to which we may offer and sell shares of common stock having an aggregate offering price of up to $50.0 million from time to time, in any method that is deemed to be an "at the market" offering as defined in Rule 415(a)(4) of the Securities Act. Equity financing, if obtained, could result in substantial dilution to our existing stockholders. At its sole discretion, our board of directors may issue additional securities without seeking stockholder approval, and we do not know when we will need additional capital or, if we do, whether it will be available to us.

Upon the exercise of our outstanding warrant, holders of our common stock may experience immediate dilution and the market price of our common stock may be adversely affected.

Our founder, Chief Executive Officer and President, Alan H. Auerbach, holds a warrant for 2,116,250 shares with an exercise price of $16.00 per share. If any portion of the outstanding warrant is exercised for shares of our common stock when the market price is higher than the exercise price prior to its expiration in October 2026, our stockholders may experience immediate dilution and the market price of our common stock may be adversely affected.

We incur increased costs and demands upon management as a result of complying with the laws and regulations affecting public companies.

As a public company, we incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also incur costs associated with current corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act"), as well as rules implemented by the SEC, or NASDAQ or any stock exchange or inter-dealer quotations system on which our common stock may be listed in the future. The expenses incurred by public companies for reporting and corporate governance purposes have increased dramatically in recent years. These rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

These rules and regulations may also make it difficult and expensive for us to maintain the appropriate level of director and officer insurance for a company with our market capitalization. If we are unable to maintain an appropriate level of such insurance, we may be required to accept reduced policy limits and coverage or larger deductible limits. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as our executive officers.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.

We are subject to the rules and regulations of the SEC, including those rules and regulations mandated by the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to include in their annual report a statement of management's responsibilities for establishing and maintaining adequate internal control over financial reporting, together with an assessment of the effectiveness of those internal controls. Section 404 also requires the independent auditors of certain public companies to attest to, and report on, this management assessment. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us, and our business may be harmed.

If securities or industry analysts do not publish, or cease publishing, research reports about us, our business or our market, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock is and will be influenced by whether industry or securities analysts publish research and reports about us, our business, our market or our competitors and, if any analysts do publish such reports, what they publish in those reports. We may not obtain analyst coverage in the future. Any analysts who do cover us may make adverse recommendations regarding our stock, adversely change their recommendations from time to time, and/or provide more favorable relative recommendations about our competitors. If any analyst who may cover us in the future were to cease coverage of our company or fail to regularly publish reports on us, or if analysts fail to cover us or publish reports about us at all, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We do not foresee paying cash dividends in the foreseeable future.

We currently intend to retain any future earnings for funding growth. We do not anticipate paying any dividends in the foreseeable future, and the payment of dividends is also restricted under our Note Purchase Agreement with Athyrium. As a result, you should not rely on an investment in our securities if you require dividend income. Capital appreciation, if any, of our shares may be your sole source of gain for the foreseeable future. Moreover, you may not be able to re-sell your shares in us at or above the price you paid for them.

Our ability to use our net operating losses and research and development credit carryforwards to offset future taxable income may be subject to certain limitations.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), a corporation that undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, is subject to limitations on its ability to utilize its pre-change net operating losses ("NOLs"), and its research and development credit carryforwards to offset future taxable income. Our existing NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs and research and development credit carryforwards could be further limited by Sections 382 and 383 of the Code. Future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Sections 382 and 383 of the Code. Furthermore, our ability to utilize NOLs and research and development credit carryforwards of any companies we may acquire in the future may be subject to limitations, in accordance with Sections 382 and 383 of the Code. For these reasons, in the event we experience a change of control, we may not be able to utilize a material portion of the NOLs and research and development credit carryforwards, even if we attain profitability.

Additionally, valuation allowances needed for deferred tax assets that we estimate are more likely than not to be unusable, based on available evidence at the time the estimate is made. For the year ended December 31, 2025, we recorded a partial release of $3.8 million of our valuation allowance related to deferred tax assets, resulting in a total valuation allowance of $324.8 million as of December 31, 2025. See Note 12–Income Taxes in the notes to the financial statements included in this Annual Report for further information. The recording of any future increase in or release of all or any portion of our valuation allowance could have a material impact on our reported results and could cause fluctuations in our quarterly and annual results of operations. Moreover, potential changes in the tax law or in our projections could impact our assessment and valuation allowance estimates, which could have a material adverse effect on our business, financial condition and results of operations.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 1C. CYBERSECURITY

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity, and availability of our critical systems and information.

We design and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework ("NIST CSF"). This does not imply that we meet any particular technical standards, specifications or requirements, only that we use the NIST CSF as a guide to help us identify, assess and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program is integrated into our overall risk management program, and shares common methodologies, reporting channels and governance processes that apply across the risk management program to other legal, compliance, strategic, operational, and financial risk areas.

Key elements of our cybersecurity risk management program include, but are not limited to the following:

- risk assessments designed to help identify material cybersecurity threats to our critical systems and information;
- a management team responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls and (3) our response to cybersecurity incidents;
- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security processes;
- cybersecurity awareness training of our employees, including incident response personnel and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- a third-party risk management process for key service providers, based on our assessment of their criticality to our operations and respective risk profile.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected us, including our operations, business strategy, results of operations, or financial condition. We face risks from cybersecurity threats that, if realized, are reasonably likely to materially affect us, including our operations, business strategy, results of operations, or financial condition. See "Risk Factors – *We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm us.*"

Cybersecurity Governance

Our Board considers cybersecurity risk as part of its risk oversight function and has delegated to the Audit Committee (the "Committee") oversight of cybersecurity risks, including oversight of management's implementation of our cybersecurity risk management program.

The Committee receives periodic reports from management on our cybersecurity risks. In addition, management updates the Committee, where it deems appropriate, regarding any cybersecurity incidents it considers to be potentially significant.

The Committee reports to the full Board regarding its activities, including those related to cybersecurity. The full Board also periodically receives briefings from management on our cyber risk management program. Board members receive presentations on cybersecurity topics from internal security staff or external experts as part of the Board's continuing education on topics that impact public companies. Our management team, including our Senior Director of Information Technology and Senior Vice President, Quality Assurance, who report to the Chief Financial Officer and Chief Executive Officer, respectively, are primarily responsible for assessing and managing our material risks from cybersecurity threats. The Senior Director of Information Technology and Senior Vice President, Quality Assurance have primary responsibility for our overall cybersecurity risk management program and supervise both our internal technology and

quality assurance compliance personnel and our retained external cybersecurity consultants. Our Senior Director of Information Technology has more than 20 years of experience in IT Management, including cybersecurity, and our Senior Vice President, Quality Assurance has more than 20 years of experience in computerized system and IT infrastructure controls, compliance, and risk management.

Our management team takes steps to stay informed about and monitor efforts to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in our information technology environment.

ITEM 2. PROPERTIES

We lease approximately 65,656 square feet of office space in the building located at 10880 Wilshire Boulevard, Los Angeles, California for use as our corporate headquarters. This lease commenced in December 2011 and over time has been amended to add rentable square footage. In February 2019, we entered into a long-term sublease agreement whereby we sublease 12,429 square feet of this office space to a third party subtenant. This sublease was terminated in December 2024. Also, in August 2023, we entered into a long-term sublease agreement whereby we sublease 13,916 square feet of this office space to a third party subtenant. The rental amounts payable to us pursuant to both subleases increase approximately 3% and terminate in March 2026. In July 2025, we executed an amendment to our office space in Los Angeles, California to surrender certain suites effective March 31, 2026 and extend the lease term for the remaining 26,700 rentable square feet in suite 17 for an additional five years and five months through August 31, 2031. We also lease approximately 29,470 square feet of office space in the building located at 701 Gateway Blvd, South San Francisco, California. The lease for the South San Francisco facility commenced in October 2012. The South San Francisco lease will terminate around March 2026. We believe that our office space in Los Angeles is adequate to meet current and anticipated future requirements and that additional or substitute space will be available as needed to accommodate any expansions that our operations require.

ITEM 3. LEGAL PROCEEDINGS

Legal Malpractice Suit

On September 17, 2020, the Company filed a lawsuit against Hedrick Gardner Kincheloe & Garofalo, L.L.P. and David L. Levy, the attorneys who previously represented the Company in *Eshelman v. Puma Biotechnology, Inc., et al*. in the Superior Court of Mecklenburg County, North Carolina. The Company is alleging legal malpractice based on the defendants' negligent handling of the defense of the Company in *Eshelman v. Puma Biotechnology, Inc., et al*. The Company is seeking recovery of the entire amount awarded in *Eshelman v. Puma Biotechnology, Inc., et al*. and all legal fees and expenses incurred in appealing from the judgment and retrying the damages phase of the trial. On November 23, 2020, the defendant filed an answer to the complaint denying the allegations of negligence. On August 19, 2022, the Company filed a voluntary dismissal of the legal malpractice action, without prejudice, to allow the *Eshelman v. Puma Biotechnology, Inc., et al*. to conclude before proceedings. On June 2, 2023, the Company re-filed the lawsuit against Hedrick Gardner Kincheloe & Garofalo, L.L.P. and David L. Levy, the attorneys who previously represented the Company in *Eshelman v. Puma Biotechnology, Inc., et al.* in the Superior Court of Mecklenburg County, North Carolina. On August 22, 2023, the defendants filed motions to dismiss the case. These motions were presented at a hearing on February 20, 2024. The Superior Court Judge granted the motions to dismiss on March 20, 2024. The Company appealed this ruling to the North Carolina Court of Appeals. On September 3, 2025, the Court of Appeals reversed the dismissal of the Company's claim for legal malpractice and remanded the case to the Superior Court for further proceedings. The defendants filed a petition for discretionary review of this decision by the North Carolina Supreme Court on October 8, 2025. The Supreme Court has not decided whether to accept the case for review.

Patent-Related Proceedings

AstraZeneca Litigation

On September 22, 2021, the Company filed suit against AstraZeneca Pharmaceuticals, LP, AstraZeneca AB, and AstraZeneca PLC for infringement of United States Patent Nos. 10,603,314 ("the '314 patent") and 10,596,162 ("the '162 patent") (*Puma Biotechnology, Inc. et al. v. AstraZeneca Pharmaceuticals LP et al*., 1:21CV01338 (D. Del. Sep. 22, 2021)). The Company's complaint alleges that AstraZeneca's commercial manufacture, use, offer for sale, sale, distribution, and/or importation of Tagrisso® (osimertinib) products for the treatment of gefitinib and/or erlotinib-resistant non-small cell lung cancer infringes the '314 and '162 patents. The Company is an exclusive licensee of the '314 and '162 patents under the Pfizer Agreement. Wyeth is a co-plaintiff. Plaintiffs seek a judgment that AstraZeneca's product infringes

the asserted patents and an award of monetary damages in an amount to be proven at trial. AstraZeneca AB and AstraZeneca Pharmaceuticals LP filed an answer and counterclaims on November 5, 2021, including claims challenging the asserted patents as not infringed and/or invalid, and accusing plaintiffs of unclean hands and patent misuse. The parties stipulated to dismiss AstraZeneca PLC as a defendant and Pfizer as a Counterclaim Defendant on December 10, 2021, which the Court so ordered on December 13, 2021. The Company filed its answer to AstraZeneca's counterclaims on December 17, 2021, denying those claims. The case was reassigned to visiting Judge Matthew Kennelly of the Northern District of Illinois. A Markman Hearing was conducted on March 17, 2023, and the Court issued its claim construction decision on March 29, 2023. Fact discovery closed on May 19, 2023, and expert discovery closed on November 17, 2023. The Court denied the parties' respective motions for summary judgment and Daubert motions, other than to clarify that Plaintiffs' damages cannot extend to any time period before the asserted patents were issued. The Court granted AstraZeneca's motion to dismiss the Company as a Plaintiff on constitutional standing grounds but denied the motion to dismiss Wyeth as a Plaintiff on constitutional standing grounds. On April 29, 2024, the Court granted AstraZeneca's motion to dismiss AstraZeneca's counterclaims against the Company, which removed the Company from the case. Wyeth remained in the case as a Plaintiff and counterclaim-defendant. Under the Company's worldwide exclusive license agreement with Pfizer, Inc. (the parent of Wyeth) as amended, the Company also maintains contractual rights to recover monetary damages in the AstraZeneca litigation, and those contractual rights are unaffected by the court's March 18, 2024 and April 29, 2024 orders. A jury trial was held May 13-17, 2024. The jury found in favor of Wyeth and against AstraZeneca. In particular, the jury found that use of Tagrisso® according to each of the three FDA-approved indications infringes the asserted claims of the '314 and '162 patents, and that AstraZeneca induces that infringement. The jury further rejected AstraZeneca's challenges to the validity of the patents, finding that they are not invalid. The jury awarded damages to Wyeth for past acts of infringement through December 31, 2023, in the amount of $107,500,000. A separate bench trial related to certain equitable claims and defenses raised by AstraZeneca was held before Judge Kennelly on June 20 and 25, 2024. On August 6, 2024, Judge Kennelly issued his ruling on the issues that were tried in the bench trial, finding for Wyeth and against AstraZeneca on all claims and defenses. The Court found that AstraZeneca had not proved its claim that Wyeth's asserted patents were invalid as indefinite, or that Wyeth had committed acts that would give rise to findings of unclean hands, implied waiver, or patent misuse. AstraZeneca filed a motion challenging the jury's verdict and requesting a new trial. Wyeth filed a motion requesting supplemental damages for past infringement from January 1, 2024, through the date of judgment; pre-and-post judgment interest, and ongoing royalties through the remaining term of the patents. Briefing on these motions from both sides was completed on July 16, 2024. On August 14, 2024, Judge Kennelly ruled on AstraZeneca's motion challenging the jury's verdict, granting it in part and denying it in part. The Court granted AstraZeneca's motion for judgment as a matter of law that the '314 and '162 patents are invalid under 35 U.S.C. § 112 for lacking enablement and adequate written description as to a particular claim limitation. In all other respects, the Court denied AstraZeneca's motion. The Court entered its final and appealable judgment accordingly. The Company respectfully disagrees with the Court's ruling regarding invalidity with respect to the particular claim limitation. Wyeth filed a notice of appeal on September 12, 2024, appealing the District Court's judgment as a matter of law, as well as other rulings and opinions of the Court adverse to Wyeth. On December 18, 2024, Wyeth filed its opening brief. On March 13, 2025, AstraZeneca filed its response brief. On March 20, 2025, non-parties Regeneron Pharmaceuticals, Inc. and Sanofi-Aventis U.S. LLC filed a motion for leave to file an amicus curiae brief in the Federal Circuit. The motion was granted on May 16, 2025. On June 6, 2025, Wyeth filed its reply brief. Briefing on the appeal is now complete, and the parties await further order from the Court.

Acebright China Litigation

On January 18, 2022, Shanghai Acebright Pharmaceuticals Group Co., Ltd. ("Acebright") filed an abbreviated new drug application ("ANDA") with the National Medical Products Administration in China ("NMPA") seeking approval to market a generic version of the Company's NERLYNX® (neratinib) tablet, 40mg in China. Acebright seeks approval prior to the expiration of three patents listed on the China Patent Information Registration Platform for Marketed Drugs ("Chinese Orange Book"), namely, Chinese Patent Nos. ZL201410082103.7, ZL201080060546.6, and ZL200880118789.3 (the "'789 patent" and collectively, the "NERLYNX® Patents"), alleging in a Type 4.2 patent declaration that its generic version of NERLYNX does not fall within the scope of the claims of NERLYNX® Patents listed in the Chinese Orange Book. The patent declaration of Acebright was published in the Chinese Orange Book on January 19, 2022. On March 2, 2022, the Company filed petitions with the China National Intellectual Property Administration ("CNIPA") and requested administrative determination that Acebright's generic neratinib tablet falls within the scope of the claims of NERLYNX® Patents listed in the Chinese Orange Book. The Company's request for administrative determination was accepted by CNIPA on March 18, 2022. The Company has notified NMPA of the acceptance of the request for administrative determination for NMPA to institute a stay of Acebright's ANDA for nine months. On July 11, 2022, CNIPA decided that claims 5 and 6 of Patent No. ZL200880118789.3 are not eligible for registration in the Chinese Orange Book on the ground that these two pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On September 9, 2022, CNIPA decided that the generic drug in Acebright's ANDA does not fall within the protection scope of claims 1, 3, 5 and 6 of Patent No. ZL201410082103.7 and claims 1-4, 7

and 9-13 of Patent No. ZL201080060546.6. The three CNIPA administrative decisions on NERLYNX® Patents have lifted the stay of Acebright's ANDA by NMPA. The Company has appealed each CNIPA administrative decision in January 2023 at the Beijing Intellectual Property Court ("BJIPC"). The three appeals were accepted by BJIPC on February 20, 2023. The Company also filed three civil complaints based on the three NERLYNX® Patents against Acebright with the BJIPC in July 2022 and requested court determination that Acebright's generic neratinib tablet falls within the scope of the claims of NERLYNX® Patents. On May 6, 2023, the Company withdrew two civil lawsuits and two appeals in relation to Chinese Patent Nos. ZL201410082103.7 and ZL201080060546.6 at the BJIPC. On May 24, 2023, the BJIPC accepted the Company's withdrawal request. On July 24, 2023, the Company withdrew the one remaining civil lawsuit and one appeal in relation to Chinese Patent No. ZL200880118789.3 at the BJIPC. On August 15, 2023, the BJIPC accepted the Company's withdrawal request. On September 12, 2023, the NMPA approved Acebright's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20234141.

On December 28, 2023, the Company filed a civil lawsuit against Acebright for infringement of the '789 patent under Article 11 of the Chinese Patent Law before Jiangsu Nanjing Intermediate People's Court. The Company's complaint alleges that Acebright's offer for sale of a generic version of the Company's NERLYNX® product infringes the '789 patent. The Company seeks a judgment that Acebright's product infringes the '789 patent and Acebright's act of offer for sale shall be enjoined. On January 2, 2024, Jiangsu Nanjing Intermediate People's Court accepted the civil complaint. An oral hearing was held on June 19, 2024, during which the Company amended its complaint to allege that Acebright making, selling and offering to sell the generic version of NERLYNX® infringes the '789 patent. On July 24, 2024, the Company submitted a request to withdraw the lawsuit. On August 8, 2024, Jiangsu Nanjing Intermediate People's Court accepted the withdrawal request.

On September 27, 2024, the Company filed an additional patent infringement claim against Acebright at Jiangsu Nanjing Intermediate People's Court. On October 14, 2024, the Court accepted the complaint and designated case number (2024) Su 01 Min Chu 2192 to this case. On December 16, 2024, the Court conducted an evidence exchange hearing. On January 10, 2025, the Court conducted a hearing of party experts on the evaluation of evidence. On July 14, 2025, the Court conducted a hearing to examine evidence and debate merits of party arguments. On September 28, 2025, the Court issued a first-instance decision, deciding that Acebright's product does not fall within the scope of the patent-in-suit, and Acebright did not infringe the NERLYNX® Patents; the Court also decided that the Company's enforcement efforts were not malicious and did not amount to unfair competition.

Aosaikang China Litigation

On November 17, 2022, Jiangsu Aosaikang Pharmaceutical Co. Ltd. ("Aosaikang") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2202006. Aosaikang made Type 4.2 declarations against the four Orange Book Patents ZL201410082103.7, ZL201080060546.6, ZL200880118789.3 and ZL201710057547.9, alleging that its generic version of NERLYNX does not fall within the scope of the claims of the Orange Book patents. Aosaikang also alleged that Patents ZL200880118789.3 and ZL201710057547.9 are not eligible for Chinese Orange Book listing.

On December 28, 2022, the Company submitted four Article 76 petitions against the Aosaikang ANDA with the CNIPA and requested administrative determination that Aosaikang's generic neratinib tablet falls within the scope of the claims of the four Orange Book patents. On January 6, 2023, the CNIPA accepted the Company's request for administrative determination in relation to Patent Nos. ZL201410082103.7 and ZL201080060546.6. Also on January 6, 2023, the CNIPA declined to accept the Company's request for administrative determination in relation to Patent Nos. ZL200880118789.3 and ZL201710057547.9, alleging that the listed claims are not eligible for registration in the Chinese Orange Book on the ground that these pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On January 28, 2023, the Company requested the NMPA to institute a nine-month stay against Aosaikang ANDA starting from the CNIPA's acceptance of the Company's request for administrative determination. On June 2, 2023, CNIPA decided that the generic drug in Aosaikang's ANDA does not fall within the protection scope of claims 1, 3, 5 and 6 of Patent No. ZL201410082103.7 and claims 1-4, 7 and 9-13 of Patent No. ZL201080060546.6. The two CNIPA administrative decisions on NERLYNX® Patents have lifted the stay of Aosaikang's ANDA by NMPA. On October 22, 2024, the NMPA approved Aosaikang's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20249180.

Convalife China Litigation

Convalife Pharmaceuticals (Shanghai) Co., Ltd ("Convalife") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2202095. On December 23, 2022, Convalife made Type 4.2 declarations against the four Orange Book Patents ZL201410082103.7, ZL201080060546.6, ZL200880118789.3 and ZL201710057547.9, alleging that its generic version of NERLYNX does not fall within the scope of the claims of the Orange Book patents. Convalife also alleged that Patents ZL200880118789.3 and ZL201710057547.9 are not eligible for Chinese Orange Book listing.

On February 1, 2023, the Company submitted four Article 76 petitions against the Convalife ANDA with the CNIPA and requested administrative determination that Convalife's generic neratinib tablet falls within the scope of the claims of the four Orange Book patents. On February 3, 2023, the CNIPA accepted the Company's request for administrative determination in relation to Patent Nos. ZL201410082103.7 and ZL201080060546.6. Also on February 3, 2023, the CNIPA declined to accept the Company's request for administrative determination in relation to Patent Nos. ZL200880118789.3 and ZL201710057547.9, alleging that the listed claims are not eligible for registration in the Chinese Orange Book on the ground that these pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On February 24, 2023, the Company requested the NMPA to institute a nine-month stay against Convalife ANDA starting from the CNIPA's acceptance of the Company's request for administrative determination. On June 2, 2023, CNIPA decided that the generic drug in Convalife's ANDA does not fall within the protection scope of claims 1, 3, 5 and 6 of Patent No. ZL201410082103.7 and claims 1-4, 7 and 9-13 of Patent No. ZL201080060546.6. The two CNIPA administrative decisions on NERLYNX® Patents have lifted the stay of Convalife's ANDA by NMPA. On June 28, 2024, the NMPA approved Convalife's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20244222.

Kelun China Litigation

Hunan Kelun Pharmaceutical Co., Ltd. ("Kelun") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2300221. On January 28, 2023, Kelun made Type 4.2 declarations against the four Orange Book Patents ZL201410082103.7, ZL201080060546.6, ZL200880118789.3 and ZL201710057547.9, alleging that its generic version of NERLYNX does not fall within the scope of the claims of the Orange Book patents. Kelun also alleged that Patents ZL200880118789.3 and ZL201710057547.9 are not eligible for Chinese Orange Book listing.

On March 13, 2023, the Company submitted four Article 76 petitions against the Kelun ANDA with the CNIPA and requested administrative determination that Kelun's generic neratinib tablet falls within the scope of the claims of the four Orange Book patents. On March 21, 2023, the CNIPA declined to accept the Company's request for administrative determination in relation to Patent Nos. ZL200880118789.3 and ZL201710057547.9, alleging that the listed claims are not eligible for registration in the Chinese Orange Book on the ground that these pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On March 24, 2023, the CNIPA accepted the Company's request for administrative determination in relation to Patent Nos. ZL201410082103.7 and ZL201080060546.6. On April 17, 2023, the Company requested the NMPA to institute a nine-month stay against Kelun's ANDA starting from the CNIPA's acceptance of the Company's request for administrative determination. On September 14, 2023, the Company withdrew the two requests for administrative determination in relation to Chinese Patent Nos. ZL201410082103.7 and ZL201080060546.6 at the CNIPA. On September 25, 2023, the CNIPA accepted the Company's withdrawal request. On September 9, 2025, the NMPA approved Kelun's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20255337.

