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, 2023

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 0-30739

INSMED INCORPORATED

(Exact name of registrant as specified in its charter)

Virginia	**54-1972729**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. employer identification no.)**
700 US Highway 202/206 Bridgewater, New Jersey 08807 (Address of principal executive offices)	**(908) 977-9900 (Registrant's telephone number including area code)**

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

Title of each class	Trading symbols	Name of each exchange on which registered
Common Stock, par value $0.01 per share	**INSM**	**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 an emerging growth company (See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act). Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐ Emerging growth company ☐

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant on June 30, 2023, was $3.0 billion (based on the closing price for shares of the registrant's common stock as reported on the Nasdaq Global Select Market on that date). In determining this figure, the registrant has assumed solely for this purpose that all of its directors, executive officers, persons beneficially owning 10% or more of the registrant's outstanding common stock and certain other stockholders of the registrant may be considered to be affiliates. This assumption shall not be deemed conclusive as to affiliate status for this or any other purpose.

On February 19, 2024, there were 148,491,583 shares of the registrant's common stock, $0.01 par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for its 2024 Annual Meeting of Shareholders to be filed with the Securities and Exchange Commission no later than April 29, 2024 and to be delivered to shareholders in connection with the 2024 Annual Meeting of Shareholders, are herein incorporated by reference in Part III of this Annual Report on Form 10-K.

INSMED INCORPORATED

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Unless the context otherwise indicates, references in this Annual Report on Form 10-K to “Insmed Incorporated” refer to Insmed Incorporated, a Virginia corporation, and the “Company,” “Insmed,” “we,” “us” and “our” refer to Insmed Incorporated together with its consolidated subsidiaries. INSMED, PULMOVANCE, ARIKARES and ARIKAYCE are trademarks of Insmed Incorporated. This