Demai Litigation

Zhengzhou Demai Pharmaceutical Co., Ltd ("Demai") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2402776. On August 26, 2024, Demai made a Type 4.2 declaration against Orange Book Patent ZL201410082103.7, alleging that its generic version of NERLYNX does not fall within the scope of the claims of this Orange Book patent. On September 30, 2024, the Company filed a lawsuit against Demai at the BJIPC based on Nerlynx Patent No. ZL201080060546.6 and on October 8, 2024, the Company filed a lawsuit against Demai at the BJIPC based on Nerlynx Patent No. ZL201410082103.7. On February 13, 2025, the Company withdrew the lawsuits from BJIPC, filed an Article 76 petition with the CNIPA against the Demai ANDA and requested administrative determination that Demai's generic neratinib maleate tablet falls within the scope of the claims of Nerlynx Patent No. ZL201080060546.6. On February 21, 2025, the CNIPA accepted the Company's petition and started examination. On March 18, 2025, the Company filed a request with the NMPA to set up a nine-month stay on Demai's ANDA.

Hexal European Patent Opposition

An opposition was filed by Hexal AG ("Hexal") on August 3, 2016 against European Patent No. EP2416774 which was licensed from Pfizer in 2011, and which claims neratinib for use in a method for treating HER-2/neu overexpressed/amplified cancer and improving IDFS, wherein the method comprises delivering neratinib therapy to HER-2/neu overexpressed/amplified cancer patients following the completion of at least one year of trastuzumab adjuvant therapy, and wherein the neratinib therapy comprises treating the cancer patients with neratinib for at least twelve months. An oral hearing was held on December 8, 2017, wherein the patent was maintained as granted. Following an appeal filed by Hexal, the Board of Appeal of the European Patent Office rejected the claims as granted and all pending auxiliary requests during the oral hearing of September 2, 2021. Before issuance of a decision, we withdrew approval of the text in which the patent was granted and all pending auxiliary requests, thereby revoking the patent and concluding the appeal. One European divisional application, namely EP15188350.1, was granted with the European patent number EP3000467 on March 1, 2023. Oppositions against EP3000467 were filed by Hexal on November 3, 2023, by Alfred E. Tiefenbacher (GmbH & Co. KG) on November 28, 2023 and by Generics (UK) Limited ("Generics") on December 1, 2023. EP3000467 is used as the basic patent for Supplementary Protection Certificate applications for the EMA-approved NERLYNX® product, 17 of which have been granted, three proceedings have been stayed, and 11 are in active prosecution. The patentee response to the notice of opposition was filed on April 15, 2024, following which, all three opponents filed additional arguments in reply to the patentee's submission. On February 6, 2025, the Company filed its response to the summons to attend oral proceedings, including six auxiliary requests. Alfred E. Tiefenbacher and Hexal filed their responses to the summons to oral proceedings on February 6 and 7, 2025, respectively. Hexal filed a further brief on March 19, 2025. Oral proceedings took place on April 9 and 10, 2025. EP3000467 was upheld as amended after the first instance hearing based on Auxiliary Request 1, which covers the EMA approved indication for NERLYNX® as an extended adjuvant therapy for treating early stage hormone receptor-positive HER-2-overexpressed/amplified breast cancer. The first instance decision may be appealed. Hexal filed an appeal on June 6, 2025, Generics filed an appeal on June 20, 2025 and Wyeth filed an appeal on June 30, 2025. On September 5, 2025, Wyeth filed its grounds of appeal, including nine auxiliary requests. On the same day, Hexal filed its grounds of appeal. Generics filed its grounds of appeal on September 4, 2025, and Alfred E. Tiefenbacher filed its grounds of appeal on September 1, 2025. On December 16, 2025, Alfred E. Tiefenbacher withdrew its appeal. Wyeth responded to the opponents' grounds of appeal on January 12, 2026. One European divisional application is pending in the same family, namely EP 23157078.8. A response to the European Search Opinion (ESO) for this application was filed February 14, 2024. The first office action was issued on January 28, 2025 with a response to the first office action filed on July 22, 2025.

ITEM 4. MINE SAFETY DISCLOSURE

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market for Common Stock

Our common stock has been quoted on the NASDAQ Global Select Market ("NASDAQ"), under the symbol "PBYI" since January 3, 2017. Prior to January 3, 2017, shares of our common stock had been listed on the New York Stock Exchange since October 19, 2012.

Record Holders

As of February 23, 2026, there were 9 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have never declared or paid any cash dividends on our capital stock. Currently, we anticipate that we will retain all available funds for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination relating to dividend policy will be made at the discretion of our board of directors and will depend on our future earnings, capital requirements, financial condition, prospects, applicable Delaware law, which provides that dividends are only payable out of surplus or current net profits, and other factors that our board of directors deems relevant. Additionally, we are restricted from paying cash dividends under our Note Purchase Agreement with Athyrium.

Securities Authorized for Issuance Under Equity Compensation Plans

The information included under Item 12 of Part III of this Annual Report, "Securities Authorized for Issuance Under Equity Compensation Plans," is hereby incorporated by reference into this Item 5 of Part II of this Annual Report.

Recent Sales of Unregistered Securities

None.

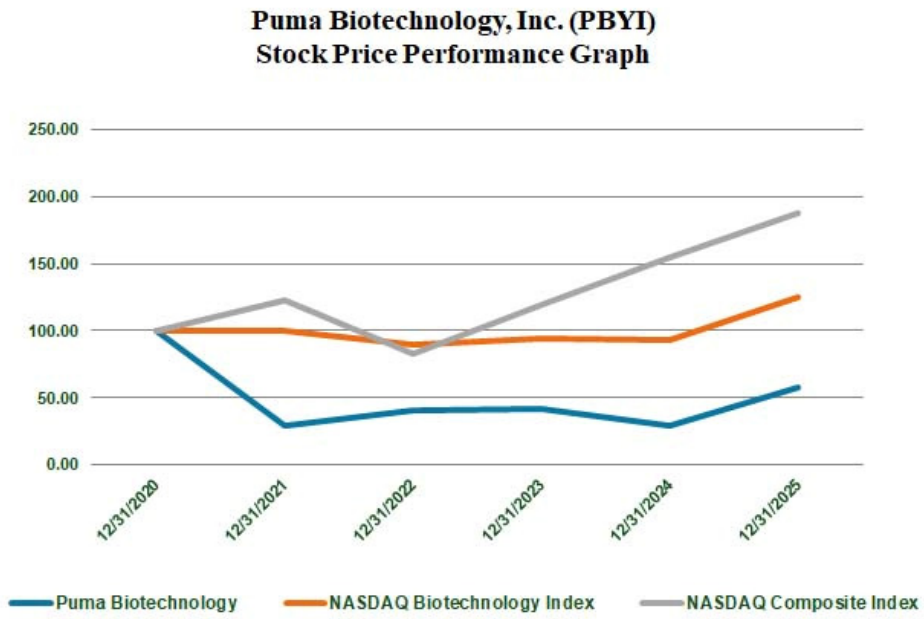
Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Performance Graph

The graph and table below compare the cumulative total return of Puma Biotechnology common stock from December 31, 2020, through December 31, 2025, with the cumulative total returns on (i) the NASDAQ Biotechnology Index and (ii) the NASDAQ Composite Index. The comparison assumes investment of $100 on December 31, 2020, in our common stock and in each index and, for each index, assumes reinvestment of all dividends.

The historical price performance included below is not necessarily indicative of future stock price performance.



Cumulative Total Return

Puma Biotechnology, Inc. Compared to the Nasdaq Biotechnology Index and Nasdaq Composite Index

	12/31/20	12/31/21	12/31/22	12/31/23	12/31/24	12/31/25
Puma Biotechnology, Inc.	**100.00**	**29.63**	**41.23**	**42.20**	**29.73**	**57.99**
NASDAQ Biotechnology Index	**100.00**	**100.02**	**89.90**	**94.03**	**93.49**	**124.75**
NASDAQ Composite Index	**100.00**	**122.18**	**82.43**	**119.22**	**154.48**	**187.14**

The material in this performance graph is not soliciting material, is not deemed filed with the SEC and is not incorporated by reference in any filing of the Company under the Exchange Act, whether made on, before or after the date of this filing and irrespective of any general incorporation language in such filing.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Annual Report contains forward-looking statements within the meanings of the federal securities laws. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those expressed or implied by such forward-looking statements. For a detailed discussion of these risks and uncertainties, see the "Risk Factors" section in Item 1A of Part I of this Annual Report. We caution the reader not to place undue reliance on these forward-looking statements, which reflect management's analysis only as of the date of this Annual Report. We undertake no obligation to update forward-looking statements to reflect events or circumstances occurring after the date of this Annual Report.

Overview

We are a biopharmaceutical company that develops and commercializes innovative products to enhance cancer care and improve treatment outcomes for patients. We are currently commercializing NERLYNX, an oral version of neratinib, for the treatment of certain HER2-positive breast cancers. Additionally, we have in-licensed, and are responsible for global development and commercialization of, alisertib. Alisertib is a selective, small-molecule inhibitor of Aurora Kinase A that is designed to disrupt mitosis leading to apoptosis of rapidly proliferating tumor cells that are dependent on Aurora Kinase A. Prior to our licensing alisertib from Takeda, alisertib was tested in over 1,300 patients who were treated across 22 company-sponsored trials resulting in a large, well-characterized clinical safety database. Based on information in this database, we believe alisertib has potential application in the treatment of a range of different cancer types, including hormone receptor-positive breast cancer, triple negative breast cancer and small cell lung cancer. We intend to pursue development of alisertib initially in small cell lung cancer and hormone receptor-positive breast cancer.

NERLYNX is currently approved in the United States for two indications: the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy and for use in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.

We currently market NERLYNX in the United States using our direct specialty sales force consisting of approximately 35 sales specialists. Our sales specialists are supported by an experienced sales leadership team consisting of five regional business leaders a Senior Vice President of Sales and a Senior Vice President of Marketing, as well as experienced professionals in marketing, managed markets, access and reimbursement, research, and sales planning and operations. Outside the United States, we seek to enter into exclusive sub-license agreements with third parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved. As of December 31, 2025, NERLYNX has received approval for the treatment of certain patients with extended adjuvant or metastatic HER2-positive breast cancer in over 40 countries outside the United States. We are currently party to several sub-licenses in various regions outside the United States, including Europe (excluding Ukraine), Australia, Canada, China, Southeast Asia, Israel, South Korea, Russia and various countries and territories in Central America, South America, Africa and the Middle East.

In September 2022, we entered into an exclusive license agreement with Takeda to license the worldwide research and development and commercial rights to alisertib. Alisertib is an investigational, reversible, ATP-competitive inhibitor that is designed to be highly selective for Aurora Kinase A. Inhibition of Aurora Kinase A can lead to disruption of mitotic spindle apparatus assembly, disruption of chromosome segregation, and inhibition of cell proliferation. In clinical trials to date, alisertib has shown single agent activity and activity in combination with other cancer drugs in the treatment of many different types of cancers, including hormone receptor-positive breast cancer, triple negative breast cancer, small cell lung cancer and head and neck cancer. We initiated the ALISertib in CAncer (ALISCA™ -Lung1) Phase II trial (PUMA-ALI-4201) of alisertib monotherapy for the treatment of patients with extensive stage small cell lung cancer in February 2024, and we commenced the ALISCA™ -Breast1 Phase II trial (PUMA-ALI-1201) in November 2024.

Under the terms of the exclusive license agreement, we assumed sole responsibility for the global development and commercialization of alisertib. We paid Takeda an upfront license fee of $7.0 million in October 2022, and it is eligible to receive potential future milestone payments of up to $287.3 million upon our achievement of certain regulatory and commercial milestones over the course of the exclusive license agreement, as well as tiered royalty payments for any net sales of alisertib. We recorded in-process research and development expense of $7.0 million during the year ended December 31, 2022, in connection with the upfront payment related to the asset acquisition. As of December 31, 2025, no milestones had been accrued as the underlying contingencies were not probable or estimable.

Our expenses to date have been related to hiring staff, commencing company-sponsored clinical trials, building out of our corporate infrastructure and, since 2017, the commercial launch of NERLYNX. Going forward, we anticipate significant expenses as we continue to develop alisertib in 2026. Accordingly, our success depends not only on the safety and efficacy of our drug candidates, but also on our ability to finance product development. To date, our major sources of working capital have been proceeds from product and license revenue, public offerings of our common stock, proceeds from our credit facility and sales of our common stock in private placements. We intend to satisfy our near-term liquidity requirements through a combination of our existing cash and cash equivalents and marketable securities as of December 31, 2025, and proceeds that will become available to us through product sales, royalties and sub-license milestone payments. However, this intention is based on assumptions that may prove to be wrong. Changes may occur that would consume our available capital faster than anticipated, including changes in and progress of our development activities, the impact of commercialization efforts, acquisitions of additional drug candidates and changes in regulation. Some of these developments have had and may continue to have an adverse effect on our revenue and thus could have an adverse effect on our ability to satisfy the minimum revenue and cash balance covenants contained in the Athyrium Notes.

Tariffs

We do not believe that tariffs imposed or proposed to be imposed by the United States, particularly with the EU and China, will have a material impact on our product costs or results of operations. However, shifts in trade policies in the United States and other countries have been rapidly evolving and are difficult to predict. The ultimate impact of any announced or future tariffs will depend on various factors, including what tariffs are ultimately implemented, the timing of implementation and the amount, scope and nature of such tariffs and potential exclusions from the application of those tariffs.

Taxes

On July 4, 2025, the "One Big Beautiful Bill" was signed into law, which includes significant changes to federal tax law and other regulatory provisions that may impact us. As of the date of these financial statements, we have evaluated the impact of the changes to Section 174 – *Amortization of Research and Experimental Expenditures* on the valuation allowance release. We intend to deduct the capitalized costs over two years. This deduction reduces the amount of net operating losses being utilized but results in a net zero change to the deferred tax asset balance. In 2025, we adjusted a portion of our valuation allowance related to our deferred tax assets in the amount of $3.8 million, which reduced our net income for the year.

Summary of Income and Expenses

Product revenue, net

Product revenue, net consists of revenue from sales of NERLYNX. We sell NERLYNX to a limited number of specialty pharmacies and specialty distributors in the United States. We record revenue at the net sales price, which includes an estimate for variable consideration for which reserves are established. Variable consideration consists of trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates and other incentives.

Product revenue also consists of product sales under sub-license agreements to our sub-licensees, who then sell into their respective international territories.

License revenue

License revenue consists of consideration earned for performance obligations satisfied pursuant to our sub-license agreements.

Royalty revenue

Royalty revenue consists of consideration earned related to product sales made by our sub-licensees in their respective territories pursuant to our sub-license agreements.

Cost of sales

Cost of sales consists of third-party manufacturing costs, freight, and indirect overhead costs associated with sales of NERLYNX. Cost of product sales also includes period costs related to royalty charges payable to Pfizer, the amortization of milestone payments made under our license agreement with Pfizer, certain inventory manufacturing services, inventory adjustment charges, unabsorbed manufacturing and overhead costs, and manufacturing variances. Cost of sales includes applicable license termination fees.

Selling, general and administrative expenses

Selling, general and administrative expenses ("SG&A expenses"), consist primarily of salaries and payroll-related costs, stock-based compensation expense, professional fees, business insurance, rent, general legal activities, credit loss expense and other corporate expenses. We expense SG&A expenses as they are incurred.

Research and development expenses

Research and development expenses ("R&D expenses") include costs associated with services provided by consultants who conduct and perform clinical services on our behalf and contract organizations for the manufacturing of clinical materials. During the years ended December 31, 2025, 2024 and 2023, our R&D expenses consisted primarily of CRO fees, manufacturing of clinical materials, fees paid to consultants, salaries and related personnel costs and stock-based compensation. We expense our R&D expenses as they are incurred. Internal R&D expenses primarily consist of payroll-related costs and also include equipment costs, travel expenses and supplies. We expect R&D expenses to increase in 2026 as we expand the development of alisertib.

Reclassifications

Certain prior year amounts in the Consolidated Statements of Cash Flows have been reclassified to correct an error in the prior year's presentation. Specifically, for the year ended December 31, 2024, a change in deferred tax assets of $7.1 million was previously classified within "Changes in operating assets and liabilities." This amount has been reclassified to non-cash items within the operating activities section of the Consolidated Statements of Cash Flows. This reclassification had no impact on the total net cash provided by (used in) operating activities, net income, or the Consolidated Balance Sheets for any period presented.

Results of Operations

The following summarizes our results of operations for the years ended December 31, 2025 and 2024. For discussion related to the results of operations and changes in financial condition for the year ended December 31, 2024, compared to the year ended December 31, 2023, please refer to Item 7 of Part II, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2024, which was filed with the SEC on February 27, 2025.

Total revenue

Total revenue was approximately $228.4 million for the year ended December 31, 2025, compared to $230.5 million for the year ended December 31, 2024. This decrease in total revenue of $2.1 million was due to a decrease in royalty revenue of $11.0 million, partially offset by an increase in product revenue, net of approximately $8.9 million.

Product revenue, net

Product revenue, net was approximately $204.1 million for the year ended December 31, 2025, compared to $195.2 million for the year ended December 31, 2024. The increase in product revenue, net was primarily attributable to a volume increase of approximately 5.5% in bottles of NERLYNX sold and an increase in net selling price. Reserves for variable consideration were approximately 24.3% and 19.5% of product revenue for the years ended December 31, 2025 and 2024, respectively. The increase in the variable consideration (gross-to-net reserve) was primarily due to government chargebacks and payor mix.

License revenue

There was no license revenue for the years ended December 31, 2025 and December 31, 2024.

Royalty revenue

Royalty revenue was approximately $24.3 million for the year ended December 31, 2025, compared to $35.3 million for the year ended December 31, 2024. The decrease was due to decreased product sales by our sub-licensees in international territories, primarily in China.

Cost of sales

Cost of sales was approximately $58.2 million for the year ended December 31, 2025, compared to $64.4 million for the year ended December 31, 2024. The $6.2 million decrease was primarily due to the decrease of product unit sales to our sub-licensees and the related cost of sales (primarily sales in China), partially offset by higher domestic sales.

Selling, general and administrative expenses:

Selling, general, and administrative expenses (in thousands)	**For the Year Ended December 31,**		**Change**	
			$	**%**
	2025	**2024**	**2025/2024**	**2025/2024**
Payroll and related costs	$ 34,662	$ 31,555	$ 3,107	9.8%
Provision for credit loss recovery	(362)	(519)	157	-30.3%
Professional fees and expenses	19,060	29,873	(10,813)	-36.2%
Travel and meetings	5,257	5,344	(87)	-1.6%
Facilities and equipment costs	4,677	4,960	(283)	-5.7%
Stock-based compensation	4,283	5,566	(1,283)	-23.1%
Other	3,270	3,384	(114)	-3.4%
	$ 70,847	$ 80,163	$ (9,316)	-11.6%

Total SG&A expenses were approximately $70.8 million and $80.2 million for the years ended December 31, 2025 and December 31, 2024. The decrease is primarily attributable to the following:

- an increase in payroll and related costs of approximately $3.1 million, due to severance costs related to the departure of our Chief Commercial Officer, an increase in our commercial team compensation, merit increases and increases in our healthcare insurance premiums;
- a decrease in provision for credit loss recovery of approximately $0.2 million, primarily related to the payment history of a customer receivable;
- a decrease in professional fees and expenses of approximately $10.8 million, primarily related to legal fees associated with the AstraZeneca litigation in the prior year; and
- a decrease in stock-based compensation expense of approximately $1.3 million due to the departure of an executive in 2025 and lower fair value on equity grants due to lower market price for our common stock.

Research and development expenses:

Research and development expenses (in thousands)	**For the Year Ended December 31,**		**Change**	
			$	**%**
	2025	**2024**	**2025/2024**	**2025/2024**
Clinical trial expense	$ 20,538	$ 17,091	$ 3,447	20.2%
Internal R&D	34,440	32,248	2,192	6.8%
Consultant and contractors	4,429	2,917	1,512	51.8%
Stock-based compensation	2,661	2,679	(18)	-0.7%
	$ 62,068	$ 54,935	$ 7,133	13.0%

Total R&D expenses were approximately $62.1 million and $54.9 million for the years ended December 31, 2025 and December 31, 2024. The increase is primarily attributable to the following:

- an increase in clinical trial expense of approximately $3.4 million, primarily due to expanded alisertib development; and
- an increase in consultants and contractors of approximately $1.5 million, primarily due to expanded alisertib development.

Other income and expenses:

Other income (expenses) (in thousands)	**For the Year Ended December 31,**		**Change**	
	2025	**2024**	**$ 2025/2024**	**% 2025/2024**
Interest income	$ 4,078	$ 4,724	$ (646)	-13.7%
Interest expense	(6,622)	(12,452)	5,830	-46.8%
Other income	1,027	862	165	19.1%
	$ (1,517)	$ (6,866)	$ 5,349	-77.9%

Interest income

For the year ended December 31, 2025, we recognized approximately $4.1 million in interest income compared to approximately $4.7 million of interest income for the year ended December 31, 2024. The $0.6 million decrease in interest income was primarily the result of lower interest rates and timing of investments.

Interest expense

For the year ended December 31, 2025, we recognized approximately $6.6 million in interest expense compared to approximately $12.5 million of interest expense for the year ended December 31, 2024. The approximately $5.8 million decrease in interest expense was primarily related to a lower debt balance related to the pay down our debt principal during the year ended December 31, 2025.

Other income

For the year ended December 31, 2025, we recognized approximately $1.0 million in other income, compared to $0.9 million in other income for the year ended December 31, 2024. The increase was primarily due to increased sublease income.

Current tax expense

The $0.5 million increase in current tax expense is materially consistent with the increase in net income before taxes.

Deferred income tax expense (benefit)

In the fourth quarter of 2025, Puma recorded a $7.1 million income tax expense, offset by a $3.8 million partial release of a valuation allowance resulting in a non-cash, deferred tax expense of approximately $3.2 million. In 2024, we released a portion of our valuation allowance related to our deferred tax assets in the amount of $7.1 million, which significantly increased our net income for the year.

Non-GAAP Financial Measures:

In addition to our operating results, as calculated in accordance with generally accepted accounting principles in the United States, ("GAAP"), we use certain non-GAAP financial measures when planning, monitoring, and evaluating our operational performance. The following table presents our net income and net income per share, as calculated in accordance with GAAP, as adjusted to remove the impact of stock-based compensation. For the year ended December 31, 2025, stock-based compensation represented approximately 5.2% of the total of SG&A and R&D expenses. Our management believes that these non-GAAP financial measures are useful to enhance understanding of our financial performance, are more indicative of our operational performance and facilitate a better comparison among fiscal periods. These non-GAAP financial measures are not, and should not be viewed as, substitutes for GAAP reporting measures.

Reconciliation of GAAP Net Income to Non-GAAP Adjusted Net Income and GAAP Net Income Per Share to Non-GAAP Adjusted Net Income Per Share
(in thousands except share and per share data)

	For the Year Ended December 31,	
	2025	2024
GAAP net income	$ 31,111	$ 30,278
Adjustments:		
Stock-based compensation -		
Selling, general and administrative [1]	4,283	5,566
Research and development [2]	2,661	2,679
Non-GAAP adjusted net income	$ 38,055	$ 38,523
GAAP net income per share—basic	$ 0.62	$ 0.62
Adjustment to net income (as detailed above)	0.14	0.17
Non-GAAP adjusted basic net income per share	$ 0.76 [3]	$ 0.79 [3]
GAAP net income per share—diluted	$ 0.61	$ 0.62
Adjustment to net income (as detailed above)	0.14	0.16
Non-GAAP adjusted diluted net income per share	$ 0.75 [4]	$ 0.78 [4]

(1) To reflect a non-cash charge to operating expense for selling, general, and administrative stock-based compensation.
(2) To reflect a non-cash charge to operating expense for research and development stock-based compensation.
(3) Non-GAAP adjusted basic net income per share was calculated based on 50,011,485 and 48,648,701 weighted-average shares of common stock outstanding for the years ended December 31, 2025 and 2024, respectively.
(4) Non-GAAP adjusted diluted net income per share was calculated based on 50,653,283 and 49,100,433 weighted-average shares of common stock outstanding for the years ended December 31, 2025 and 2024, respectively.

Liquidity and Capital Resources

The following table summarizes our liquidity and capital resources as of and for the years ended December 31, 2025 and 2024 and is intended to supplement the more detailed discussion that follows:

Liquidity and capital resources (in thousands)	As of December 31, 2025	As of December 31, 2024
Cash and cash equivalents	$ 29,635	$ 69,219
Marketable securities	$ 67,893	$ 31,746
Working capital	$ 81,433	$ 51,547
Current portion of long-term debt	$ 22,523	$ 45,329
Long-term debt	$ —	$ 21,719
Stockholders' equity	$ 130,340	$ 92,125

The following table summarizes our cash flows (uses) for the years ended December 31, 2025 and 2024

	Year Ended December 31, 2025	Year Ended December 31, 2024
Cash provided by (used in):		
Operating activities	$ 41,802	$ 38,918
Investing activities	(36,188)	(20,438)
Financing activities	(45,198)	(33,846)
Net decrease in cash, cash equivalents and restricted cash	$ (39,584)	$ (15,366)

Operating Activities

We recorded net income of approximately $31.1 million and $30.3 million for the years ended December 31, 2025 and 2024, respectively. We recorded cash flows from operating activities of approximately $41.8 million for the year ended December 31, 2025 and recorded cash flows from operating activities of approximately $38.9 million for the year ended December 31, 2024.

Net cash provided by operating activities for the year ended December 31, 2025 was $41.8 million which consisted of net income of $31.1 million, adjusted for non-cash items of approximately $20.6 million, including stock-based compensation of $6.9 million, depreciation and amortization of $10.9 million, deferred income taxes of $3.2 million and recovery of credit loss of $0.4 million. Total changes in cash flows from operations were due to a change in working capital related primarily to an increase in accrued expenses of approximately $13.2 million, a decrease in inventory of approximately $3.2 million, offset by an increase in accounts receivable of $21.3 million, a decrease in post-marketing commitment liability of $2.4 million and a decrease in operating lease assets and liabilities, net of $1.8 million.

Net cash provided by operating activities for the year ended December 31, 2024 was $38.9 million which consisted of net income of $30.3 million, adjusted for non-cash items of approximately $12.1 million, including stock-based compensation of $8.2 million, depreciation and amortization of $11.5 million and recovery of credit loss of $0.5 million. Total changes in cash flows from operations were due to a change in working capital related primarily to a decrease in accrued expenses of approximately $15.8 million, an increase in inventory of approximately $1.6 million (increase in inventory purchases), offset by a decrease in accounts receivable of $16.3 million, primarily related to collection of royalties receivable.

Investing Activities

During the year ended December 31, 2025, cash used in investing activities was approximately $36.2 million. Cash used in investing activities was primarily due to the purchase of available-for-sale securities of approximately $108.1 million, partially offset by the maturities of available-for-sale securities of approximately $72.0 million.

During the year ended December 31, 2024, cash used in investing activities was approximately $20.4 million. Cash used in investing activities was primarily due to the purchase of available-for-sale securities of approximately $76.2 million, partially offset by the maturities of available-for-sale securities of approximately $55.8 million.

Financing Activities

Cash used in financing activities for the year ended December 31, 2025 was approximately $45.2 million. Of this amount, $44.4 million related to the payment of principal, as well as exit fees of approximately $0.9 million, on our debt with Athyrium, partially offset by approximately $0.1 million of proceeds from employee stock options exercised.

Cash used in financing activities for the year ended December 31, 2024 was approximately $33.8 million. Of this amount, $34.0 million related to the payment of principal, as well as exit fees, on our debt with Athyrium, partially offset by approximately $0.2 million of proceeds from employee stock options exercised.

Athyrium Note Purchase Agreement

We issued senior notes for an aggregate principal amount of $100.0 million pursuant to the note purchase agreement dated July 23, 2021 by us, and our subsidiary, and Athyrium, as Administrative Agent, and certain other investor parties (the "Note Purchase Agreement"), with an initial maturity date of July 23, 2026 (the "Athyrium Notes"). The Athyrium Notes were issued for face amount of $100.0 million, net of an original issue discount of $1.5 million. The Athyrium Notes also require a 2.0% exit payment to be made on each payment of principal. The borrowings under the Athyrium Notes, together with cash on hand, were used to repay our outstanding indebtedness, including the applicable exit and prepayment fees owed to lenders under our prior credit facility with Oxford. The Athyrium Notes are secured by substantially all of our assets. We incurred $1.9 million of deferred financing costs with the initial borrowing of the Athyrium Notes.

Interest on the Athyrium Notes is calculated in part based on the Secured Overnight Financing Rate ("SOFR"), which replaced the "London Interbank Offering Rate" as the floating benchmark for interest rate calculations applicable to the Athyrium Notes pursuant to the terms of the Third Amendment to the Note Purchase Agreement dated as of September 16, 2022 (the "Third Amendment"). The modification of the Note Purchase Agreement pursuant to the Third Amendment did not meet the requirements of a debt extinguishment under ASC Topic 470-50 - *Debt Modifications and Exchanges* and no gain or loss was recognized. We performed a quantitative analysis and determined that the terms of the new debt and original debt instrument are not substantially different. Accordingly, the Third Amendment is accounted for as a debt modification.

Following the effectiveness of the Third Amendment, the Athyrium Notes bear interest at an annual rate equal to the sum of (a) eight percent (8.00%) plus (b) the lesser of (i) the sum of (x) three-month term SOFR for an interest period of three months plus (y) 0.26161% (26.161 basis points) and (ii) three and one-half of one percent (3.50%) per annum. Interest is payable quarterly on the last business day of March, June, September and December each year. In the second quarter of 2024, we began paying the principal payments required to be made quarterly at 11.11% of the original face amount. The remaining balance will be paid at maturity. Each principal payment also includes a 2.0% exit payment. Each quarterly principal payment approximates $11.1 million, and each quarterly exit fee payment approximates $0.2 million. As of December 31, 2025, the effective interest rate for the loan was 12.99%.

As of December 31, 2025, we may prepay the outstanding principal balance of the notes, in whole or in part, without premium or penalty.

The Athyrium Notes include affirmative and negative covenants applicable to us. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage, and satisfy certain requirements regarding deposit accounts. The negative covenants include, among others, restrictions on our transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions. We are also required to maintain minimum cash balances and achieve certain minimum product revenue targets, measured as of the last day of each fiscal quarter on a trailing year-to-date basis. As of December 31, 2025, we were in compliance with such covenants.

As of December 31, 2025, the principal balance outstanding under the Athyrium Notes was $22.5 million, representing all of our debt.

Current and Future Financing Needs

We did not receive or record any product revenue until the third quarter of 2017. We have spent, and expect to continue to spend, substantial amounts in connection with implementing our business strategy, including our planned product development efforts, our clinical trials, our R&D efforts and our commercialization efforts.

We may choose to begin new R&D efforts, launch additional marketing efforts or pursue other in-licensing opportunities. These efforts will require funding in addition to the cash and cash equivalents totaling approximately $29.6 million and approximately $67.9 million in marketable securities available at December 31, 2025. While our consolidated financial statements have been prepared on a going concern basis, we may incur significant losses in the future and will need to generate significant revenue to sustain operations and successfully commercialize neratinib and develop alisertib. While we have been successful in raising financing in the past, there can be no assurance that we will be able to do so in the future. Our ability to obtain funding may be adversely impacted by uncertain market conditions, our success in commercializing neratinib, our success in developing alisertib, unfavorable decisions of regulatory authorities or adverse clinical trial results. The outcome of these matters cannot be predicted at this time. We believe that our existing cash and

cash equivalents and marketable securities as of December 31, 2025, and proceeds that will become available to us through product sales and sub-license payments are sufficient to satisfy our operating cash and capital needs for at least one year after the filing of this Annual Report.

In addition, we have based our estimate of capital needs on assumptions that may prove to be wrong. Changes may occur that would consume our available capital faster than anticipated, including changes in and progress of our development activities, the impact of commercialization efforts, acquisitions of additional drug candidates and changes in regulation. Potential sources of financing include strategic relationships, public or private sales of equity or debt and other sources of funds. We may seek to access the public or private equity markets when conditions are favorable due to our long-term capital requirements. If we raise funds by selling additional shares of common stock or other securities convertible into common stock, the ownership interests of our existing stockholders will be diluted. If we are not able to obtain financing when needed, we may be unable to carry out our business plan. As a result, we may have to significantly limit our operations, and our business, financial condition and results of operations would be materially harmed. In such an event, we will be required to undertake a thorough review of our programs, and the opportunities presented by such programs, and allocate our resources in the manner most prudent.

Off-Balance Sheet Arrangements

We do not have any "off-balance sheet arrangements," as defined by SEC regulations.

Contractual Obligations

Contractual obligations represent future cash commitments and liabilities under agreements with third parties and exclude contingent liabilities for which we cannot reasonably predict future payment. Our contractual obligations result from leases for office space and office equipment and the principal and interest owed under our Note Purchase Agreement. We also have unrecognized tax benefits that, if recognized, would affect the effective tax rate at December 31, 2025. We do not have tax positions for which it is reasonably possible that the total amounts of unrecognized tax benefit will significantly increase or decrease within 12 months of the reporting date. Additionally, the expected timing of payment of the obligations presented below is estimated based on current information.

The following table represents our contractual obligations as of December 31, 2025, aggregated by type (in thousands):

Contractual Obligations	Total	Less than 1 year	1 - 3 years	3 - 5 years
Operating Lease Obligations	8,126	1,913	3,878	2,335
Long Term Debt Obligations (principal and interest)	23,719	23,719	—	—
Total	**31,845**	**25,632**	**3,878**	**2,335**

We also engage with CROs and contract manufacturing organizations ("CMOs") in addition to engaging in contracts for the management of our ongoing clinical trials and pre-commercialization efforts. We may cancel these agreements with a 30 to 45 day written notice to the outside vendor. We would be obligated to pay for services rendered up to that point, which amounts to total contractual obligations of $54.9 million within the next twelve months. The contracts also contain variable costs that are hard to predict as they are based on such things as patients enrolled and clinical trial sites, which can vary, and therefore, are not included in the total obligations amount. The remaining milestone amounts were not included in the table above as the timing of when or if these payments will be made is uncertain. As of December 31, 2025, our obligations for potential milestone payments totaled approximately $15.7 million. This amount will be paid by us if all milestones are reached and would reduce the overall contractual obligation if one or more milestone is never reached.

In regard to our contractual obligations in relation to the Pfizer in-license agreement, as consideration for the license, we are required to make substantial payments upon the achievement of certain milestones totaling approximately $187.5 million if all such milestones are achieved, of which $102.5 million have been achieved as of December 31, 2025. The remaining milestone amounts were not included in the table above as the timing of when or if these payments will be made is uncertain. In connection with the FDA approval of NERLYNX in July 2017, we triggered a one-time milestone payment pursuant to the agreement. In June 2020, we entered into a letter agreement with Pfizer relating to the method of payment associated with a milestone payment under our license agreement with Pfizer (see Note 13–Commitments and Contingencies in the accompanying notes to the financial statements). In addition, we reached a commercial milestone by

achieving aggregate worldwide net sales of $250.0 million in calendar year 2022, resulting in a payable to Pfizer of $12.5 million. The commercial milestone payable was paid in February 2023. Should we commercialize any more of the compounds licensed from Pfizer or any products containing any of these compounds, we will be obligated to pay to Pfizer annual royalties at a fixed rate in the low to mid-teens of net sales of all such products, subject to certain reductions and offsets in some circumstances. Our royalty obligation continues, on a product-by-product and country-by-country basis, until the later of (i) the last to expire licensed patent covering the applicable licensed product in such country, or (ii) the earlier of generic competition for such licensed product reaching a certain level in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. In the event that we sublicense the rights granted to us under the license agreement with Pfizer to a third party, the same milestone and royalty payments are required. We can terminate the license agreement at will, or for safety concerns, in each case upon specified advance notice.

In regard to our contractual obligations with Takeda, as consideration for the license, we are required to make substantial payments upon the achievement of certain milestones totaling $287.3 million if all such milestones are achieved. As of December 31, 2025, no milestones had been achieved.

See Note 12–Income Taxes and Note 13–Commitments and Contingencies in the accompanying notes to the financial statements for a summary of our uncertain tax positions and contracts held by us as of December 31, 2025. As of December 31, 2025, the amount of unrecognized tax benefit was $3.4 million, and is also not included in the table above as the timing of when or if these payments will be made is uncertain.

Critical Accounting Estimates

The discussion and analysis of our consolidated financial condition and results of operations are based upon our consolidated financial statements, which have been prepared in conformity with GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, and expenses, and related disclosure of contingent assets and liabilities reported in our consolidated financial statements. The estimation process requires assumptions to be made about future events and conditions and, as a result, is inherently subjective and uncertain. Actual results could differ materially from our estimates.

The SEC defines critical accounting policies as those that are, in management's view, most important to the portrayal of our financial condition and results of operations and most demanding of our judgment. We consider the following policies to be critical to an understanding of our consolidated financial statements and the uncertainties associated with the complex judgments made by us that could impact our results of operations, financial position, and cash flows.

Revenue Recognition

Under Accounting Standards Codification ("ASC") Topic 606 - *Revenue from Contracts with Customers ("*ASC 606") we recognize revenue when a customer obtains control of the promised goods or services, in an amount that reflects the consideration which we expect to be entitled in exchange for those goods or services. We had no contracts with customers until the FDA approved NERLYNX on July 17, 2017. Subsequent to receiving FDA approval, we entered into a limited number of arrangements with specialty pharmacies and specialty distributors in the United States to distribute NERLYNX. These arrangements are our initial contracts with customers. We have determined that these sales channels with customers are similar.

Product Revenue, Net:

We sell NERLYNX to a limited number of specialty pharmacies and specialty distributors in the United States. These customers subsequently resell our products to patients and certain medical centers or hospitals. In addition to distribution agreements with these customers, we enter into arrangements with healthcare providers and payors that provide for government mandated and/or privately negotiated rebates, chargebacks and discounts with respect to the purchase of our products. Product revenue also consists of product sales under sub-license agreements to our sub-licensees, who then sell into their respective international territories.

We recognize revenue on product sales when the specialty pharmacy or specialty distributor, as applicable, obtains control of our product, which occurs at a point in time (upon delivery). Product revenue is recorded net of applicable reserves for variable consideration.

Shipping and handling costs for product shipments occur prior to the customer obtaining control of the goods and are recorded in cost of sales.

Reserves for Variable Consideration:

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between us and our customers, payors, and other indirect customers relating to the sale of our products. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable or a current liability. These estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Our analyses also contemplated application of the constraint in accordance with the guidance, under which we determined a significant reversal of revenue would not occur in a future period for the estimates detailed below as of December 31, 2025 and, therefore, the transaction price was not reduced further during the year ended December 31, 2025. 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.

Trade Discounts and Allowances:

We generally provide customers with discounts which include incentive fees that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we compensate (through trade discounts and allowances) our customers for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations.

Product Returns:

Consistent with industry practice, we offer the specialty pharmacies and specialty distributors limited product return rights for damaged and expiring products, provided it is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reduction to accounts receivables, net on the consolidated balance sheets. We currently estimate product returns using our sales information, including our visibility into the inventory remaining in the distribution channel. We have an insignificant amount of returns to date and believe that returns of our products will continue to be minimal.

Provider Chargebacks and Discounts:

Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and a reduction to accounts receivable, net on the consolidated balance sheets. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and we generally issue credits for such amounts within a few weeks of the customer's notification to us of the resale. Chargebacks consist of credits that we expect to issue for units that remain in the distribution channel at each reporting period end that we expect will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which we have not yet issued a payment.

Government Rebates:

We are subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the consolidated balance sheets. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Payor Rebates:

We contract with certain private payor organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of our products. We estimate these rebates and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Incentives:

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

License Revenue:

We recognize license revenue under certain of our sub-license agreements that are within the scope of ASC 606. The terms of these agreements may contain multiple performance obligations, which may include licenses and research and development activities. We evaluate these agreements under ASC 606 to determine the distinct performance obligations. Non-refundable, upfront fees that are not contingent on any future performance and require no consequential continuing involvement by us, are recognized as revenue when the license term commences and the licensed data, technology or product is delivered. We defer recognition of non-refundable upfront license fees if the performance obligations are not satisfied.

Prior to recognizing revenue, we make estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration 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 and when the uncertainty associated with the variable consideration is subsequently resolved. Variable consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, we allocate the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure.

Royalty Revenue:

For sub-license agreements that are within the scope of ASC 606, we recognize revenue when the related sales occur in accordance with the sales-based royalty exception under ASC 606-10-55-65. Royalty revenue consists of consideration earned related to international sales of NERLYNX made by our sub-licensees in their respective territories. We recognize royalty revenue when the performance obligations have been satisfied.

Legal Contingencies and Expense

For legal contingencies, we accrue a liability for an estimated loss if the potential loss from any claim or legal proceeding is considered probable and the amount can be reasonably estimated. Legal fees and expenses are expensed as incurred based on invoices or estimates provided by legal counsel. We periodically evaluate available information, both internal and external, relative to such contingencies and adjust the accrual as necessary. We determine whether a contingency should be disclosed by assessing whether a material loss is deemed reasonably possible. In determining whether a loss should be accrued, we evaluate, among other factors, the degree of probability of an unfavorable outcome and the ability to make a reasonable estimate of the amount of the loss (see Note 13–Commitments and Contingencies in the accompanying notes to the financial statements).

Accounting Pronouncements Adopted During the Current Year

ASU 2023-09, Improvements to Income Tax Disclosures

On December 14, 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures (*"*ASU 2023-09*"*).* ASU 2023-09 amends ASC 740, Income Taxes to expand income tax disclosures and requires that the Company disclose (i) the income tax rate reconciliation using both percentages and reporting currency amounts; (ii) specific categories within the income tax rate reconciliation; (iii) additional information for reconciling items that meet a quantitative threshold; (iv) the composition of state and local income taxes by jurisdiction; and (v) the amount of income taxes paid disaggregated by jurisdiction. The Company adopted ASU 2023-09 for the year ended December 31, 2025 on a prospective basis. Accordingly, the expanded disclosures are provided for the year ended December 31, 2025, while prior period disclosures have not been retroactively adjusted and continue to be presented under the previous disclosure requirements. As this update only impacts disclosures, its adoption did not have a material impact on the Company's consolidated financial position, results of operations, or cash flows. See Note 12 *Income Taxes* for additional information.

Recently Issued Accounting Standards

In November 2024, the FASB issued ASU 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures*: The ASU requires more detailed information about specified categories of expenses included in certain expense captions presented on the face of the income statement. This ASU is effective for fiscal years beginning after December 15, 2026, and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The amendments may be applied either (i) prospectively to financial statements issued for reporting periods after the effective date of this ASU or (ii) retrospectively to all prior periods presented in the financial statements. We are currently evaluating the impact of adopting this ASU on our consolidated financial statements and related disclosures.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Some of the securities in which we invest have market risk in that a change in prevailing interest rates may cause the principal amount of the cash equivalents to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents. We invest our excess cash primarily in cash equivalents such as money market investments as of December 31, 2025. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our cash and cash equivalents without significantly increasing risk. Additionally, we established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Because of the short-term maturities of our cash equivalents, we do not believe that a 10% increase in interest rates would have a material effect on the realized value of our cash equivalents.

We also have interest rate exposure as a result of borrowings outstanding under the Athyrium Notes. As of December 31, 2025, the aggregate outstanding principal amounts of the Athyrium Notes was $22.5 million. The Athyrium Notes bear interest at a rate per annum equal to the sum of 8.00% plus the adjusted three-month term SOFR and the lesser of (a) the sum of (i) three-month term SOFR and (ii) 0.26161% (26.161 basis points) and (b) three and one-half of one percent (3.50%) per annum. If overall interest rates had increased by one hundred basis points during the year ended December 31, 2025, our interest expense would have increased by $0.2 million.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

All financial statements and supplementary data required by this Item are listed in Part IV, Item 15 of this Annual Report and are presented beginning on Page F-1.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Exchange Act, is recorded, processed, summarized and reported within the timelines specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosures. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we have evaluated the effectiveness of our disclosure controls and procedures (as defined under Exchange Act Rule 13a-15(e)) as of December 31, 2025. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that these disclosure controls and procedures were effective as of December 31, 2025.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the year ended December 31, 2025, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. 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 accounting principles generally accepted in the United States of America.

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

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2025. Management based its assessment on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework - 2013* (COSO 2013 framework). Based on this evaluation, our management concluded that, as of December 31, 2025, our internal control over financial reporting was effective.

Our internal control over financial reporting as of December 31, 2025 has been audited by KPMG LLP, our independent registered public accounting firm, as stated in their report, which expresses an unqualified opinion on the effectiveness of our internal control over financial reporting as of December 31, 2025.

ITEM 9B. OTHER INFORMATION

During the three months ended December 31, 2025, no director or officer (as defined in Rule 16a-1(f) under the Exchange Act) of the Company adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

Part III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We have adopted an insider trading and compliance policy applicable to our directors, officers and employees, that we believe is reasonably designed to promote compliance with insider trading laws and regulations and the NASDAQ stock exchange listing standards. A copy of our policy is included with this Annual Report on Form 10-K as Exhibit 19.1.

The other information required by this Item will be included in our 2026 Proxy Statement, which will be filed with the SEC in connection with our 2026 Annual Meeting of Stockholders within 120 days after December 31, 2025, and is incorporated by reference herein.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item will be included in our 2026 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

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

The information required by this Item will be included in our 2026 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

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

The information required by this Item will be included in our 2026 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item will be included in our 2026 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

Part IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

Reference is made to the Index to Consolidated Financial Statements beginning on Page F-1 hereof.

Consolidated Financial Statement Schedules

(a) Documents Filed as Part of Report

(1) Consolidated Financial Statements

(2) Consolidated Financial Statement Schedules

Consolidated Financial Statement Schedules have been omitted because they are either not required or not applicable, or because the information required to be presented is included in the consolidated financial statements or the notes thereto included in this Annual Report.

(3) Exhibits

The exhibits listed on the accompanying Exhibit Index are filed or incorporated by reference as part of this Annual Report and such Exhibit Index is incorporated by reference herein.

ITEM 16. FORM 10-K SUMMARY

None.

EXHIBIT INDEX

Exhibit Number	Description
2.1	Agreement and Plan of Merger, dated September 29, 2011, by and among Innovative Acquisitions Corp., IAC Merger Corporation, a Delaware corporation and wholly-owned subsidiary of the Company, and Puma Biotechnology, Inc., a Delaware corporation (filed as Exhibit 2.1 to the Company's Current Report on Form 8-K filed with the SEC on October 4, 2011 and incorporated herein by reference)
3.1	Certificate of Merger relating to the merger of IAC Merger Corporation with and into Puma Biotechnology, Inc., filed with the Secretary of State of Delaware on October 4, 2011 (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)
3.2	Certificate of Ownership and Merger relating to the merger of Puma Biotechnology, Inc. with and into Innovative Acquisitions Corp., filed with the Secretary of State of the State of Delaware on October 4, 2011 (filed as Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)
3.3	Second Amended and Restated Certificate of Incorporation of the Company, as filed with the Secretary of State of the State of Delaware on June 14, 2016 (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on June 15, 2016 and incorporated herein by reference)
3.4	Fifth Amended and Restated Bylaws of the Company (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on June 24, 2025 and incorporated herein by reference)
4.1	Form of Common Stock Certificate (filed as Exhibit 4.1 to the Company's Registration Statement on Form S-1/A filed with the SEC on February 1, 2012 and incorporated herein by reference)
4.2#	Warrant to Purchase Shares of Common Stock of Puma Biotechnology, Inc., dated October 4, 2011, issued to Alan H. Auerbach (filed as Exhibit 4.2 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)
4.2(a)#	Amendment to Warrant to Purchase Shares of Common Stock of Puma Biotechnology, Inc., dated April 1, 2021, by and between the Company and Alan H. Auerbach (filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed with the SEC on June 17, 2021 and incorporated herein by reference)
4.3+	Description of the Company's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934
10.1(a)*	License Agreement, dated August 18, 2011, by and between the Company, as successor to Puma Biotechnology, Inc., and Pfizer Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed with the SEC on December 16, 2011 and incorporated herein by reference)
10.1(b)*	Amendment No. 1 to License Agreement dated July 18, 2014, between the Company and Pfizer Inc. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 10, 2014 and incorporated herein by reference)
10.1(c)**	Pfizer Letter Agreement dated June 8, 2020, by and between the Company and Pfizer Inc. (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 6, 2020 and incorporated herein by reference)
10.1(d)**	Amendment No. 2 to License Agreement dated October 29, 2020, between the Company and Pfizer Inc. (filed as Exhibit 10.1(d) to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2021 and incorporated by reference)
10.2(a)#	Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)

10.2(b)#	First Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Appendix A to the Company's Proxy Statement on Form DEFR14A filed with the SEC on June 4, 2014 and incorporated herein by reference)
10.2(c)#	Second Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 10, 2015 and incorporated herein by reference)
10.2(d)#	Third Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 14, 2017 and incorporated herein by reference)
10.2(e)#	Fourth Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the SEC on June 14, 2017 and incorporated herein by reference)
10.2(f)#	Fifth Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 17, 2021 and incorporated herein by reference)
10.2(g)#	Sixth Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 24, 2024 and incorporated herein by reference)
10.2(h)#	Puma Biotechnology, Inc. 2017 Employment Inducement Incentive Award Plan (filed as Exhibit 99.1 to the Company's Registration Statement on Form S-8 filed with the SEC on February 28, 2020 and incorporated herein by reference)
10.2(i)#	First Amendment to Puma Biotechnology, Inc. 2017 Employment Inducement Incentive Award Plan (filed as Exhibit 99.2 to the Company's Registration Statement on Form S-8 filed with the SEC on February 28, 2020 and incorporated herein by reference)
10.2(j)#	Second Amendment to Puma Biotechnology, Inc. 2017 Incentive Award Plan (filed as Exhibit 99.12 to the Company's Current Report on Form S-8 filed with the SEC on September 16, 2021 and incorporated herein by reference)
10.2(k)#	Form of Stock Option Grant Notice and Stock Option Agreement, issued pursuant to the 2011 Incentive Award Plan (filed as Exhibit 10.5 to the Company's Annual Report on Form 10-K filed with the SEC on March 29, 2012 and incorporated herein by reference)
10.2(l)#	Form of Restricted Stock Unit Award Agreement, issued pursuant to the 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on October 17, 2016 and incorporated herein by reference)
10.2(m)#	Form of Stock Option Grant Notice and Stock Option Agreement, issued pursuant to the 2017 Employment Inducement Incentive Award Plan (filed as Exhibit 10.2(k) to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2019 and incorporated herein by reference)
10.2(n)#	Form of Restricted Stock Unit Award Agreement, issued pursuant to the 2017 Employment Inducement Award Plan (filed as Exhibit 10.2(n) to the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2025 and incorporated herein by reference)
10.3(a)	Office Lease by and between the Company and CA - 10880 Wilshire Limited Partnership, executed on December 7, 2011 (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on December 13, 2011 and incorporated herein by reference)
10.3(b)	First Amendment to the Office Lease, dated as of November 28, 2012, by and between the Company and CA - 10880 Wilshire Limited Partnership (filed as Exhibit 10.13(b) to the Company's Annual Report on Form 10-K filed with the SEC on April 1, 2013 and incorporated herein by reference)

10.3(c)	Second Amendment to the Office Lease, dated as of December 3, 2013, by and between the Company and CA - 10880 Wilshire Limited Partnership (filed as Exhibit 10.6(c) to the Company's Annual Report on Form 10-K filed with the SEC on March 3, 2014 and incorporated herein by reference)
10.3(d)	Third Amendment to the Office Lease, dated as of March 18, 2014, by and between the Company and CA - 10880 Wilshire Limited Partnership (filed as Exhibit 10.5(d) to the Company's Annual Report on Form 10-K filed with the SEC on March 2, 2015 and incorporated herein by reference)
10.3(e)	Fourth Amendment to the Office Lease, dated as of July 31, 2015, by and between the Company and CA - 10880 Wilshire Limited Partnership (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 9, 2015 and incorporated herein by reference)
10.3(f)	Fifth Amendment to Office Lease, dated as of October 27, 2017, by and between the Company and DE PARK AVENUE 10880, LLC (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 7, 2025 and incorporated herein by reference)
10.3(g)	Sixth Amendment to Office Lease, dated as of July 23, 2025, by and between the Company and DE PARK AVENUE 10880, LLC (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 7, 2025 and incorporated herein by reference)
10.4#	Employment Agreement, dated January 19, 2012, by and between the Company and Alan H. Auerbach (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on January 24, 2012 and incorporated herein by reference)
10.5(a)	Office Lease by and between DWF III Gateway, LLC and the Company, executed June 7, 2012 (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 13, 2012 and incorporated herein by reference)
10.5(b)	First Amendment to Lease, dated as of May 19, 2014, by and between DWF III Gateway, LLC and Puma Biotechnology, Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on May 23, 2014 and incorporated herein by reference)
10.5(c)	Second Amendment to Lease, dated as of June 10, 2014, by and between DWF III Gateway, LLC and Puma Biotechnology, Inc. (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 10, 2015 and incorporated herein by reference)
10.5(d)	Third Amendment to Lease, dated as of July 21, 2015, by and between PR 707 Gateway, LLC (as successor in interest to DWF III Gateway, LLC) and the Company (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 9, 2015 and incorporated herein by reference)
10.6#	Form of Indemnification Agreement (filed as Exhibit 10.17 to the Company's Registration Statement on Form S-1/A filed with the SEC on October 15, 2012 and incorporated herein by reference)
10.7(a)#+	Amended Non-Employee Director Compensation Program, effective April 1, 2026
10.7(b)#	Amended Non-Employee Director Compensation Program, dated April 27, 2022 (filed as Exhibit 10.1 to the Company's Current Report on Form 10-Q filed with the SEC on May 5, 2022 and incorporated herein by reference)
10.8(a)*	License Agreement, dated November 20, 2017, by and between the Company and Specialised Therapeutics Asia Pte Ltd. (filed as Exhibit 10.13 to the Company's Annual Report on Form 10-K filed with the SEC on March 9, 2018 and incorporated herein by reference)
10.8(b)*	Amendment No. 1, dated April 20, 2018, to the License Agreement by and between the Company and Specialised Therapeutics Asia Pte Ltd. (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018 and incorporated herein by reference)

10.9#	Letter Agreement, dated December 8, 2017, between the Company and Douglas Hunt (filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K filed with the SEC on March 9, 2018 and incorporated herein by reference)
10.10(a)*	Collaboration and License Agreement, dated January 30, 2018, between the Company and CANbridge Biomed Limited (as successor in interest to CANbridgepharma Limited) (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2018 and incorporated herein by reference)
10.10(b)*	Side Letter Agreement, dated November 19, 2018, between the Company and CANbridge Biomed Limited (as successor in interest to CANbridgepharma Limited) (filed as Exhibit 10.15(b) to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2019 and incorporated herein by reference)
10.10(c)**	Termination Agreement, dated February 24, 2021, by and between the Company and CANbridge BIOMED Limited (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 6, 2021 and incorporated herein by reference)
10.11*	License Agreement, dated March 30, 2018, between the Company and Pint Pharma International SA (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2018 and incorporated herein by reference)
10.12*	Supply Agreement, dated April 20, 2018, by and between the Company and Specialised Therapeutics Asia Pte. Ltd. (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018 and incorporated herein by reference)
10.13#	Letter Agreement, dated September 28, 2018, between the Company and Maximo F. Nougues (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on November 9, 2018 and incorporated herein by reference)
10.14(a)*	License Agreement, dated January 9, 2019, by and between the Company and Knight Therapeutics Inc. (filed as Exhibit 10.19 to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2019 and incorporated herein by reference)
10.14(b)**	Amendment to the License Agreement, dated December 18, 2019, by and between the Company and Knight Therapeutics, Inc. (filed as Exhibit 10.17(b) to the Company's Annual Report on Form 10-K filed with the SEC on February 28, 2020 and incorporated herein by reference)
10.15(a)**	License Agreement, dated March 29, 2019, by and between the Company and Pierre Fabre Medicament SAS (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2019 and incorporated herein by reference)
10.15(b)**	First Amendment to the License Agreement, dated September 17, 2019, by and between the Company and Pierre Fabre Medicament SAS (filed as Exhibit 10.18(b) to the Company's Annual Report on Form 10-K filed with the SEC on February 28, 2020 and incorporated herein by reference)
10.15(c)**	Second Amendment to the License Agreement, dated November 25, 2019, by and between the Company and Pierre Fabre Medicament SAS (filed as Exhibit 10.18(c) to the Company's Annual Report on Form 10-K filed with the SEC on February 28, 2020 and incorporated herein by reference)
10.15(d)**	Amendment No. 3 to the License Agreement, dated February 24, 2021, by and between the Company and Pierre Fabre Medicament SAS (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 6, 2021 and incorporated herein by reference)
10.16(a)**	Note Purchase Agreement, dated July 23, 2021, by and between the Company and Athyrium Opportunities IV Co-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 4, 2021 and incorporated herein by reference)

10.16(b)**	First Amendment to Note Purchase Agreement, dated February 8, 2022, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.18(b) to the Company's Annual Report on Form 10-K filed with the SEC on March 3, 2022 and incorporated herein by reference)
10.16(c)	Second Amendment to Note Purchase Agreement, dated May 18, 2022, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.17(c) to the Company's Annual Report on Form 10-K filed with the SEC on March 2, 2023 and incorporated herein by reference)
10.16(d)	Third Amendment to Note Purchase Agreement, dated September 16, 2022, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 3, 2022 and incorporated herein by reference)
10.16(e)**	Fourth Amendment to Note Purchase Agreement, dated November 29, 2022, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.17(e) to the Company's Annual Report on Form 10-K filed with the SEC on March 2, 2023 and incorporated herein by reference)
10.16(f)	Limited Waiver and Fifth Amendment to Note Purchase Agreement, dated July 7, 2023, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 3, 2023, and incorporated herein by reference)
10.16(g)	Sixth Amendment to Note Purchase Agreement, dated September 8, 2023, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 2, 2023, and incorporated herein by reference)
10.16(h)	Seventh Amendment to Note Purchase Agreement and Third Amendment to Disclosure Letter, dated April 12, 2024, by and between the Company and Athyrium Opportunities IV CO-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 2, 2024, and incorporated herein by reference)
10.16(i)	Eighth Amendment to Note Purchase Agreement and Fourth Amendment to Disclosure Letter, dated October 6, 2025, by and between the Company and Athyrium Opportunities IV Co-Invest 1 LP, as Administrative Agent (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 6, 2025, and incorporated herein by reference)
10.17	Open Market Sale Agreement[SM], dated November 4, 2021, by and between the Company and Jeffries LLC (filed as Exhibit 1.1 to the Company's Current Report on Form 8-K filed with the SEC on November 4, 2021 and incorporated herein by reference)
10.18**	Exclusive License Agreement, dated September 16, 2022, by and between the Company and Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 3, 2022 and incorporated herein by reference)
19.1	Insider Trading and Compliance Policy
21.1+	Subsidiary
23.1+	Consent of KPMG LLP
24.1+	Power of Attorney (included on signature page)

31.1+	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2+	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1++	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2++	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
97.1	Puma Biotechnology, Inc. Policy for Recovery of Erroneously Awarded Compensation (filed as Exhibit 97.1 to the Company's Annual Report on Form 10-K filed with the SEC on February 29, 2024 and incorporated herein by reference)
101.INS+	Inline XBRL Instance Document
101.SCH+	Inline XBRL Taxonomy Extension Schema Document
101.CAL+	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF+	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB+	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE+	Inline XBRL Taxonomy Extension Linkbase Document
104+	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)
+	Filed herewith
++	Furnished herewith
*	Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 24b-2 under the Securities Exchange Act of 1934.
**	Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Regulation S-K, Item 601(b)(10) or certain schedules and attachments to this exhibit have been omitted pursuant to Regulation S-K, Item 601(a)(5). Such omitted information is not material and would likely cause competitive harm to the registrant if publicly disclosed.
#	Management contract or compensatory plan or arrangement.

Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on February 26, 2026.

PUMA BIOTECHNOLOGY, INC.

By: /s/ Alan H. Auerbach
Alan H. Auerbach
President & Chief Executive Officer

Power of Attorney

KNOWN BY ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Alan H. Auerbach and Maximo Nougues, or either of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K and any documents related to this report and filed pursuant to the Securities Exchange Act of 1934, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitute or substitutes may lawfully do or cause to be done by virtue hereof. This power of attorney shall be governed by and construed with the laws of the State of Delaware and applicable federal securities laws.

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

Signature	Date
/s/ Alan H. Auerbach Alan H. Auerbach (Principal Executive Officer)	February 26, 2026
/s/ Maximo Nougues Maximo Nougues (Principal Financial Officer and Principal Accounting Officer)	February 26, 2026
/s/ Alessandra Cesano Alessandra Cesano	February 26, 2026
/s/ Allison Dorval Allison Dorval	February 26, 2026
/s/ Michael P. Miller Michael P. Miller	February 26, 2026
/s/ Jay M. Moyes Jay M. Moyes	February 26, 2026
/s/ Adrian M. Senderowicz Adrian M. Senderowicz	February 26, 2026
/s/ Brian M. Stuglik Brian M. Stuglik	February 26, 2026
/s/ Troy E. Wilson Troy E. Wilson	February 26, 2026

PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARY
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Puma Biotechnology, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Puma Biotechnology, Inc. and subsidiary (the Company) as of December 31, 2025 and 2024, the related consolidated statements of operations, comprehensive income, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2025, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2025, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2025, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025 based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated 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 consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Estimate of certain variable consideration related to product revenue, net

As discussed in Note 2 to the consolidated financial statements, the Company recognizes product revenue, net that includes estimates of variable consideration. For the year ended December 31, 2025, the Company recorded product revenue, net of $204.1 million. The components of variable consideration include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives. These estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method in Accounting Standards Codification (ASC) 606, Revenue from Contracts with Customers. The range of possible outcomes is driven by relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns.

We identified the estimate of variable consideration for provider chargebacks and government rebates, including consideration of the constraint on variable consideration, related to product revenue, net as a critical audit matter. Evaluating the key assumptions of forecasted patient buying and payment patterns underlying the estimate for provider chargebacks and government rebates involved especially challenging auditor judgment due to their measurement uncertainty. These key assumptions relate to estimating which of the Company's revenue transactions will ultimately be subject to a related provider chargeback or government rebate.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to the development of the key assumptions used to determine variable consideration for provider chargebacks and government rebates, including consideration of the constraint on variable consideration. We evaluated the forecasted patient buying and payment patterns used to determine the provider chargebacks and government rebates by comparing them to the Company's historical data, statutory information, and executed third-party contracts. We assessed the Company's assumed patient buying and payment patterns by (1) independently recalculating historical actual patient buying and payment pattern rates based on historical actual claim data, and (2) comparing current period forecasts to historical actual rates. We evaluated the Company's ability to accurately estimate provider chargebacks and government rebates, including consideration of the constraint on variable consideration, by comparing historically recorded accruals to the actual amount that was ultimately paid by the Company.

KPMG LLP

We have served as the Company's auditor since 2017.

Los Angeles, California
February 26, 2026

PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARY
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31, 2025	December 31, 2024
ASSETS		
Current assets:		
Cash and cash equivalents	$ 29,635	$ 69,219
Marketable securities	67,893	31,746
Accounts receivable, net of allowance for credit loss of $0 and $362	53,654	32,011
Inventory	5,515	8,724
Prepaid expenses, current	3,642	5,867
Restricted cash, current	2,091	—
Other assets, current	256	91
Total current assets	162,686	147,658
Lease right-of-use assets, net	5,373	4,579
Property and equipment, net	187	515
Intangible assets, net	41,392	51,131
Restricted cash, long-term	—	2,091
Deferred tax assets	3,830	7,075
Prepaid expenses and other, long-term	2,834	284
Total assets	$ 216,302	$ 213,333
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 5,056	$ 5,509
Accrued expenses, current	50,031	36,898
Lease liabilities, current	1,314	5,540
Post-marketing commitment liability	2,187	2,835
Current portion of long-term debt	22,523	45,329
Other liabilities, current	142	—
Total current liabilities	81,253	96,111
Lease liabilities, long-term	4,709	1,494
Post-marketing commitment liability, long-term	—	1,763
Long-term debt, net	—	21,719
Other liabilities, long-term	—	121
Total liabilities	85,962	121,208
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Common stock - $.0001 par value per share; 100,000,000 shares authorized; 50,408,023 shares issued and outstanding at December 31, 2025 and 49,105,834 issued and outstanding at December 31, 2024	5	5
Additional paid-in capital	1,414,074	1,407,000
Accumulated other comprehensive income	36	6
Accumulated deficit	(1,283,775)	(1,314,886)
Total stockholders' equity	130,340	92,125
Total liabilities and stockholders' equity	$ 216,302	$ 213,333

See Accompanying Notes to the Consolidated Financial Statements

PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)

	For the Year Ended December 31,		
	2025	**2024**	**2023**
Revenues:			
Product revenue, net	$ 204,074	$ 195,186	$ 203,107
Royalty revenue	24,297	35,282	32,530
Total revenue	228,371	230,468	235,637
Operating costs and expenses:			
Cost of sales	58,157	64,404	62,682
Selling, general and administrative	70,847	80,163	89,933
Research and development	62,068	54,935	50,382
Total operating costs and expenses	191,072	199,502	202,997
Income from operations	37,299	30,966	32,640
Other income (expenses):			
Interest income	4,078	4,724	2,605
Interest expense	(6,622)	(12,452)	(13,330)
Other income	1,027	862	759
Total other expenses, net	(1,517)	(6,866)	(9,966)
Net income before income taxes	$ 35,782	$ 24,100	$ 22,674
Current income tax (expense)	(1,426)	(897)	(1,083)
Deferred income tax (expense) benefit	(3,245)	7,075	—
Net income	$ 31,111	$ 30,278	$ 21,591
Net income per share of common stock—basic	$ 0.62	$ 0.62	$ 0.46
Net income per share of common stock—diluted	$ 0.61	$ 0.62	$ 0.45
Weighted-average shares of common stock outstanding—basic	50,011,485	48,648,701	47,134,331
Weighted-average shares of common stock outstanding—diluted	50,653,283	49,100,433	47,550,852

See Accompanying Notes to the Consolidated Financial Statements

PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME
(in thousands)

	For the Year Ended December 31,		
	2025	**2024**	**2023**
Net income	$ 31,111	$ 30,278	21,591
Other comprehensive income:			
Unrealized gain (loss) on available-for-sale securities, net of tax of $0	30	10	(4)
Comprehensive income	$ 31,141	$ 30,288	$ 21,587

See Accompanying Notes to the Consolidated Financial Statements

PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share and per share data)

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	Common Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	
	Shares	Amount	Capital	Income (Loss)	Deficit	Total
Balance at December 31, 2022	46,345,660	$ 5	$ 1,388,358	$ —	$ (1,366,755)	$ 21,608
Stock-based compensation	—	—	10,247	—	—	10,247
Shares issued or restricted stock units vested under employee stock plans	1,301,127	—	—	—	—	—
Unrealized loss on available-for-sale securities	—	—	—	(4)	—	(4)
Net income	—	—	—	—	21,591	21,591
Balance at December 31, 2023	47,646,787	$ 5	$ 1,398,605	$ (4)	$ (1,345,164)	$ 53,442
Stock-based compensation	—	—	8,245	—	—	8,245
Shares issued or restricted stock units vested under employee stock plans	1,459,047	—	150	—	—	150
Unrealized gain on available-for-sale securities	—	—	—	10	—	10
Net income	—	—	—	—	30,278	30,278
Balance at December 31, 2024	49,105,834	$ 5	$ 1,407,000	$ 6	$ (1,314,886)	$ 92,125
Stock-based compensation	—	—	6,944	—	—	6,944
Shares issued or restricted stock units vested under employee stock plans	1,302,189	—	130	—	—	130
Unrealized gain on available-for-sale securities	—	—	—	30	—	30
Net income	—	—	—	—	31,111	31,111
Balance at December 31, 2025	50,408,023	$ 5	$ 1,414,074	$ 36	$ (1,283,775)	$ 130,340

See Accompanying Notes to the Consolidated Financial Statements

PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARY
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	For the Year Ended December 31,		
	2025	**2024**	**2023**
Operating activities:			
Net income	$ 31,111	$ 30,278	$ 21,591
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation and amortization	10,938	11,524	11,519
Stock-based compensation	6,944	8,245	10,247
Deferred income taxes	3,245	(7,075)	—
Provision for credit loss recovery	(362)	(519)	881
Loss on disposal of property and equipment	4	—	—
Loss on impairment of asset	—	—	625
Changes in operating assets and liabilities:			
Accounts receivable, net	(21,281)	16,345	(8,368)
Inventory, net	3,209	(1,644)	(2,554)
Prepaid expenses and other	(325)	1,000	820
Other current assets	(165)	821	1,517
Accounts payable	(453)	(1,380)	449
Operating lease assets and liabilities, net	(1,805)	(1,587)	(1,195)
Accrued expenses and other	13,154	(15,823)	(7,583)
Post-marketing commitment liability	(2,412)	(1,267)	(940)
Net cash provided by operating activities	41,802	38,918	27,009
Investing activities:			
Purchase of property and equipment	(71)	(56)	(140)
Purchase of available-for-sale securities	(108,141)	(76,230)	(23,813)
Maturity of available-for-sale securities	72,024	55,848	17,328
Purchase of intangible assets	—	—	(12,500)
Net cash used in investing activities	(36,188)	(20,438)	(19,125)
Financing activities:			
Net proceeds from shares issued under employee stock plans	130	150	—
Payment of debt	(44,440)	(33,330)	—
Payment of exit costs	(888)	(666)	—
Net cash used in financing activities	(45,198)	(33,846)	—
Net (decrease) increase in cash, cash equivalents and restricted cash	(39,584)	(15,366)	7,884
Cash, cash equivalents and restricted cash, beginning of period	71,310	86,676	78,792
Cash, cash equivalents and restricted cash, end of period	31,726	71,310	86,676
Supplemental disclosures of non-cash investing and financing activities:			
Property and equipment purchases in accounts payable	$ 5	$ —	$ 26
Supplemental disclosure of cash flow information:			
Interest paid	$ 5,818	$ 10,769	$ 11,628
Income taxes paid	$ 1,524	$ 1,218	$ 737

See Accompanying Notes to the Consolidated Financial Statements

Note 1—Business and Basis of Presentation

Puma Biotechnology, Inc., (the "Company") is a biopharmaceutical company based in Los Angeles, California that develops and commercializes innovative products to enhance cancer care and improve treatment outcomes for patients. The Company is currently commercializing NERLYNX®, an oral version of neratinib ("NERLYNX"), for the treatment of *HER2*-positive breast cancer. Additionally, the Company in-licensed, and is responsible for global development and commercialization of, alisertib. Alisertib is a selective, small molecule inhibitor of Aurora Kinase A that is designed to disrupt mitosis leading to apoptosis of rapidly proliferating tumor cells dependent on Aurora Kinase. The Company believes alisertib has potential application in the treatment of a range of different cancer types, including hormone receptor-positive breast cancer, triple negative breast cancer and small cell lung cancer.

The Company has one subsidiary, Puma Biotechnology, B.V., a Netherlands company. This subsidiary was established for the purpose of legal representation in the European Union ("EU"). The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All intercompany accounts and transactions have been eliminated.

The accompanying consolidated financial statements of the Company and its subsidiary have been prepared in accordance with generally accepted accounting principles in the United States ("US GAAP").

The Company has incurred significant operating losses since its inception. While the Company has previously reported net income, the Company cannot assure that it will continue to do so and will need to continue to generate significant revenue to sustain operations and successfully commercialize neratinib. In 2017, the Company received U.S. Food and Drug Administration ("FDA") approval for its first product, NERLYNX® (neratinib), formerly known as PB272 (neratinib, oral), for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. Following FDA approval in July 2017, NERLYNX became available by prescription in the United States, and the Company commenced commercialization.

In February 2020, NERLYNX was also approved by the FDA in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.

In 2018, the European Commission ("EC") granted marketing authorization for NERLYNX in the EU for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who are less than one year from the completion of prior adjuvant trastuzumab-based therapy.

The Company is required to make substantial payments to Pfizer upon the achievement of certain milestones and has contractual obligations for clinical trial contracts.

The Company has entered into other exclusive sub-license agreements with various parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved, in many regions outside the United States, including Europe (excluding Ukraine), Australia, Canada, China, Southeast Asia, Israel, South Korea, Russia and various countries and territories in Central America, South America, Africa and the Middle East. The Company plans to continue to pursue commercialization of NERLYNX in other countries outside the United States, if approved.

In September 2022, the Company entered into an exclusive license agreement with a subsidiary of Takeda Pharmaceutical Company Limited ("Takeda") to license the worldwide research and development and commercial rights to alisertib, a selective, small-molecule, orally administered inhibitor of Aurora Kinase A. Alisertib is an adenosine triphosphate–competitive and reversible inhibitor of Aurora Kinase A and results in disruption of mitosis leading to apoptosis of rapidly proliferating tumor cells that are dependent on Aurora Kinase A. Alisertib has been tested in clinical trials in patients with metastatic cancers including breast cancer, small cell lung cancer, head and neck cancer, ovarian cancer, peripheral T cell lymphoma and acute myeloid leukemia. Under the terms of the exclusive license agreement, the Company assumed sole responsibility for the global development and commercialization of alisertib. The Company paid Takeda an upfront license fee of $7.0 million in October 2022 and Takeda is eligible to receive potential future milestone payments of up to $287.3 million upon the Company's achievement of certain regulatory and commercial milestones over the course of the exclusive license agreement, as well as tiered royalty payments for any net sales of alisertib. As of December 31, 2025, no milestones had been accrued as the underlying contingencies were not probable or estimable.

The Company has reported net income of approximately $31.1 million and cash provided by operations of approximately $41.8 million for the year ended December 31, 2025. The Company's commercialization, research and development or marketing efforts may require funding in addition to the cash and cash equivalents and marketable securities totaling approximately $97.5 million at December 31, 2025. The Company believes that its existing cash and cash equivalents and marketable securities as of December 31, 2025 and proceeds that will become available to the Company through product sales and sub-license payments are sufficient to satisfy its operating cash needs, including amounts due under the Company's Note Purchase Agreement with Athyrium, Opportunities IV Co-Invest 1 LP ("Athyrium") (see Note 9—Debt), for at least one year after the filing of the Annual Report on Form 10-K in which these financial statements are included. The Company continues to remain dependent, in part, on its ability to obtain sufficient funding to sustain operations and continue to successfully commercialize neratinib in the United States. While the Company has been successful in raising capital in the past, there can be no assurance that it will be able to do so in the future. The Company's ability to obtain funding may be adversely impacted by uncertain market and economic conditions, including the Company's success in commercializing neratinib and unfavorable decisions of regulatory authorities or adverse clinical trial results. The outcome of these matters cannot be predicted at this time. Additionally, the terms of the Company's Note Purchase Agreement place restrictions on the Company's ability to operate the business and on the Company's financial flexibility, and the Company may be unable to achieve the revenue necessary to satisfy the minimum revenue and cash balance covenants as specified in the agreement.

Since its inception through December 31, 2025, the Company's financing has primarily been proceeds from product, royalty, and license revenue, public offerings of its common stock, private equity placements, and various debt instruments.

The Company does not believe that tariffs imposed or proposed to be imposed by the United States, particularly with the EU and China, will have a material impact on our product costs or results of operations. However, shifts in trade policies in the United States and other countries have been rapidly evolving and are difficult to predict. The ultimate impact of any announced or future tariffs will depend on various factors, including what tariffs are ultimately implemented, the timing of implementation and the amount, scope and nature of such tariffs and potential exclusions from the application of those tariffs.

Note 2—Significant Accounting Policies

The significant accounting policies followed in the preparation of these consolidated financial statements are as follows:

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All intercompany balances and transactions have been eliminated in consolidation.

Segment Reporting

Management has determined that the Company operates in one reporting segment, which is the development and commercialization of innovative products to enhance cancer care. The Company derives its global product, license and royalty revenue through the sales of NERLYNX®. The majority of our royalty revenue is derived from our sub-licensee sales into China. The accounting policies of this operating segment are the same as those described below in Note 2– Significant Accounting Policies.

The Company's Chief Operating Decision Maker ("CODM") is its President, Chief Executive Officer and Chairman of the Board, Alan H. Auerbach. The CODM primarily uses our Consolidated Statement of Operations and related revenues, expenses and net income in evaluating the performance of the single operating segment and determining how to allocate resources of the Company as a whole, including its sales force and related marketing, research and development programs, including alisertib, and licensing strategy. Consolidated revenue, expenses and net income are also used to monitor budget versus actual results.

In addition to the significant expense categories included within consolidated net income presented on the Company's Consolidated Statements of Operations, see below for disaggregated amounts that comprise operating expenses:

	For the Year Ended December 31,		
	2025	2024	2023
Cost of sales	$ 58,157	$ 64,404	$ 62,682
General and administrative	25,553	36,749	37,892
Commercialization	41,010	37,849	45,132
Research and development:			
Clinical research and development	31,754	24,715	17,784
Medical affairs	5,494	4,605	6,751
Other research and development (1)	22,160	22,935	22,508
Operating costs and expenses	184,128	191,257	192,750
Stock based compensation	6,944	8,245	10,247
Total operating costs and expenses	$ 191,072	$ 199,502	$ 202,997

(1) Other research and development expense includes regulatory affairs, pharmacovigilance, quality assurance, chemical manufacturing and other costs.

Use of Estimates

The preparation of consolidated financial statements in conformity with Generally Accepted Accounting Principles ("GAAP") in the United States requires management to make estimates and assumptions that affect reported amounts of assets and liabilities, and disclosure of contingent assets and liabilities at the date of the balance sheet, and reported amounts of revenues and expenses for the period presented. Accordingly, actual results could differ from those estimates.

Significant estimates include estimates for variable consideration for which reserves were established. These estimates are included in the calculation of net revenues and include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between the Company and its customers, payors, and other indirect customers relating to the Company’s sale of its products. Other significant estimates include those related to the valuation of deferred income taxes, legal and other expense accruals.

Reclassifications

Certain prior year amounts in the Consolidated Statements of Cash Flows have been reclassified to correct an error in the prior year's presentation. Specifically, for the year ended December 31, 2024, a change in deferred tax assets of $7.1 million was previously classified within "Changes in operating assets and liabilities." This amount has been reclassified to non-cash items within the operating activities section of the Consolidated Statements of Cash Flows. This reclassification had no impact on the total net cash provided by (used in) operating activities, net income, or the Consolidated Balance Sheets for any period presented.

Net Income per Share of Common Stock

Basic net income per share of common stock is computed by dividing net income available to common stockholders by the weighted average number of shares of common stock outstanding during the periods presented, as required by Accounting Standard Codification ("ASC 260"), *Earnings per Share*. For purposes of calculating diluted net income per share of common stock, the denominator includes both the weighted average number of shares of common stock outstanding and the number of dilutive common stock equivalents, such as stock options, restricted stock units (“RSUs”) and warrants. A common stock equivalent is not included in the denominator when calculating diluted earnings per common share if the effect of such common stock equivalent would be anti-dilutive.

Our potentially dilutive securities include potential common shares related to our stock options and RSUs granted in connection with the Puma Biotechnology, Inc. 2011 Incentive Award Plan and the Puma Biotechnology, Inc. 2017 Employment Inducement Incentive Award Plan. Diluted earnings per share (“Diluted EPS”) considers the impact of potentially dilutive securities except in periods in which there is a loss because the inclusion of the potential common shares would have an anti-dilutive effect. Diluted EPS excludes the impact of potential common shares related to our stock options in periods in which the option exercise price is greater than the average market price of our common stock for the

period. The following potentially dilutive outstanding common stock equivalents for the respective periods were excluded from diluted net income per share because of their anti-dilutive effect:

	For the Year Ended December 31,	
	2025	2024
Options outstanding	3,504,811	3,533,693
Warrant outstanding	2,116,250	2,116,250
Unvested restricted stock units	110,902	734,236
Totals	5,731,963	6,384,179

Revenue Recognition

Under ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606") the Company recognizes revenue when its customer obtains control of the promised goods or services in an amount that reflects the consideration that the entity expects to be entitled in exchange for those goods or services. The Company had no contracts with customers until the FDA approved NERLYNX on July 17, 2017. Subsequent to receiving FDA approval, the Company entered into a limited number of arrangements with specialty pharmacies and specialty distributors in the United States to distribute NERLYNX. These arrangements are the Company's initial contracts with customers. The Company has determined that these sales channels with customers are similar.

Product Revenue, Net

The Company sells NERLYNX to a limited number of specialty pharmacies and specialty distributors in the United States. These customers subsequently resell the Company's products to patients and certain medical centers or hospitals. In addition to distribution agreements with these customers, the Company enters into arrangements with healthcare providers and payors that provide for government mandated and/or privately negotiated rebates, chargebacks and discounts with respect to the purchase of the Company's products.

The Company recognizes revenue on product sales when the specialty pharmacy or specialty distributor, as applicable, obtains control of the Company's product, which occurs at a point in time (upon delivery). Product revenue is recorded net of applicable reserves for variable consideration, including discounts and allowances. The Company's payment terms range between 10 and 68 days.

Product revenue also consists of product sales under sub-license agreements to our sub-licensees, who then sell into their respective international territories.

Shipping and handling costs for product shipments occur prior to the customer obtaining control of the goods and are recorded in cost of sales.

If taxes relating to product sales should be collected from customers and remitted to governmental authorities, they will be excluded from revenue. The Company expenses incremental costs of obtaining a contract when incurred if the expected amortization period of the asset that the Company would have recognized is one year or less. However, no such costs were incurred during the year ended December 31, 2025.

For the year ended December 31, 2025, five customers individually comprised approximately 27.3%, 17.0%, 16.4%, 13.1% and 10.6%, respectively, of the Company's total product revenue. For the year ended December 31, 2024, four customers individually comprised approximately 28.4%, 18.8%, 14.1% and 12.3%, respectively, of the Company's total product revenue. For the year ended December 31, 2023, four customers individually comprised approximately 31.4%, 17.2%, 15.2% and 11.9%, respectively, of the Company's total product revenue.

Reserves for Variable Consideration

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between the Company and its customers, payors, and other indirect customers relating to the Company's sale of its products. These reserves, as detailed below, are based on the related sales, and are classified as reductions of accounts receivable, net when the right of offset

exists in accordance with Accounting Standards Update ("ASU") 2013-1, *Balance Sheet (Topic 210): Clarifying the Scope of Disclosures about Offsetting Assets and Liabilities*, or as a current liability. These estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. The Company's analyses also contemplated application of the constraint in accordance with the guidance, under which it determined a significant reversal of revenue would not likely occur in a future period for the estimates detailed below as of December 31, 2025 and, therefore, the transaction price was not reduced further during the year ended December 31, 2025. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances

The Company generally provides customers with discounts, which include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. The reserve for discounts is established in the same period that the related revenue is recognized, together with reductions to accounts receivable, net on the consolidated balance sheets. In addition, the Company compensates its customers for sales order management, data, and distribution services. The Company has determined such services received to date are not distinct from the Company's sale of products to its customers and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations.

Product Returns

Consistent with industry practice, the Company offers the specialty pharmacies and specialty distributors that are its customers limited product return rights for damaged and expiring product, provided it is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reduction to accounts receivables, net on the consolidated balance sheets. The Company currently estimates product returns using its own sales information, including its visibility into the inventory remaining in the distribution channel. The Company has an insignificant number of returns to date and believes that returns of its products will continue to be minimal.

Provider Chargebacks and Discounts

Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to its customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. The reserve for chargebacks is established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and a reduction to accounts receivable, net on the consolidated balance sheets. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the customer's notification to the Company of the resale. Chargebacks consist of credits the Company expects to issue for units that remain in the distribution channel at each reporting period end that the Company expects will be sold to qualified healthcare providers and chargebacks that customers have claimed, but for which the Company has not yet issued a payment.

Government Rebates

The Company is subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue, net and the establishment of a current liability, which is included in accrued expenses on the consolidated balance sheets. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Payor Rebates

The Company contracts with certain private payor organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue, net and the establishment of a current liability, which is included in accrued expenses on the consolidated balance sheets.

Other Incentives

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

License Revenue

The Company also recognizes license revenue under certain of the Company's sub-license agreements that are within the scope of ASC 606. The terms of these agreements may contain multiple performance obligations, which may include licenses and research and development activities. The Company evaluates these agreements under ASC 606 to determine the distinct performance obligations. Non-refundable, upfront fees that are not contingent on any future performance and require no consequential continuing involvement by the Company, are recognized as revenue when the license term commences and the licensed data, technology or product is delivered. The Company defers recognition of non-refundable upfront license fees if the performance obligations are not satisfied. The Company's payment terms range between the execution date of the sub-license agreement and 45 days.

Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration 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 and when the uncertainty associated with the variable consideration is subsequently resolved.

If there are multiple distinct performance obligations, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure.

Since 2018, the Company has entered into sub-license agreements with certain sub-licensees in territories outside of the United States. These sub-licensing agreements grant certain intellectual property rights and set forth various obligations with respect to actions such as development, pursuit and maintenance of regulatory approvals, commercialization and supply of NERLYNX in the sub-licensees' respective territories.

License fees under the sub-license agreements include one-time upfront payments when each sub-license agreement was executed and potential additional one-time milestone payments due to the Company upon successful completion of certain performance obligations, such as achieving regulatory approvals or sales target thresholds, and potential double-digit royalties on sales of the licensed product, calculated as a percentage of net sales of the licensed product throughout each sub-licensee's respective territory. As of December 31, 2025, the total potential milestone payments that would be due to the Company upon achievement of all respective performance obligations under the sub-license agreements is approximately $579.8 million. At this time, the Company cannot estimate if or when these milestone-related performance obligations might be achieved.

Royalty Revenue

For sub-license agreements that are within the scope of ASC 606, the Company recognizes revenue when the related sales occur in accordance with the sales-based royalty exception under ASC 606-10-55-65. Royalty revenue consists of consideration earned related to international sales of NERLYNX made by the Company's sub-licensees in their respective territories. The Company recognizes royalty revenue when the performance obligations have been satisfied. The Company's payment terms range between 10 and 60 days.

Royalty Expenses

Royalties incurred in connection with the Company's license agreement with Pfizer, as disclosed in Note 13– Commitments and Contingencies, are expensed to cost of sales as revenue from product sales is recognized.

Legal Contingencies and Expense

For legal contingencies, the Company accrues a liability for an estimated loss if the potential loss from any claim or legal proceeding is considered probable and the amount can be reasonably estimated. Legal fees and expenses are expensed as incurred based on invoices or estimates provided by legal counsel. The Company periodically evaluates available information, both internal and external, relative to such contingencies and adjusts the accrual as necessary. The Company determines whether a contingency should be disclosed by assessing whether a material loss is deemed reasonably possible. In determining whether a loss should be accrued, the Company evaluates, among other factors, the degree of probability of an unfavorable outcome and the ability to make a reasonable estimate of the amount of the loss (see Note 13-Commitments and Contingencies).

Research and Development Expenses

Research and development ("R&D") expenses are charged to operations as incurred. The major components of research and development costs include clinical manufacturing costs, clinical trial expenses, consulting and other third-party costs, salaries and employee benefits, stock-based compensation expense, supplies and materials, and allocations of various overhead costs. Clinical trial expenses include, but are not limited to, investigator fees, site costs, comparator drug costs, and clinical research organization ("CRO") costs. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the ongoing development of potential products. The financial terms of these agreements are subject to negotiation and variations from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful enrollment of patients and the completion of portions of the clinical trial or similar conditions. The Company's accruals for clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with numerous clinical trial sites, cooperative groups and CROs. As actual costs become known, the Company adjusts its accruals in that period.

In instances where the Company enters into agreements with third parties for clinical trials and other consulting activities, upfront amounts are recorded to prepaid expenses and other in the accompanying consolidated balance sheets and expensed as services are performed or as the underlying goods are delivered. If the Company does not expect the services to be rendered or goods to be delivered, any remaining capitalized amounts for non-refundable upfront payments are charged to expense immediately. Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments and payments upon the completion of milestones or receipt of deliverables.

Costs related to the acquisition of technology rights and patents for which development work is still in process are charged to operations as incurred and considered a component of research and development costs.

Stock-Based Compensation

Stock Option Awards

ASC Topic 718, *Compensation-Stock Compensation* ("ASC 718") requires the fair value of all share-based payments to employees and non-employees, including grants of stock options, to be recognized in the statement of operations over the requisite service period. Under ASC 718, employee and non-employee option grants are generally valued at the grant date and those valuations do not change once they have been established. The fair value of each option award is estimated on the grant date using the Black-Scholes Option Pricing Method. The Company's estimate of expected volatility is based on its average volatility using its expected life, or approximately the last six years of publicly traded history. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant valuation. Option forfeitures are estimated when the option is granted to reduce the option expense to be recognized over the life of the award. The estimated forfeiture rate considers historical employee turnover rates stratified into employee pools, actual forfeiture experience and other factors. The option expense is adjusted upon the actual forfeiture of a stock option grant and the Company periodically revises the estimated forfeiture rate in subsequent periods if actual forfeitures differ from those estimates. Due to its limited history of stock option exercises, the Company uses the simplified method to determine the expected life of the option grants. Compensation expense related to modified stock options is measured based on the fair value for the awards as of the modification date. Any incremental compensation expense arising from the excess of the fair value of the awards on the modification date compared to the fair value of the awards immediately before the modification date is recognized at the modification date or ratably over the requisite service period, as appropriate.

Restricted Stock Units

RSUs are valued on the grant date and the fair value of the RSUs is equal to the market price of the Company's common stock on the grant date. The RSU expense is recognized over the requisite service period. When the requisite service period begins prior to the grant date (because the service inception date occurs prior to the grant date), the Company is required to begin recognizing compensation cost before there is a measurement date (i.e., the grant date). The service inception date is the beginning of the requisite service period. If the service inception date precedes the grant date, accrual of compensation cost for periods before the grant date shall be based on the fair value of the award at the reporting date. In the period in which the grant date occurs, cumulative compensation cost shall be adjusted to reflect the cumulative effect of measuring compensation cost based on fair value at the grant date rather than the fair value previously used at the service inception date (or any subsequent reporting date). RSU forfeitures are estimated when the RSU is granted to reduce the RSU expense to be recognized over the life of the award. The estimated forfeiture rate considers historical employee turnover rates stratified into employee pools, actual forfeiture experience and other factors. The RSU expense is adjusted upon the actual forfeiture of an RSU grant and the Company periodically revises the estimated forfeiture rate in subsequent periods if actual forfeitures differ from those estimates. Compensation expense related to modified RSUs is measured based on the fair value for the awards as of the modification date. Any incremental compensation expense arising from the excess of the fair value of the awards on the modification date compared to the fair value of the awards immediately before the modification date is recognized at the modification date or ratably over the requisite service period, as appropriate.

Warrants

Warrants (see Note 10–Stockholders' Equity for further details) granted to employees and non-employees are normally valued at the fair value of the instrument on the grant date and are recognized in the statement of operations over the requisite service period. When the requisite service period precedes the grant date and a market condition exists in the warrant, the Company values the warrant using the Monte Carlo Simulation Method. When the terms of the warrant become fixed, the Company values the warrant using the Black-Scholes Option Pricing Method. The Company's estimate of expected volatility is based on its average volatility using its past nine years of publicly traded history. The risk-free rate for periods within the contractual life of the warrant is based on the U.S. Treasury yield curve in effect at the time of grant valuation. In determining the value of the warrant until the terms are fixed, the Company factors in the probability of the market condition occurring and several possible scenarios. When the requisite service period precedes the grant date and is deemed to be complete, the Company records the fair value of the warrant at the time of issuance as an equity stock-based compensation transaction. The grant date is determined when all pertinent information, such as exercise price and quantity are known.

Income Taxes

The Company follows ASC Topic 740, *Income Taxes* ("ASC 740") which requires recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Under this method, deferred tax assets and liabilities are based on the differences between the consolidated financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance to the extent management concludes it is more likely than not that the asset will not be realized. 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 standard addresses the determination of whether tax benefits claimed or expected to be claimed on a tax return should be recorded in the consolidated financial statements. Under ASC 740, the Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the tax authorities, based on the technical merits of the position. The tax benefits recognized in the consolidated financial statements from such a position should be measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. ASC 740 also provides guidance on de-recognition, classification, interest and penalties on income taxes, accounting in interim periods and requires increased disclosures. As of December 31, 2025, the Company's uncertain tax positions include a reserve for its Research and Development credits.

On July 4, 2025, the "One Big Beautiful Bill" was signed into law, which includes significant changes to federal tax law and other regulatory provisions that may impact the Company. As of the date of these financial statements, the Company has evaluated the impact of the changes to Section 174 – Amortization of research and experimental expenditures on the valuation allowance release. The Company intends to deduct the capitalized costs over two years. This deduction reduces the amount of net operating losses being utilized but results in a net zero change to the deferred tax asset balance. In 2025, we released a portion of our valuation allowance related to our deferred tax assets in the amount of $3.8 million, which reduced our net income for the year.

Financial Instruments

The carrying value of financial instruments, such as cash equivalents, accounts receivable and accounts payable, approximate their fair value because of their short-term nature. The carrying value of long-term debt approximates its fair value as the principal amounts outstanding are subject to variable interest rates that are based on market rates that are regularly reset.

Cash and Cash Equivalents

The Company classifies all highly liquid instruments with an original maturity of three months or less as cash equivalents.

Restricted Cash

Restricted cash represents cash held at financial institutions that is pledged as collateral for stand-by letters of credit for office leases. The lease related letters of credit will lapse at the end of the respective lease terms through 2026. At December 31, 2025 and 2024, the Company had restricted cash in the amount of $2.1 million.

Investment Securities

The Company classifies all investment securities (short-term and long-term) as available-for-sale, as the sale of such securities may be required prior to maturity to implement management's strategies. These securities are carried at fair value, with the unrealized gains and losses, reported as a component of accumulated other comprehensive income in stockholders' equity until realized. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis. In accordance with ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, credit losses on available-for-sale securities are reported using an expected loss model and recorded to an allowance. Premiums and discounts are amortized or accreted over the life of the related security as an adjustment to yield using the straight-line method. Interest income is recognized when earned.

Assets Measured at Fair Value on a Recurring Basis

ASC Topic 820, *Fair Value Measurement ("*ASC 820") provides a single definition of fair value and a common framework for measuring fair value as well as disclosure requirements for fair value measurements used in financial statements. Under ASC 820, fair value is determined based upon the exit price that would be received by a company to sell an asset or paid by a company to transfer a liability in an orderly transaction between market participants, exclusive of any transaction costs. Fair value measurements are determined by either the principal market or the most advantageous market. The principal market is the market with the greatest level of activity and volume for the asset or liability. Absent a principal market to measure fair value, the Company uses the most advantageous market, which is the market from which the Company would receive the highest selling price for the asset or pay the lowest price to settle the liability, after considering transaction costs. However, when using the most advantageous market, transaction costs are only considered to determine which market is the most advantageous and these costs are then excluded when applying a fair value measurement. ASC 820 creates a three-level hierarchy to prioritize the inputs used in the valuation techniques to derive fair values. The basis for fair value measurements for each level within the hierarchy is described below, with Level 1 having the highest priority and Level 3 having the lowest.

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Quoted prices for similar assets or liabilities in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations in which all significant inputs are observable in active markets.

Level 3: Valuations derived from valuation techniques in which one or more significant inputs are unobservable.

Following are the major categories of assets measured at fair value on a recurring basis as of December 31, 2025 and 2024, using quoted prices in active markets for identical assets (Level 1), significant other observable inputs (Level 2), and significant unobservable inputs (Level 3) (in thousands):

December 31, 2025	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 5,060	$ 18,710	$ —	$ 23,770
U.S. Government securities	27,903	14,873	—	42,776
Corporate Bonds	—	6,865	—	6,865
Commercial paper	—	18,252	—	18,252
	$ 32,963	$ 58,700	$ —	$ 91,663

December 31, 2024	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 16,996	$ 38,102	$ —	$ 55,098
U.S. Government securities	17,568	8,617	—	26,185
Commercial paper	—	5,561	—	5,561
Totals	$ 34,564	$ 52,280	$ —	$ 86,844

The Company's investments in commercial paper and U.S. government securities are exposed to price fluctuations. The fair value measurements for commercial paper, corporate bonds and U.S. government securities are based upon the quoted prices of identical and similar items in active markets multiplied by the number of securities owned.

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

December 31, 2025	Maturity (in years)	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
Cash equivalents		$ 23,772	$ —	$ (2)	$ 23,770
U.S. Government securities	Less than 1	42,739	37	—	42,776
Corporate Bonds	Less than 1	6,866	1	(2)	6,865
Commercial paper	Less than 1	18,250	3	(1)	$ 18,252
Totals		$ 91,627	$ 41	$ (5)	$ 91,663

December 31, 2024	Maturity (in years)	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
Cash equivalents		$ 55,096	$ 4	$ (2)	$ 55,098
U.S. Government securities	Less than 1	26,186	$ 7	$ (8)	26,185
Commercial paper	Less than 1	5,556	5	—	5,561
Totals		$ 86,838	$ 16	$ (10)	$ 86,844

Concentration of Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash and cash equivalents, marketable securities, and accounts receivable, net. The Company's cash and cash equivalents and restricted cash in excess of the Federal Deposit Insurance Corporation and the Securities Investor Protection Corporation insured limits at December 31, 2025, were approximately $36.6 million. The Company does not believe it is exposed to any significant credit risk due to the quality nature of the financial instruments in which the money is held. Pursuant to the Company's internal investment policy, investments must be rated A-1/P-1 or better by Standard and Poor's Rating Service and Moody's Investors Service at the time of purchase.

The Company sells its products in the United States primarily through specialty pharmacies and specialty distributors. Therefore, wholesale distributors and large pharmacy chains account for a large portion of its accounts receivables, net and product revenues, net. The creditworthiness of its customers is continuously monitored, and the Company has internal policies regarding customer credit limits. The Company estimates an allowance for credit loss primarily based on the creditworthiness of its customers, historical payment patterns, aging of receivable balances and general economic conditions. The Company recorded $0.4 million credit loss recovery in the year ended December 31, 2025, and $0.5 million in the year ended December 31, 2024.

As of December 31, 2025 and 2024, accounts receivable from individual customers with balances due in excess of 10% of total accounts receivable totaled $38.9 million and $22.9 million, respectively.

The Company's success depends on its ability to successfully commercialize NERLYNX. The Company currently has a single product and limited commercial sales experience, which makes it difficult to evaluate its current business, predict its future prospects and forecast financial performance and growth. The Company has invested a significant portion of its efforts and financial resources in the development and commercialization of its lead product, NERLYNX, and expects NERLYNX to constitute the vast majority of product revenue for the foreseeable future.

The Company relies exclusively on third parties to formulate and manufacture NERLYNX and its drug candidates. The commercialization of NERLYNX and any other drug candidates, if approved, could be stopped, delayed or made less profitable if those third parties fail to provide sufficient quantities of product or fail to do so at acceptable quality levels or prices. The Company has no experience in drug formulation or manufacturing and does not intend to establish its own manufacturing facilities. The Company lacks the resources and expertise to formulate or manufacture NERLYNX and other drug candidates. While the drug candidates were developed by Pfizer, both the drug substance and drug product are manufactured by third-party contractors. The Company is using the same third-party contractors to manufacture, supply, store and distribute drug supplies for clinical trials and the commercialization of NERLYNX. If the Company is unable to continue its relationships with one or more of these third-party contractors, it could experience delays in the development or commercialization efforts as it locates and qualifies new manufacturers. The Company intends to rely on one or more third-party contractors to manufacture the commercial supply of drugs.

Inventory

The Company values its inventories at the lower of cost and estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis and uses standard costing. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within the cost of sales in the consolidated statements of operations. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as a cost of sales in the consolidated statements of operations.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval, if any, when, based on management's judgment, future commercialization is considered probable, and the future economic benefit is expected to be realized. Inventory that can be used in either the production of clinical or commercial product is recorded as research and development expense when selected for use in a clinical trial. Starter kits, provided to patients prior to insurance approval, are expensed by the Company to selling, general and administrative expense as incurred. Of the total inventory amounts noted below, approximately $4.5 million and $1.2 million was located at contract manufacturing organizations in Europe as of December 31, 2025 and 2024, respectively.

The Company's inventory balances are as follows:

	December 31, 2025	December 31, 2024
Raw materials	$ 3,212	$ 7,183
Work-in-process (materials, labor and overhead)	1,343	758
Finished goods (materials, labor and overhead)	960	783
Total inventories	$ 5,515	$ 8,724

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the useful lives of the assets, which is generally three years for computer hardware and software, three years for phone equipment, and seven years for furniture and fixtures. Leasehold improvements are amortized using the straight-line method over the lesser of the useful life or the lease term. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is credited or charged to operations. Repairs and maintenance costs are expensed as incurred.

The Company reviews its long-lived assets used in operations for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable, as required by ASC Topic 360, *Property, Plant, and Equipment* ("ASC 360"). The Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows over the life of the asset to its carrying value on the consolidated balance sheet. If the undiscounted cash flows used in the recoverability test are less than the carrying value, the Company would then determine the fair value of the long-lived asset and recognize an impairment loss for the amount in excess of the carrying value. No material impairments were recorded during the years ended December 31, 2025 and 2024.

Leases

ASC Topic 842, *Leases*, as adopted in the first quarter of 2019, requires lessees to recognize most leases on the balance sheet with a corresponding right-of-use asset ("ROU asset"). ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. The assets and lease liabilities are recognized at the lease commencement date based on the estimated present value of fixed lease payments over the lease term. ROU assets are evaluated for impairment using the long-lived assets impairment guidance, as required by ASC 360. A significant indication of impairment of an ROU asset would include a change in the extent or manner in which the asset is being used. The Company must make assumptions that underlie the most significant and subjective estimates in determining whether any impairment exists. Those estimates, and the underlying assumptions, include estimates of future cash flow utilizing market lease rates and determination of fair value. If an ROU asset related to an operating lease is impaired, the carrying value of the ROU asset post-impairment should be amortized on a straight-line basis through the earlier of the end of the useful life of the ROU asset or the end of the lease term. Post impairment, a lessee must calculate the amortization of the ROU asset and interest expense on the lease liability separately, although the sum of the two continues to be presented as a single lease cost. If a lease is planned to be abandoned with no intention of subleasing, the ROU asset should be assessed for impairment.

Leases are classified as financing or operating, which will drive the expense recognition pattern. The Company elects to exclude short-term leases if and when the Company has them. For additional information, see Note 6–Leases.

The Company leases office space and copy machines, all of which are operating leases. Most leases include the option to renew, and the exercise of the renewal options is at the Company's sole discretion. Options to extend or terminate a lease are considered in the lease term to the extent that the option is reasonably certain of exercise. The leases do not include options to purchase the leased property. The depreciable life of assets and leasehold improvements is limited by the expected lease term. Covenants imposed by the leases include letters of credit required to be obtained by the lessee.

The Company is required to remeasure the lease liability and make an adjustment in the following instances:

- The term of the lease has been modified or there has been a change in the Company's assessment of a purchase option being exercised, in which case the lease liability is remeasured by discounting the revised lease payments using a revised discount rate;

- A lease contract is modified, and the lease modification is not accounted for as a separate lease, in which case the lease liability is remeasured by discounting the revised lease payments using a revised discount rate; and

- The lease payments are adjusted due to changes in the index or a change in expected payment under a guaranteed residual value, in which cases the lease liability is remeasured by discounting the revised lease payments using the initial discount rate.

The incremental borrowing rate ("IBR") represents the rate of interest the Company would expect to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. As the implicit rate on the Company's leases are not readily determinable, the Company uses its IBR based on the information available at the commencement date in determining the present value of lease payments. The Company's average IBR for existing leases as of December 31, 2025 was 12.2%.

The Company decided to cease the use of a portion of its leased office space in 2023. In connection with the decreased need for the right to use the ROU asset, the Company entered into a sublease for the underlying asset, in which the sublease income is less than the original lease payments, indicating impairment. In performing the recoverability test on the effective date, the undiscounted future estimated cash flows and carrying value were identified for the subleased portion of the leased building, as an individual asset group, defined under ASC 360. A reduction to the carrying value of the ROU asset of approximately $0.6 million was recorded, representing the fair value amount in excess of the carrying value, with a corresponding impairment charge recorded as selling, general and administration expense, in the consolidated statements of operations for the year ended December 31, 2023.

License Fees and Intangible Assets

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain and the technology has no alternative future use when acquired. Acquisitions of technology licenses are charged to expense or capitalized based upon the asset achieving technological feasibility in accordance with management's assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that technological feasibility for its drug candidates is reached when the requisite regulatory approvals are obtained to make the product available for sale. The Company capitalizes technology licenses upon reaching technological feasibility.

The Company maintains definite-lived intangible assets related to the license agreement with Pfizer. These assets are amortized over their remaining useful lives, which are estimated based on the shorter of the remaining patent life or the estimated useful life of the underlying product. Intangible assets are amortized using the economic consumption method if anticipated future revenues can be reasonably estimated. The straight-line method is used when future revenues cannot be reasonably estimated. Amortization costs are recorded as part of cost of sales.

In September 2022, the Company entered into an exclusive license agreement with Takeda to license the worldwide research and development and commercial rights to alisertib, a selective, small-molecule, orally administered inhibitor of Aurora Kinase A. The upfront payment of $7.0 million was expensed as acquired in-process research and development as the drug candidate has not achieved regulatory approval for marketing and has no alternative future use.

The Company assesses its intangible assets for impairment if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or non-clinical data regarding one of the Company's drug candidates or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate, or new information regarding potential sales of the drug. If impairment indicators are present or changes in circumstance suggest that impairment may exist, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of each asset group to its carrying value on the consolidated balance sheet. If the undiscounted cash flows used in the recoverability test are less than the carrying value, the Company would determine the fair value of the intangible asset and recognize an impairment loss if the carrying value of the intangible asset exceeds its fair value. In connection with the FDA approval of NERLYNX in July 2017, the Company triggered a one-time milestone payment pursuant to its license agreement with Pfizer. In June 2020, the Company entered into a letter agreement with Pfizer relating to the method of payment associated with a milestone payment under the Company's license agreement with Pfizer (see Note 13–Commitments and Contingencies). The Company capitalized the milestone payments as an intangible asset and is amortizing the asset to cost of sales on a straight-line basis over the estimated useful life of the licensed patent through 2030. In addition, the Company reached a commercial milestone by achieving aggregate worldwide net sales of $250 million in calendar year 2022, resulting in a payable to Pfizer of $12.5 million as of December 31, 2022. The Company capitalized this milestone as an intangible asset and accrued in-licensed rights on the accompanying consolidated balance sheets and payment was made in the first quarter of 2023. The Company recorded amortization expense related to its intangible assets of $9.7 million, $9.7 million, and $8.0 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, estimated future amortization expense related to the Company's intangible asset was approximately $9.7 million for each year from 2026 through 2029, and $2.4 million for 2030.

Accounting Pronouncements Adopted During the Current Year

ASU 2023-09, Improvements to Income Tax Disclosures

On December 14, 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures ("ASU 2023-09").* ASU 2023-09 amends ASC 740, *Income Taxes* to expand income tax disclosures and requires that the Company disclose (i) the income tax rate reconciliation using both percentages and reporting currency amounts; (ii) specific categories within the income tax rate reconciliation; (iii) additional information for reconciling items that meet a quantitative threshold; (iv) the composition of state and local income taxes by jurisdiction; and (v) the amount of income taxes paid disaggregated by jurisdiction. The Company adopted ASU 2023-09 for the year ended December 31, 2025 on a prospective basis. Accordingly, the expanded disclosures are provided for the year ended December 31, 2025, while prior period disclosures have not been retroactively adjusted and continue to be presented under the previous disclosure requirements. As this update only impacts disclosures, its adoption did not have a material impact on the Company's consolidated financial position, results of operations, or cash flows. See Note 12 *Income Taxes* for additional information.

Recently Issued Accounting Standards

In November 2024, the FASB issued ASU 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures*: The ASU requires more detailed information about specified categories of expenses included in certain expense captions presented on the face of the income statement. This ASU is effective for fiscal years beginning after December 15, 2026, and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The amendments may be applied either (1) prospectively to financial statements issued for reporting periods after the effective date of this ASU or (2) retrospectively to all prior periods presented in the financial statements. The Company is currently evaluating the impact of adopting this ASU on its consolidated financial statements and related disclosures.

Note 3—Accounts Receivable, Net

Accounts receivable, net consisted of the following (in thousands):

	December 31, 2025	December 31, 2024
Trade accounts receivable	$ 38,146	$ 26,362
Royalty revenue receivable	15,508	6,011
Total accounts receivable	$ 53,654	$ 32,373
Allowance for credit losses	—	(362)
Total accounts receivable, net	$ 53,654	$ 32,011

Trade accounts receivable consist entirely of amounts owed from the Company's customers related to product sales. Royalty revenue receivable represents amounts owed related to royalty revenue recognized based on the Company's sub-licensees' sales in their respective territories in the years ended December 31, 2025 and 2024.

For all accounts receivable, the Company recognizes credit losses based on lifetime expected losses to selling and general administrative expense in the consolidated statements of operations. In determining estimated credit losses, the Company evaluates its historical loss rates, current economic conditions and reasonable and supportable forecasts of future economic conditions. The Company recorded a recovery to the provision for credit loss recovery of $0.4 million in the year ended December 31, 2025. The Company recorded $0.5 million recovery to the provision for credit loss recovery in the year ended December 31, 2024 and a $0.9 million credit loss expense in the year ended December 31, 2023.

Note 4—Prepaid Expenses and Other

Prepaid expenses and other consisted of the following at December 31 (in thousands):

	December 31, 2025	December 31, 2024
Current:		
CRO services	$ 37	$ 81
Other clinical development	324	347
Insurance	1,128	1,078
Professional fees	381	731
Prepaid Taxes	117	21
Other	1,655	3,609
	3,642	5,867
Long-term:		
CRO services	52	52
Insurance	8	11
Other clinical development	101	102
Other	2,673	119
	2,834	284
Totals	$ 6,476	$ 6,151

Other current prepaid amounts consist primarily of deposits, signing bonuses, licenses, subscriptions and software. Other long-term prepaid amounts consist primarily of funding for commercial copay support programs.

Note 5—Property and Equipment

Property and equipment consisted of the following at December 31 (in thousands):

	December 31, 2025	December 31, 2024
Leasehold improvements	$ 2,549	$ 3,779
Computer equipment	761	2,150
Telephone equipment	—	95
Furniture and fixtures	1,475	2,359
Total property and equipment	4,785	8,383
Less: accumulated depreciation	(4,598)	(7,868)
Property and equipment, net	$ 187	$ 515

For the years ended December 31, 2025, 2024 and 2023, the Company incurred depreciation expense of $0.4 million for each of the years ended December 31, 2025 and 2024.

Note 6—Leases

In December 2011, the Company entered into a non-cancelable operating lease for office space in Los Angeles, California, which was subsequently amended in November 2012, December 2013, March 2014, July 2015 and December 2017. The initial term of the lease was for seven years and commenced on December 10, 2011. As amended, the Company rents approximately 65,656 square feet. The term of the lease runs until March 2026. In July 2025, the Company executed an additional amendment to its office space in Los Angeles, California to surrender certain suites effective March 31, 2026 and extend the lease term for the remaining 26,700 rentable square feet on the 17th floor for an additional five years and five months through August 31, 2031. Base rent escalates annually and is abated from April 2026 through August 2026. Lease payments also include variable charges for the Company's proportionate share of building operating expenses and real estate taxes based on a 2026 base year. The Company has the option to renew such lease for an additional five year term. Management determined that the renewal option is not reasonably certain to occur. The Company accounted for this amendment as a lease modification. There was no change in the lease classification as a result of this modification and the Company continues to recognize such a lease as an operating lease. The Company remeasured its ROU assets and operating lease liabilities using an updated incremental borrowing rate. The change in ROU assets and operating lease liabilities related to this lease modification amounted to $4.1 million.

In June 2012, the Company entered into a long-term lease agreement for office space in South San Francisco, California, which was subsequently amended in May 2014 and July 2015. As amended, the Company rents approximately 29,470 square feet. The term of this lease runs until March 2026, with the option to extend for an additional five-year term, and rents payable by the Company increase approximately 3% per year. The Company provided the landlord an automatically renewable stand-by letter of credit in the amount of $1.1 million. The stand-by letter of credit is collateralized by a high-yield savings account, which is classified as restricted cash, current on the accompanying consolidated balance sheets.

The Company also leases copier equipment for use in the office spaces. Components of copier lease expense include both fixed and variable lease expenses.

Total rent expense for the years ended December 31, 2025, 2024 and 2023 was approximately $4.5 million, $4.9 million and $4.9 million, respectively. For purposes of determining straight-line rent expense, the lease term is calculated from the date the Company first takes possession of the facility, including any periods of free rent and any renewal option periods that the Company is reasonably certain of exercising. The Company's office leases generally have contractually specified minimum rent and annual rent increases that are included in the measurement of the ROU asset and related lease liability. Additionally, under these lease arrangements, the Company may be required to pay directly, or reimburse the lessors, for real estate taxes, insurance, utilities, maintenance and other operating costs. Such amounts are generally variable and therefore not included in the measurement of the ROU asset and related lease liability but are instead recognized as variable lease expense in selling, general and administrative costs in the consolidated statements of operations when they are incurred. Variable lease payments not included in the lease liability were $0.5 million and $0.7 million for the years ended December 31, 2025 and 2024, respectively.

The future minimum lease payments under ASC 842 as of December 31, 2025 were as follows (in thousands):

	Amount
2026	1,913
2027	1,248
2028	1,292
2029	1,338
2030	1,385
2031	951
Total minimum lease payments	$ 8,127
Less: imputed interest	(2,104)
Total lease liabilities	$ 6,023

In February 2019, the Company entered into a long-term sublease agreement for 12,429 square feet of the office space in Los Angeles, California. The term of the lease ran until March 2026 and rent amounts payable to the Company increased approximately 3% per year. The February 2019 sublease was terminated in December 2024. As a result, the Company received $0.7 million, which approximated the sublease rental payments on the remaining lease term.
In March 2025, the Company signed another sublease agreement for the 12,429 square feet of office space with a sublease commencement date of April 1, 2025.

In August 2023, the Company entered into a long-term sublease agreement for 13,916 square feet of the office space in Los Angeles, California, which commenced in November 2023. The term of the lease runs until March 2026 and the rent amounts payable to the Company increase approximately 3% per year. The Company has recorded sublease income in other income (expenses) in the condensed consolidated statements of operations since November 2023.

The Company recorded operating sublease income of $0.7 million and $1.4 million for the years ended December 31, 2025 and 2024, respectively, in other income (expenses) in the consolidated statements of operations.

The future minimum lease payments to be received as of December 31, 2025 were as follows (in thousands):

	Amount
2026	81
Total	$ 81

Supplemental cash flow information related to leases for the year ended December 31, 2025:

Supplemental cash flow information related to leases for the twelve months ended December 31, 2025:	
Operating cash flows used for operating leases (in thousands)	$ 6,469
Right-of-use assets obtained in exchange for new operating lease liabilities	4,123
Weighted-average remaining lease term (in years)	4.7
Weighted average discount rate	12.2%

Note 7—Intangible Assets

Intangible assets consisted of the following at December 31 (in thousands):

	December 31, 2025	December 31, 2024
Acquired and in-licensed rights	$ 102,500	$ 102,500
Less: accumulated amortization	(61,108)	(51,369)
Total intangible assets, net	$ 41,392	$ 51,131

Estimated future intangible amortization expense as of December 31, 2025 is as follows (in thousands):

2026	9,739
2027	9,739
2028	9,739
2029	9,739
2030	2,436
Totals	$ 41,392

Note 8—Accrued Expenses

Accrued expenses consisted of the following at December 31 (in thousands):

	December 31, 2025	December 31, 2024
Current:		
Accrued royalties	$ 15,858	$ 10,169
Accrued CRO services	3,793	1,035
Accrued variable consideration	14,215	10,829
Accrued bonus	8,377	7,976
Accrued compensation	5,797	4,368
Accrued other clinical development	567	935
Accrued professional fees	132	341
Accrued legal fees	990	1,095
Accrued manufacturing costs	93	39
Other	209	111
	$ 50,031	$ 36,898
Long-term:		
Accrued other liabilities	—	121
	—	121
Totals	$ 50,031	$ 37,019

Accrued variable consideration represents estimates of adjustments to product revenue, net for which reserves are established. Accrued royalties represent royalties incurred in connection with the Company's license agreement with Pfizer. Accrued CRO services, accrued other clinical development expenses, and accrued legal fees represent the Company's estimates of such costs and are recognized as incurred. Accrued compensation includes severance, commissions and vacation.

Note 9—Debt

Long-term debt consisted of the following at December 31, 2025 (in thousands):

	December 31, 2025	Maturity Date
Total debt, inclusive of $2.0 million exit payment	$ 102,000	July 23, 2026
Less: unamortized debt issuance costs and discounts	(152)	
Less: current portion	(22,523)	
Less: debt repayment	(79,325)	
Total long-term debt, net	$ (0)	

Athyrium Note Purchase Agreement

The Company issued senior notes for an aggregate principal amount of $100.0 million pursuant to a note purchase agreement dated July 23, 2021 by the Company, and its subsidiary, and Athyrium, as Administrative Agent, and certain other investor parties (the "Note Purchase Agreement"), with an initial maturity date of July 23, 2026 (the "Athyrium Notes"). The Athyrium Notes were issued for face amount of $100.0 million net of an original issue discount of $1.5 million. The Athyrium Notes also require a 2.0% exit payment to be made on each payment of principal. The borrowings under the Athyrium Notes, together with cash on hand, were used to repay the Company's outstanding indebtedness, including the applicable exit and prepayment fees owed to lenders under its prior credit facility with Oxford. The Athyrium Notes are secured by substantially all of the Company's assets. The Company incurred $1.9 million of deferred financing costs with the initial borrowing of the Athyrium Notes.

Interest on the Athyrium Notes is calculated in part based on the Secured Overnight Financing Rate ("SOFR"), which replaced the "London Interbank Offering Rate" as the floating benchmark for interest rate calculations applicable to the Athyrium Notes pursuant to the terms of the Third Amendment to Note Purchase Agreement dated as of September 16, 2022. (the "Third Amendment"). The modification of the Note Purchase Agreement pursuant to the Third Amendment did not meet the requirements of a debt extinguishment under ASC Topic 470-50 - *Debt Modifications and Exchanges* and no gain or loss was recognized. The Company performed a quantitative analysis and determined that the terms of the new debt and original debt instrument were not substantially different. Accordingly, the Third Amendment is accounted for as a debt modification.

Following the effectiveness of the Third Amendment, the Athyrium Notes bear interest at an annual rate equal to the sum of (a) eight percent (8.00%) plus (b) the lesser of (i) the sum of (x) three-month term SOFR for an interest period of three months plus (y) 0.26161% (26.161 basis points) and (ii) three and one-half of one percent (3.50%) per annum. Interest is payable quarterly on the last business day of March, June, September and December each year. In the second quarter of 2024, the Company began paying the principal payments required to be made quarterly at 11.11% of the original face amount. The remaining balance will be paid at maturity. Each principal payment also includes a 2.0% exit payment. Each quarterly principal payment approximates $11.1 million, and each quarterly exit fee payment approximates $0.2 million. As of December 31, 2025, the effective interest rate for the loan was 12.99%. The carrying amounts of the Company's debt approximate fair value because of the short-term nature and near-term maturity of the instruments.

As of December 31, 2025, the Company may prepay the outstanding principal balance of the notes, in whole or in part, without premium or penalty.

The Athyrium Notes include affirmative and negative covenants applicable to the Company. The affirmative covenants include, among others, covenants requiring the Company to maintain its legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage, and satisfy certain requirements regarding deposit accounts. The negative covenants include, among others, restrictions on the Company's transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions. The Company is also required to maintain minimum cash balances and achieve certain minimum product revenue targets, measured as of the last day of each fiscal quarter on a trailing year-to-date basis. As of December 31, 2025, the Company was in compliance with such covenants.

As of December 31, 2025, the principal balance outstanding under the Athyrium Notes was $22.5 million, representing all of the Company's debt.

The future minimum principal and exit payments under the Athyrium Notes as of December 31, 2025, were as follows (in thousands):

	Amount
2026	22,675
Total	$ 22,675

Debt Issuance Costs and Discounts

Debt issuance costs and discounts consist of the following (in thousands):

	December 31, 2025	December 31, 2024
Debt issuance costs and discounts (Athyrium Notes)	$ 5,410	$ 5,410
Less: accumulated amortization	(5,258)	(4,454)
Included in current portion of debt	$ 152	$ 956

Debt issuance costs and discounts are financing costs related to the Company's outstanding debt. Amortization of debt issuance costs is expensed using the effective interest method and is included in interest expense in the consolidated statements of operations. For the years ended December 31, 2025, 2024 and 2023, the Company recorded approximately $0.8 million, $1.4 million and $1.3 million, respectively, of interest expense related to the amortization of debt issuance costs, discounts and exit fees in the consolidated statements of operations.

Note 10—Stockholders' Equity

Common Stock

The Company issued 55,882 and 64,118 shares of common stock upon exercise of stock options for the years ended December 31, 2025 and 2024, respectively. The Company did not issue any shares of common stock in 2023. The Company issued 1,246,307, 1,394,929 and 1,301,127 shares of common stock upon vesting of RSUs during the years ended December 31, 2025, 2024 and 2023, respectively.

Authorized Shares

The Company has 100,000,000 shares of stock authorized for issuance, all of which are common stock, par value $0.0001 per share.

Warrants

In October 2011, the Company issued an anti-dilutive warrant to Alan H. Auerbach, the Company's Founder and Chief Executive Officer. The warrant was issued to provide Mr. Auerbach with the right to maintain ownership of at least 20% of the Company's common stock in the event that the Company raised capital through the sale of its securities in the future.

In connection with the closing of a public offering in October 2012, the exercise price and number of shares underlying the warrant issued to Mr. Auerbach were established and, accordingly, the final value of the warrant became fixed. Pursuant to the terms of the warrant, Mr. Auerbach may exercise the warrant to acquire 2,116,250 shares of the Company's common stock at $16 per share until October 4, 2021. On April 1, 2021, the Company's Board of Directors approved an amendment to the terms of the warrant by extending the term until October 4, 2026. The amendment was approved by the Company's stockholders on June 15, 2021.

Stock Options and Restricted Stock Units

The Company's 2011 Incentive Award Plan ("2011 Plan"), as amended, was adopted by the Company's Board of Directors on September 15, 2011. Pursuant to the 2011 Plan, the Company may grant incentive stock options and nonqualified stock options, as well as other forms of equity-based compensation. Incentive stock options may be granted only to employees, while consultants, employees, officers and directors are eligible for the grant of nonqualified options under the 2011 Plan. The maximum term of stock options granted under the 2011 Plan is 10 years and the awards generally vest over a three-year period. The exercise price of incentive stock options granted under the 2011 Plan must be at least equal to the fair value of such shares on the date of grant. On April 1, 2021, the Board of Directors adopted an amendment to the 2011 Plan to increase the number of shares of the Company's common stock reserved for issuance thereunder by 2,000,000 shares. The amendment was approved by the Company's stockholders on June 15, 2021. On June 18, 2024, the stockholders of the Company approved an amendment to the Company's 2011 Plan, increasing the number of authorized shares of the Company's common stock that may become issuable under the 2011 Plan by 3,000,000 shares and extending the period during which incentive stock options may be granted. As of December 31, 2025, a total of 17,529,412 shares of the Company's common stock have been reserved for issuance under the 2011 Plan.

All of the options awarded by the Company have been "plain vanilla options" as determined by the SEC Staff Accounting Bulletin 107 - *Share Based Payment.* As of December 31, 2025, 4,157,795 shares of the Company's common stock are issuable upon the exercise of outstanding stock options and vesting RSUs granted under the 2011 Plan and 3,668,856 shares of the Company's common stock are available for future issuance under the 2011 Plan. The fair value of options granted to employees and non-employees was estimated using the Black-Scholes Option Pricing Method (see Note 2–Significant Accounting Policies) with the following weighted-average assumptions used during the years ended December 31:

	2025	2024
Dividend yield	0.0%	0.0%
Expected volatility	81.5%	85.8%
Risk-free interest rate	4.4%	4.1%
Expected life in years	5.55	5.55

The Company's 2017 Employment Inducement Incentive Award Plan ("2017 Plan"), as amended, was adopted by the Company's Board of Directors on April 27, 2017. Pursuant to the 2017 Plan, the Company may grant stock options and RSUs, as well as other forms of equity-based compensation to employees, as an inducement to join the Company. The maximum term of stock options granted under the 2017 Plan is 10 years and the awards generally vest over a three-year period. The exercise price of stock options granted under the 2017 Plan must be at least equal to the fair market value of such shares on the date of grant. On July 15, 2021, the Board of Directors adopted an amendment to the 2017 Plan to increase the number of shares of the Company's common stock reserved for issuance thereunder by 1,000,000 shares. As of December 31, 2025, a total of 3,000,000 shares of the Company's common stock have been reserved for issuance under the 2017 Plan. As of December 31, 2025, 394,467 shares of the Company's common stock are issuable upon the exercise of outstanding stock options and vesting of RSUs granted under the 2017 Plan, and 1,306,714 shares of the Company's common stock are available for future issuance under the 2017 Plan.

Stock-based compensation expense was as follows for the years ended December 31 (in thousands):

	For the Year Ended December 31,		
	2025	2024	2023
Stock-based compensation:			
Options:			
Selling, general, and administrative	$ 1,036	$ 1,625	$ 2,510
Research and development	170	290	611
Restricted stock units:			
Selling, general, and administrative	3,247	3,941	4,398
Research and development	2,491	2,389	2,728
Total stock-based compensation expense	$ 6,944	$ 8,245	$ 10,247

Stock Option Roll Forward

Activity with respect to options granted under the 2011 Plan and 2017 Plan is summarized as follows:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2024	4,051,928	$ 33.80		
Granted	492,514	2.78		
(Forfeited)	(84,954)	3.57		
(Exercised)	(55,882)	2.33		
(Expired)	(1,186,317)	67.35		
Outstanding at December 31, 2025	3,217,289	$ 16.13	5.4	$ 3,609
Vested and expected to vest at December 31, 2025	3,217,289	$ 16.13	5.4	$ 3,609
Exercisable	2,811,562	$ 17.95	4.9	$ 2,593

On December 31, 2025, total estimated unrecognized compensation cost related to non-vested stock options granted prior to that date was approximately $0.4 million, which is expected to be recognized over a weighted-average period of 1.1 years. At December 31, 2025, the total estimated unrecognized compensation cost related to non-vested RSUs was approximately $2.5 million, which is expected to be recognized over a weighted-average period of 1.3 years. The weighted-average grant date fair value of options granted during the years ended December 31, 2025, 2024 and 2023, was $1.95, $4.57 and $3.17 per share, respectively. The weighted-average grant date fair value of RSUs awarded during the year ended December 31, 2025, 2024 and 2023 was $3.36, $5.86 and $3.96, respectively.

Restricted Stock Unit Rollforward

	Shares	Weighted Average Grant-Date Fair Value
Nonvested shares at December 31, 2024	1,289,449	$ 5.14
Granted	1,430,211	$ 3.36
(Forfeited)	(138,380)	$ 4.03
(Vested)	(1,246,307)	$ 4.57
Nonvested shares at December 31, 2025	1,334,973	$ 3.88

Note 11—401(k) Savings Plan

During 2012, the Company adopted a 401(k) savings plan for the benefit of its employees. The Company is required to make matching contributions to the 401(k) plan equal to 100% of the first 3% of wages deferred by each participating employee and 50% on the next 2% of wages deferred by each participating employee. The Company incurred expenses for employer matching contributions of approximately $1.6 million for each of the years ended December 31, 2025, 2024 and 2023.

Note 12—Income Taxes

The Company uses the asset and liability method of accounting for income taxes in accordance with Accounting Standards Codification Topic 740, “Income Taxes.” Under this method, income tax expense is recognized for the amount of: (i) taxes payable or refundable for the current year and (ii) deferred tax consequences of temporary differences resulting from matters that have been recognized in an entity’s financial statements or tax returns. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date.

The components of income before income taxes for the years ended December 31 (in thousands) are as follows:

	2025	2024	2023
Domestic	$ 35,782	$ 24,100	$ 22,674
Foreign	—	—	—
Income Before Income Taxes	$ 35,782	$ 24,100	$ 22,674

The provisions of income taxes are summarized as follows (in thousands):

	2025	2024	2023
Current:			
Federal	$ —	$ —	$ —
State	1,247	722	905
Foreign	179	175	178
	1,426	897	1,083
Deferred:			
Federal	3,052	(6,632)	—
State	193	(443)	—
	3,245	(7,075)	—
Total	$ 4,671	$ (6,178)	$ 1,083

Reconciliation of Statutory Federal Income Tax Rate to the Effective Income Tax Rate

The Company has elected to prospectively adopt the guidance in ASU No. 2023-09, *Income Taxes* (Topic 740): Improvements to Income Taxes Disclosures, or ASU 2023-09. The following table is a reconciliation of the U.S. federal statutory rate of 21% to the Company's effective rate for the year ended December 31, 2025 in accordance with the guidance in ASU No. 2023-09:

	2025	
	Amount	**Percentage**
U.S. federal statutory income tax	7,514	21.0%
State and local income taxes, net of federal income tax effect (1)	1,238	3.5%
Foreign tax effects	179	0.5%
Tax credits	(1,280)	-3.6%
Change in valuation allowance	(18,639)	-52.1%
Non-taxable or non-deductible items		
SBC Options	14,619	40.9%
Section 162(m)	777	2.2%
Other nontaxable or nondeductible items	243	0.7%
Other	20	0.1%
Income tax expense	4,671	13.1%

(1) State taxes in Kentucky and Indiana comprise the majority (greater than 50%) of the tax effect in this category.

As previously disclosed for the years ended December 31, 2024 and 2023, prior to the adoption of ASU 2023-09, the effective income tax rate differs from the statutory federal income tax rate as follows:

	2024	**2023**
Tax computed at the federal statutory rate	$ 5,061	$ 4,488
State taxes	744	1,312
Foreign taxes	175	178
Permanent items	12,946	4,837
R&D credits	(1,532)	(1,806)
Prior year adjustment	1,697	(1,715)
Change in valuation allowance	(25,269)	(6,211)
Total provision	$ (6,178)	$ 1,083

Approximately $3.8 million of the $18.7 million change in valuation allowance is attributable to a partial valuation allowance release (see further discussion within the tax footnotes below). Approximately $15.0 million of tax expense is due to stock-based compensation expense shortfall, the expiration of vested stock options, and non-deductible stock-based compensation. Approximately $1.6 million of the tax benefits are due to R&D tax credits, net of a $0.4 million reserve related to unrecognized tax benefits for the method of allocation of expenses used in the R&D credit calculation.

Temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes give rise to the Company's deferred income taxes. The components of the Company's net deferred tax assets as of December 31, 2025, 2024 and 2023 are as follows (in thousands):

	2025	2024	2023
Deferred tax assets:			
Net operating loss carryforwards	$ 230,018	$ 232,184	$ 240,960
Business credit carryforwards	64,968	63,175	62,051
Compensation	13,104	26,081	37,946
Sec 174 R&D expenses	14,505	23,933	19,882
Accrued expenses	139	90	261
Carryforward of disallowed interest	—	—	1,477
Accrued legal verdict	—	—	1,976
Other deferred tax assets	5,718	4,745	4,231
Lease liabilities	1,530	1,764	3,034
Gross deferred tax assets	329,982	351,972	371,818
Valuation allowance	(324,787)	(343,482)	(368,751)
Net deferred tax assets	5,195	8,490	3,067
Deferred tax liabilities:			
Other deferred tax liabilities	—	(70)	(149)
Right of use assets	(1,365)	(1,148)	(1,997)
Inventory	—	(197)	(921)
Total deferred tax liabilities	(1,365)	(1,415)	(3,067)
Net deferred tax assets (liability)	$ 3,830	$ 7,075	$ —

As of December 31, 2024, the Company had deferred tax assets totaling $352.0 million, primarily attributable to net operating loss (NOL) carryforwards and R&D tax credit carryforwards. A valuation allowance of $343.5 million had been established in prior periods as the management concluded it was more likely than not that the asset will not be realized.

During the year ended December 31, 2025, the Company has recorded a net decrease in the valuation allowance of $18.7 million. The decrease is attributable to recognizing $14.9 million of net deferred tax assets primarily related to utilization of net operating losses and stock-based compensation. The remaining change is attributable to a partial valuation allowance release of $3.8 million driven by forecasted earnings in 2026. The remaining valuation allowance of $324.8 million reserves against deferred tax assets that are more likely than not to not be recognized, as the Company's forecasted profitability is uncertain beyond 2026.

Management's decision to release a portion of the valuation allowance was based on an assessment of both positive and negative evidence, as required under ASC 740.

Positive evidence supporting the partial release included:

- Three consecutive years of cumulative pretax income, indicating a trend of profitability.
- Projected earnings in 2026, increasing the likelihood of realizing certain deferred tax assets.

Negative evidence that led to retaining a portion of the valuation allowance included:

- Competitive pressure in the oncology market, including the risks of alternative treatments gaining market share or impacting pricing flexibility.
- Ability to generate sustained profitability remains uncertain due to dependence on NYRLYNX as a primary commercial product
- Future profits are contingent on the successful clinical development and approval of pipeline products
- Future limitations on the utilization of NOL and R&D tax credits.
- The Company does not have material deferred tax liabilities (DTLs) to offset deferred tax assets (DTAs).

As of December 31, 2025, the remaining valuation allowance of $324.8 million continues to reflect management's assessment of uncertainties related to the realization of certain net operating losses and R&D tax credit carryforwards, which remain subject to expiration or utilization limitations. The decision to retain the remaining valuation allowance was based on inherent uncertainty in forecasting taxable income beyond 2026.

The partial release of the valuation allowance decreased the effective tax rate by 9.07%.

Management will continue to evaluate the realizability of deferred tax assets on a quarterly basis.

At December 31, 2025, the Company had federal and state net operating loss carryforwards respectively of approximately $827.8 million and $819.2 million, respectively, which will begin to expire respectively in 2035 and 2036. At December 31, 2025, the Company also has federal research and development credit carryforwards of approximately $42.0 million. If not utilized, the research and development credit carryforwards will begin expiring in 2033. The Company has state research and development credit carryforwards of approximately $26.3 million which do not expire. Pursuant to the Internal Revenue Code, Sections 382 and 383, use of the Company's net operating loss and credit carryforwards could be limited if a cumulative change in ownership of more than 50% occurs within a three-year period. The Company performed an assessment of the potential limitation on net operating loss and credit carryforwards, and concluded that there will be no limitation for the tax year 2025 for federal purposes.

The following is a tabular reconciliation of the total amounts of unrecognized tax benefits at December 31 (in thousands):

	2025	2024	2023
Unrecognized tax benefits - January 1	$ 3,045	$ 2,811	$ 2,522
Gross decreases - tax positions in prior period	(50)	(143)	(163)
Gross increases - tax positions in a current period	403	377	452
Unrecognized tax benefits - December 31	$ 3,398	$ 3,045	$ 2,811

During prior period we completed research and development credit study. As a result of the study, we computed our credit under safe harbor rules which when applied consistently result in more conservative approach of calculating the amount of credit. We concluded that a release of uncertain tax benefits for the portion of the R&D credit attributable to safe harbor was appropriate and released a portion of previously recorded uncertain tax positions reserve.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by the federal and state jurisdictions where applicable. The Company is currently pending a federal income tax examination for the fiscal year ended December 31, 2022. The Company's tax years for 2012 and forward are subject to examination by the federal and California tax authorities due to the carryforward of unutilized net operating losses and research and development credits.

Income Tax Payments

Disclosed below is a summary of income taxes paid by jurisdiction pursuant to the disclosure requirements of ASU 2023-09 for the year ended December 31, 2025:

	2025
Federal income taxes paid (net of refunds)	—
State income taxes paid (net of refunds)	1,092
Foreign income taxes paid (net of refunds)	179
Total income taxes paid (net of refunds)	1,271

Income taxes paid (net of refunds) exceeded five percent of total income taxes paid (net of refunds) in the following jurisdictions:

State	2025
Alabama	172,000
California	181,700
Indiana	199,000
Kentucky	181,400
New York	77,800
Pennsylvania	121,600

Foreign	2025
South Korea	179,120

Note 13—Commitments and Contingencies

License Agreements

Pfizer License Agreement

In August 2011, the Company entered into an agreement pursuant to which Pfizer agreed to grant it a worldwide license for the development, manufacture and commercialization of PB272 (neratinib, oral), PB272 (neratinib, intravenous) and PB357, and certain related compounds. The license is exclusive with respect to certain patent rights owned by or licensed to Pfizer. Under the agreement, the Company is obligated to commence a new clinical trial for a product containing one of these compounds within a specified period of time and to use commercially reasonable efforts to complete clinical trials and to achieve certain milestones as provided in a development plan. From the closing date of the agreement through December 31, 2011, Pfizer continued to conduct the existing clinical trials on behalf of the Company at the licensor's sole expense. At the Company's request, Pfizer agreed to continue to perform certain services in support of the existing clinical trials at the Company's expense. These services will continue through the completion of the transitioned clinical trials. The license agreement "capped" the out of pocket expense the Company would be responsible to complete the then existing clinical trials. All agreed upon costs incurred by the Company above the "cost cap" would be reimbursed by Pfizer. The Company exceeded the "cost cap" during the fourth quarter of 2012. In accordance with the license agreement, the Company billed Pfizer for agreed upon costs above the "cost cap" until December 31, 2013.

On July 18, 2014, the Company entered into an amendment to the license agreement with Pfizer. The amendment amends the agreement to (i) reduce the royalty rate payable by the Company to Pfizer on sales of licensed products; (ii) release Pfizer from its obligation to pay for certain out-of-pocket costs incurred or accrued on or after January 1, 2014 to complete certain ongoing clinical studies; and (iii) provide that Pfizer and the Company will continue to cooperate to effect the transfer to the Company of certain records, regulatory filings, materials and inventory controlled by Pfizer as promptly as reasonably practicable.

As consideration for the license, the Company is required to make substantial payments upon the achievement of certain milestones totaling approximately $187.5 million if all such milestones are achieved, of which $102.5 million have been achieved as of December 31, 2025. In connection with the FDA approval of NERLYNX in July of 2017, the Company triggered a one-time milestone payment pursuant to the agreement. In June 2020, the Company entered into a letter agreement (the "Letter Agreement"), with Pfizer relating to the method of payment associated with a one-time milestone payment under the license agreement with Pfizer. The Letter Agreement permitted the Company to make the milestone payment in installments with the remaining amount payable to Pfizer (including interest). The milestone payment accrued interest at 6.25% per annum. The milestone payment including accrued interest of $1.8 million was paid in full in September 2021. In addition, the company reached a commercial milestone by achieving aggregate worldwide net sales of $250.0 million in calendar year 2022, resulting in a payable to Pfizer of $12.5 million as of December 31, 2022. The commercial milestone payable was paid in February 2023.

The Company may trigger additional milestone payments in the future. Should the Company commercialize any more of the compounds licensed from Pfizer or any products containing any of these compounds, the Company will be obligated to pay to Pfizer annual royalties at a fixed rate in the low to mid-teens of net sales of all such products, subject to certain reductions and offsets in some circumstances. The Company's royalty obligation continues, on a product-by-product and country-by-country basis, until the later of (i) the last to expire licensed patent covering the applicable licensed product in such country, or (ii) the earlier of generic competition for such licensed product reaching a certain level in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. In the event that the Company sublicenses the rights granted to the Company under the license agreement with Pfizer to a third party, the same milestone and royalty payments are required. The Company can terminate the license agreement at will, or for safety concerns, in each case upon specified advance notice.

Takeda License Agreement

In September 2022, the Company entered into an exclusive license agreement with Takeda to license the worldwide research and development and commercial rights to alisertib, a selective, small-molecule, orally administered inhibitor of Aurora Kinase A. Under the terms of the exclusive license agreement, the Company assumed sole responsibility for the global development and commercialization of alisertib. The Company paid Takeda an upfront license fee of $7.0 million in October 2022 and is eligible to receive potential future milestone payments of up to $287.3 million upon the Company's achievement of certain regulatory and commercial milestones over the course of the exclusive license agreement, as well as tiered royalty payments for any net sales of alisertib. The Company recorded in-process research and development expense of $7.0 million in connection with the upfront payment related to the asset acquisition. As of December 31, 2025, no milestones had been accrued as the underlying contingencies were not considered probable.

Clinical Trial Contracts

The Company engages with CROs and contract manufacturing organizations ("CMOs") in addition to engaging in contracts for the management of its ongoing clinical trials and pre-commercialization efforts. The Company may cancel these agreements with a 30 to 45 day written notice to the outside vendor. The Company would be obligated to pay for services rendered up to that point, which amounts to total contractual obligations of approximately $54.9 million within the next twelve months. The contracts also contain variable costs that are hard to predict as they are based on such things as patients enrolled and clinical trial sites, which can vary, and therefore, are not included in the total obligations amount. Included in the total contractual obligations amount above are payments to be made when milestones are reached. As of December 31, 2025, the Company's obligations for potential milestone payments totaled approximately $15.7 million. This amount will be paid by the Company if all milestones are reached and would reduce the overall contractual obligation if one or more milestone is never reached.

Legal Proceedings

The Company and certain of its executive officers were named as defendants in the lawsuits detailed below. The Company records a liability in the consolidated financial statements for loss contingencies when a loss is known or considered probable and the amount can be reasonably estimated. If the reasonable estimate of a known or probable loss is a range, and no amount within the range is a better estimate than any other, the minimum amount of the range is accrued. If a loss is reasonably possible but not known or probable, and can be reasonably estimated, the estimated loss or range of loss is disclosed. When determining the estimated loss or range of loss, significant judgment is required to estimate the amount and timing of a loss to be recorded.

Legal Malpractice Suit

On September 17, 2020, the Company filed a lawsuit against Hedrick Gardner Kincheloe & Garofalo, L.L.P. and David L. Levy, the attorneys who previously represented the Company in *Eshelman v. Puma Biotechnology, Inc., et al*. in the Superior Court of Mecklenburg County, North Carolina. The Company is alleging legal malpractice based on the defendants' negligent handling of the defense of the Company in *Eshelman v. Puma Biotechnology, Inc., et al*. The Company is seeking recovery of the entire amount awarded in *Eshelman v. Puma Biotechnology, Inc., et al*. and all legal fees and expenses incurred in appealing from the judgment and retrying the damages phase of the trial. On November 23, 2020, the defendant filed an answer to the complaint denying the allegations of negligence. On August 19, 2022, the Company filed a voluntary dismissal of the legal malpractice action, without prejudice, to allow the *Eshelman v. Puma Biotechnology, Inc., et al*. to conclude before proceedings. On June 2, 2023, the Company re-filed the lawsuit against Hedrick Gardner Kincheloe & Garofalo, L.L.P. and David L. Levy, the attorneys who previously represented the Company in *Eshelman v. Puma Biotechnology, Inc., et al.* in the Superior Court of Mecklenburg County, North Carolina. On August 22, 2023, the defendants filed motions to dismiss the case. These motions were presented at a hearing on February 20,

2024. The Superior Court Judge granted the motions to dismiss on March 20, 2024. The Company appealed this ruling to the North Carolina Court of Appeals. On September 3, 2025, the Court of Appeals reversed the dismissal of the Company's claim for legal malpractice and remanded the case to the Superior Court for further proceedings. The defendants filed a petition for discretionary review of this decision by the North Carolina Supreme Court on October 8, 2025. The Supreme Court has not decided whether to accept the case for review.

Patent-Related Proceedings

AstraZeneca Litigation

On September 22, 2021, the Company filed suit against AstraZeneca Pharmaceuticals, LP, AstraZeneca AB, and AstraZeneca PLC for infringement of United States Patent Nos. 10,603,314 ("the '314 patent") and 10,596,162 ("the '162 patent") (*Puma Biotechnology, Inc. et al. v. AstraZeneca Pharmaceuticals LP et al*., 1:21CV01338 (D. Del. Sep. 22, 2021)). The Company's complaint alleges that AstraZeneca's commercial manufacture, use, offer for sale, sale, distribution, and/or importation of Tagrisso® (osimertinib) products for the treatment of gefitinib and/or erlotinib-resistant non-small cell lung cancer infringes the '314 and '162 patents. The Company is an exclusive licensee of the '314 and '162 patents under the Pfizer Agreement. Wyeth is a co-plaintiff. Plaintiffs seek a judgment that AstraZeneca's product infringes the asserted patents and an award of monetary damages in an amount to be proven at trial. AstraZeneca AB and AstraZeneca Pharmaceuticals LP filed an answer and counterclaims on November 5, 2021, including claims challenging the asserted patents as not infringed and/or invalid, and accusing plaintiffs of unclean hands and patent misuse. The parties stipulated to dismiss AstraZeneca PLC as a defendant and Pfizer as a Counterclaim Defendant on December 10, 2021, which the Court so ordered on December 13, 2021. The Company filed its answer to AstraZeneca's counterclaims on December 17, 2021, denying those claims. The case was reassigned to visiting Judge Matthew Kennelly of the Northern District of Illinois. A Markman Hearing was conducted on March 17, 2023, and the Court issued its claim construction decision on March 29, 2023. Fact discovery closed on May 19, 2023, and expert discovery closed on November 17, 2023. The Court denied the parties' respective motions for summary judgment and Daubert motions, other than to clarify that Plaintiffs' damages cannot extend to any time period before the asserted patents were issued. The Court granted AstraZeneca's motion to dismiss the Company as a Plaintiff on constitutional standing grounds but denied the motion to dismiss Wyeth as a Plaintiff on constitutional standing grounds. On April 29, 2024, the Court granted AstraZeneca's motion to dismiss AstraZeneca's counterclaims against the Company, which removed the Company from the case. Wyeth remained in the case as a Plaintiff and counterclaim-defendant. Under the Company's worldwide exclusive license agreement with Pfizer, Inc. (the parent of Wyeth) as amended, the Company also maintains contractual rights to recover monetary damages in the AstraZeneca litigation, and those contractual rights are unaffected by the court's March 18, 2024 and April 29, 2024 orders. A jury trial was held May 13-17, 2024. The jury found in favor of Wyeth and against AstraZeneca. In particular, the jury found that use of Tagrisso® according to each of the three FDA-approved indications infringes the asserted claims of the '314 and '162 patents, and that AstraZeneca induces that infringement. The jury further rejected AstraZeneca's challenges to the validity of the patents, finding that they are not invalid. The jury awarded damages to Wyeth for past acts of infringement through December 31, 2023, in the amount of $107,500,000. A separate bench trial related to certain equitable claims and defenses raised by AstraZeneca was held before Judge Kennelly on June 20 and 25, 2024. On August 6, 2024, Judge Kennelly issued his ruling on the issues that were tried in the bench trial, finding for Wyeth and against AstraZeneca on all claims and defenses. The Court found that AstraZeneca had not proved its claim that Wyeth's asserted patents were invalid as indefinite, or that Wyeth had committed acts that would give rise to findings of unclean hands, implied waiver, or patent misuse. AstraZeneca filed a motion challenging the jury's verdict and requesting a new trial. Wyeth filed a motion requesting supplemental damages for past infringement from January 1, 2024, through the date of judgment; pre-and-post judgment interest, and ongoing royalties through the remaining term of the patents. Briefing on these motions from both sides was completed on July 16, 2024. On August 14, 2024, Judge Kennelly ruled on AstraZeneca's motion challenging the jury's verdict, granting it in part and denying it in part. The Court granted AstraZeneca's motion for judgment as a matter of law that the '314 and '162 patents are invalid under 35 U.S.C. § 112 for lacking enablement and adequate written description as to a particular claim limitation. In all other respects, the Court denied AstraZeneca's motion. The Court entered its final and appealable judgment accordingly. The Company respectfully disagrees with the Court's ruling regarding invalidity with respect to the particular claim limitation. Wyeth filed a notice of appeal on September 12, 2024, appealing the District Court's judgment as a matter of law, as well as other rulings and opinions of the Court adverse to Wyeth. On December 18, 2024, Wyeth filed its opening brief. On March 13, 2025, AstraZeneca filed its response brief. On March 20, 2025, non-parties Regeneron Pharmaceuticals, Inc. and Sanofi-Aventis U.S. LLC filed a motion for leave to file an amicus curiae brief in the Federal Circuit. The motion was granted on May 16, 2025. On June 6, 2025, Wyeth filed its reply brief. Briefing on the appeal is now complete, and the parties await further order from the Court.

Acebright China Litigation

On January 18, 2022, Shanghai Acebright Pharmaceuticals Group Co., Ltd. ("Acebright") filed an abbreviated new drug application ("ANDA") with the National Medical Products Administration in China ("NMPA") seeking approval to market a generic version of the Company's NERLYNX® (neratinib) tablet, 40mg in China. Acebright seeks approval prior to the expiration of three patents listed on the China Patent Information Registration Platform for Marketed Drugs ("Chinese Orange Book"), namely, Chinese Patent Nos. ZL201410082103.7, ZL201080060546.6, and ZL200880118789.3 (the "'789 patent" and collectively, the "NERLYNX® Patents"), alleging in a Type 4.2 patent declaration that its generic version of NERLYNX does not fall within the scope of the claims of NERLYNX® Patents listed in the Chinese Orange Book. The patent declaration of Acebright was published in the Chinese Orange Book on January 19, 2022. On March 2, 2022, the Company filed petitions with the China National Intellectual Property Administration ("CNIPA") and requested administrative determination that Acebright's generic neratinib tablet falls within the scope of the claims of NERLYNX® Patents listed in the Chinese Orange Book. The Company's request for administrative determination was accepted by CNIPA on March 18, 2022. The Company has notified NMPA of the acceptance of the request for administrative determination for NMPA to institute a stay of Acebright's ANDA for nine months. On July 11, 2022, CNIPA decided that claims 5 and 6 of Patent No. ZL200880118789.3 are not eligible for registration in the Chinese Orange Book on the ground that these two pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On September 9, 2022, CNIPA decided that the generic drug in Acebright's ANDA does not fall within the protection scope of claims 1, 3, 5 and 6 of Patent No. ZL201410082103.7 and claims 1-4, 7 and 9-13 of Patent No. ZL201080060546.6. The three CNIPA administrative decisions on NERLYNX® Patents have lifted the stay of Acebright's ANDA by NMPA. The Company has appealed each CNIPA administrative decision in January 2023 at the Beijing Intellectual Property Court ("BJIPC"). The three appeals were accepted by BJIPC on February 20, 2023. The Company also filed three civil complaints based on the three NERLYNX® Patents against Acebright with the BJIPC in July 2022 and requested court determination that Acebright's generic neratinib tablet falls within the scope of the claims of NERLYNX® Patents. On May 6, 2023, the Company withdrew two civil lawsuits and two appeals in relation to Chinese Patent Nos. ZL201410082103.7 and ZL201080060546.6 at the BJIPC. On May 24, 2023, the BJIPC accepted the Company's withdrawal request. On July 24, 2023, the Company withdrew the one remaining civil lawsuit and one appeal in relation to Chinese Patent No. ZL200880118789.3 at the BJIPC. On August 15, 2023, the BJIPC accepted the Company's withdrawal request. On September 12, 2023, the NMPA approved Acebright's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20234141.

On December 28, 2023, the Company filed a civil lawsuit against Acebright for infringement of the '789 patent under Article 11 of the Chinese Patent Law before Jiangsu Nanjing Intermediate People's Court. The Company's complaint alleges that Acebright's offer for sale of a generic version of the Company's NERLYNX® product infringes the '789 patent. The Company seeks a judgment that Acebright's product infringes the '789 patent and Acebright's act of offer for sale shall be enjoined. On January 2, 2024, Jiangsu Nanjing Intermediate People's Court accepted the civil complaint. An oral hearing was held on June 19, 2024, during which the Company amended its complaint to allege that Acebright making, selling and offering to sell the generic version of NERLYNX® infringes the '789 patent. On July 24, 2024, the Company submitted a request to withdraw the lawsuit. On August 8, 2024, Jiangsu Nanjing Intermediate People's Court accepted the withdrawal request.

On September 27, 2024, the Company filed an additional claim of infringement of the '789 patent against Acebright at Jiangsu Nanjing Intermediate People's Court. On October 14, 2024, the Court accepted the complaint and designated case number (2024) Su 01 Min Chu 2192 to this case. On December 16, 2024, the Court conducted an evidence exchange hearing. On January 10, 2025, the Court conducted a hearing of party experts on the evaluation of evidence. On July 14, 2025, the Court conducted a hearing to examine evidence and debate merits of party arguments. On September 28, 2025, the Court issued a first-instance decision, deciding that Acebright's product does not fall within the scope of the '789 patent, and Acebright did not infringe the '789 patent; the Court also decided that the Company's enforcement efforts were not malicious and did not amount to unfair competition.

Aosaikang China Litigation

On November 17, 2022, Jiangsu Aosaikang Pharmaceutical Co. Ltd. ("Aosaikang") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2202006. Aosaikang made Type 4.2 declarations against the four Orange Book Patents ZL201410082103.7, ZL201080060546.6, ZL200880118789.3 and ZL201710057547.9, alleging that its generic version of NERLYNX does not fall within the scope of the claims of the Orange Book patents. Aosaikang also alleged that Patents ZL200880118789.3 and ZL201710057547.9 are not eligible for Chinese Orange Book listing.

On December 28, 2022, the Company submitted four Article 76 petitions against the Aosaikang ANDA with the CNIPA and requested administrative determination that Aosaikang's generic neratinib tablet falls within the scope of the claims of the four Orange Book patents. On January 6, 2023, the CNIPA accepted the Company's request for administrative determination in relation to Patent Nos. ZL201410082103.7 and ZL201080060546.6. Also on January 6, 2023, the CNIPA declined to accept the Company's request for administrative determination in relation to Patent Nos. ZL200880118789.3 and ZL201710057547.9, alleging that the listed claims are not eligible for registration in the Chinese Orange Book on the ground that these pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On January 28, 2023, the Company requested the NMPA to institute a nine-month stay against Aosaikang ANDA starting from the CNIPA's acceptance of the Company's request for administrative determination. On June 2, 2023, CNIPA decided that the generic drug in Aosaikang's ANDA does not fall within the protection scope of claims 1, 3, 5 and 6 of Patent No. ZL201410082103.7 and claims 1-4, 7 and 9-13 of Patent No. ZL201080060546.6. The two CNIPA administrative decisions on NERLYNX® Patents have lifted the stay of Aosaikang's ANDA by NMPA. On October 22, 2024, the NMPA approved Aosaikang's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20249180.

Convalife China Litigation

Convalife Pharmaceuticals (Shanghai) Co., Ltd ("Convalife") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2202095. On December 23, 2022, Convalife made Type 4.2 declarations against the four Orange Book Patents ZL201410082103.7, ZL201080060546.6, ZL200880118789.3 and ZL201710057547.9, alleging that its generic version of NERLYNX does not fall within the scope of the claims of the Orange Book patents. Convalife also alleged that Patents ZL200880118789.3 and ZL201710057547.9 are not eligible for Chinese Orange Book listing.

On February 1, 2023, the Company submitted four Article 76 petitions against the Convalife ANDA with the CNIPA and requested administrative determination that Convalife's generic neratinib tablet falls within the scope of the claims of the four Orange Book patents. On February 3, 2023, the CNIPA accepted the Company's request for administrative determination in relation to Patent Nos. ZL201410082103.7 and ZL201080060546.6. Also on February 3, 2023, the CNIPA declined to accept the Company's request for administrative determination in relation to Patent Nos. ZL200880118789.3 and ZL201710057547.9, alleging that the listed claims are not eligible for registration in the Chinese Orange Book on the ground that these pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On February 24, 2023, the Company requested the NMPA to institute a nine-month stay against Convalife ANDA starting from the CNIPA's acceptance of the Company's request for administrative determination. On June 2, 2023, CNIPA decided that the generic drug in Convalife's ANDA does not fall within the protection scope of claims 1, 3, 5 and 6 of Patent No. ZL201410082103.7 and claims 1-4, 7 and 9-13 of Patent No. ZL201080060546.6. The two CNIPA administrative decisions on NERLYNX® Patents have lifted the stay of Convalife's ANDA by NMPA. On June 28, 2024, the NMPA approved Convalife's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20244222.

Kelun China Litigation

Hunan Kelun Pharmaceutical Co., Ltd. ("Kelun") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2300221. On January 28, 2023, Kelun made Type 4.2 declarations against the four Orange Book Patents ZL201410082103.7, ZL201080060546.6, ZL200880118789.3 and ZL201710057547.9, alleging that its generic version of NERLYNX does not fall within the scope of the claims of the Orange Book patents. Kelun also alleged that Patents ZL200880118789.3 and ZL201710057547.9 are not eligible for Chinese Orange Book listing.

On March 13, 2023, the Company submitted four Article 76 petitions against the Kelun ANDA with the CNIPA and requested administrative determination that Kelun's generic neratinib tablet falls within the scope of the claims of the four Orange Book patents. On March 21, 2023, the CNIPA declined to accept the Company's request for administrative determination in relation to Patent Nos. ZL200880118789.3 and ZL201710057547.9, alleging that the listed claims are not eligible for registration in the Chinese Orange Book on the ground that these pharmaceutical method-of-use claims fall within the scope of "patents of crystalline forms," which are not eligible for listing in the Chinese Orange Book. On March 24, 2023, the CNIPA accepted the Company's request for administrative determination in relation to Patent Nos. ZL201410082103.7 and ZL201080060546.6. On April 17, 2023, the Company requested the NMPA to institute a nine-month stay against Kelun's ANDA starting from the CNIPA's acceptance of the Company's request for administrative determination. On September 14, 2023, the Company withdrew the two requests for administrative determination in relation to Chinese Patent Nos. ZL201410082103.7 and ZL201080060546.6 at the CNIPA. On September 25, 2023, the CNIPA accepted the Company's withdrawal request. On September 9, 2025, the NMPA approved Kelun's ANDA to market a generic version of the Company's NERLYNX® in China with the approval number of GuoYaoZhunZi H20255337.

Demai Litigation

Zhengzhou Demai Pharmaceutical Co., Ltd ("Demai") filed an ANDA with NMPA in China seeking approval to market a generic version of the Company's NERLYNX®. The ANDA application No. is CYHS2402776. On August 26, 2024, Demai made a Type 4.2 declaration against Orange Book Patent ZL201410082103.7, alleging that its generic version of NERLYNX does not fall within the scope of the claims of this Orange Book patent. On September 30, 2024, the Company filed a lawsuit against Demai at the BJIPC based on Nerlynx Patent No. ZL201080060546.6 and on October 8, 2024, the Company filed a lawsuit against Demai at the BJIPC based on Nerlynx Patent No. ZL201410082103.7. On February 13, 2025, the Company withdrew the lawsuits from BJIPC, filed an Article 76 petition with the CNIPA against the Demai ANDA and requested administrative determination that Demai's generic neratinib maleate tablet falls within the scope of the claims of Nerlynx Patent No. ZL201080060546.6. On February 21, 2025, the CNIPA accepted the Company's petition and started examination. On March 18, 2025, the Company filed a request with the NMPA to set up a nine-month stay on Demai's ANDA.

Hexal European Patent Opposition

An opposition was filed by Hexal AG ("Hexal") on August 3, 2016 against European Patent No. EP2416774 which was licensed from Pfizer in 2011, and which claims neratinib for use in a method for treating HER-2/neu overexpressed/amplified cancer and improving IDFS, wherein the method comprises delivering neratinib therapy to HER-2/neu overexpressed/amplified cancer patients following the completion of at least one year of trastuzumab adjuvant therapy, and wherein the neratinib therapy comprises treating the cancer patients with neratinib for at least twelve months. An oral hearing was held on December 8, 2017, wherein the patent was maintained as granted. Following an appeal filed by Hexal, the Board of Appeal of the European Patent Office rejected the claims as granted and all pending auxiliary requests during the oral hearing of September 2, 2021. Before issuance of a decision, we withdrew approval of the text in which the patent was granted and all pending auxiliary requests, thereby revoking the patent and concluding the appeal. One European divisional application, namely EP15188350.1, was granted with the European patent number EP3000467 on March 1, 2023. Oppositions against EP3000467 were filed by Hexal on November 3, 2023, by Alfred E. Tiefenbacher (GmbH & Co. KG) on November 28, 2023 and by Generics (UK) Limited ("Generics") on December 1, 2023. EP3000467 is used as the basic patent for Supplementary Protection Certificate applications for the EMA-approved NERLYNX® product, 17 of which have been granted, three proceedings have been stayed, and 11 are in active prosecution. The patentee response to the notice of opposition was filed on April 15, 2024, following which, all three opponents filed additional arguments in reply to the patentee's submission. On February 6, 2025, the Company filed its response to the summons to attend oral proceedings, including six auxiliary requests. Alfred E. Tiefenbacher and Hexal filed their responses to the summons to oral proceedings on February 6 and 7, 2025, respectively. Hexal filed a further brief on March 19, 2025. Oral proceedings took place on April 9 and 10, 2025. EP3000467 was upheld as amended after the first instance hearing based on Auxiliary Request 1, which covers the EMA approved indication for NERLYNX® as an extended adjuvant therapy for treating early stage hormone receptor-positive HER-2-overexpressed/amplified breast cancer. The first instance decision may be appealed. Hexal filed an appeal on June 6, 2025, Generics filed an appeal on June 20, 2025 and Wyeth filed an appeal on June 30, 2025. On September 5, 2025, Wyeth filed its grounds of appeal, including nine auxiliary requests. On the same day, Hexal filed its grounds of appeal. Generics filed its grounds of appeal on September 4, 2025, and Alfred E. Tiefenbacher filed its grounds of appeal on September 1, 2025. On December 16, 2025, Alfred E. Tiefenbacher withdrew its appeal. Wyeth responded to the opponents' grounds of appeal on January 12, 2026. One European divisional application is pending in the same family, namely EP 23157078.8. A response to the European Search Opinion (ESO) for this application was filed February 14, 2024. The first office action was issued on January 28, 2025 with a response to the first office action filed on July 22, 2025.

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Alan H. Auerbach, certify that:

1. I have reviewed this Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2025;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2026

/s/ Alan H. Auerbach
Alan H. Auerbach
Principal Executive Officer

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Maximo F. Nougues, certify that:

1. I have reviewed this Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2025;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2026

/s/ Maximo F. Nougues
Maximo F. Nougues
Principal Financial and Accounting Officer

Exhibit 32.1

CERTIFICATION

PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

The following certification is being furnished solely to accompany the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2025, pursuant to 18 U.S.C. § 1350 and in accordance with SEC Release No. 33-8238. This certification shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be incorporated by reference in any filing of Puma Biotechnology, Inc. under the Securities Act of 1933, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Certification of Principal Executive Officer

I, Alan H. Auerbach, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2025, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended, and that the information contained in such report fairly presents, in all material respects, the financial condition and results of operations of Puma Biotechnology, Inc.

Date: February 26, 2026

/s/ Alan H. Auerbach
Alan H. Auerbach
Principal Executive Officer

A signed original of this written statement required by Section 906 has been provided to Puma Biotechnology, Inc. and will be retained by Puma Biotechnology, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION

PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

The following certification is being furnished solely to accompany the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2025, pursuant to 18 U.S.C. § 1350 and in accordance with SEC Release No. 33-8238. This certification shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be incorporated by reference in any filing of Puma Biotechnology, Inc. under the Securities Act of 1933, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Certification of Principal Financial Officer

I, Maximo F. Nougues, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2025, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended, and that the information contained in such report fairly presents, in all material respects, the financial condition and results of operations of Puma Biotechnology, Inc.

Date: February 26, 2026

/s/ Maximo F. Nougues
Maximo F. Nougues
Principal Financial and Accounting Officer

A signed original of this written statement required by Section 906 has been provided to Puma Biotechnology, Inc. and will be retained by Puma Biotechnology, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

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COMPANY LEADERSHIP

BOARD OF DIRECTORS

Alan H. Auerbach
Chairman, Chief Executive Officer and President
Puma Biotechnology, Inc.

Alessandra Cesano, M.D., Ph.D.
Chief Medical Officer and Executive Vice President *(former)*
ESSA Pharma Inc.

Allison Dorval
Chief Financial Officer
AIRNA

Michael P. Miller
Executive Vice President U.S. Commercial *(retired)*
Jazz Pharmaceuticals plc

Jay M. Moyes
Chief Financial Officer *(retired)*
Sera Prognostics, Inc.

Adrian M. Senderowicz, M.D.
Senior Advisor
Constellation Pharmaceuticals

Brian Stuglik, R.Ph.
Chief Executive Officer *(retired)*
Verastem, Inc.

Troy E. Wilson, Ph.D., J.D.
President, Chief Executive Officer and Chairman
Kura Oncology, Inc.

CORPORATE OFFICERS

Alan H. Auerbach
Chairman, Chief Executive Officer and President

Maximo F. Nougues
Chief Financial Officer

Douglas Hunt, B.Sc. (Hons)
Chief Regulatory Affairs, Medical Affairs,
and Pharmacovigilance Officer

STOCKHOLDER INFORMATION

Corporate Headquarters
Puma Biotechnology, Inc.
10880 Wilshire Blvd., Suite 1700
Los Angeles, CA 90024
424-248-6500

Investor Relations
Securities analysts, investment professionals and stockholders should direct inquiries to Investor Relations at (424) 248-6500 or ir@pumabiotechnology.com.

For additional information about Puma, please visit our website at https://www.pumabiotechnology.com.

Common Stock
Puma's common stock is listed on The NASDAQ Stock Market under the trading symbol "PBYI."

Transfer Agent
EQ Shareowner Services℠

Mail:
P.O. Box 64854
St. Paul, MN 55164

Courier:
1110 Centre Pointe Curve, Suite 101
Mendota Heights, MN 55120--4100

Telephone:
800-468-9716 | 651-450-4064

Website:
https://www.shareowneronline.com

Annual Meeting
The 2025 Annual Meeting of Stockholders will be held at 1:00 p.m. PDT on Thursday, June 11, 2026 at
Puma Biotechnology, Inc.
10880 Wilshire Boulevard, Suite 1700
Los Angeles, CA 90024

Independent Registered Public Accounting Firm
KPMG LLP
550 South Hope St.
Suite 1500
Los Angeles, CA 90071

Forward-Looking Statements

This document contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, including, but not limited to, statements regarding the commercialization of NERLYNX®, the potential indications of Puma's drug candidates and the development of those drug candidates, and the announcement of data relative to Puma's clinical trials. These statements are often, but not always, made through the use of words or phrases such as "anticipates," "estimates," "expects," "may," "will," "would," "plans," "projects," "continuing," "ongoing," "believes," "intends," and similar words or phrases intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Discussions containing these forward-looking statements may be found throughout this document, including the sections entitled "Item 1. Business" and "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" in Puma's Annual Report on Form 10-K for the fiscal year ended December 31, 2025. All forward-looking statements included in this document involve risks and uncertainties that could cause Puma's actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These forward-looking statements are based on current expectations, forecasts and assumptions, and actual outcomes and results could differ materially from those in the forward-looking statements due to a number of factors, which include, but are not limited to, any adverse impact on Puma's business, strategy, plans and objectives of management, future operations and/or financial position, growth opportunities in the market in which Puma operates, or the global economy and financial markets, generally, from changes in interest rates, inflationary concerns, geopolitical conflicts, tariffs and the risk factors disclosed in the periodic and current reports filed by Puma with the Securities and Exchange Commission from time to time, including Puma's Annual Report on Form 10-K for the fiscal year ended December 31, 2025, which is included herein. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made. Puma assumes no obligation to update these forward-looking statements, except as required by law.

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Los Angeles, CA 90024
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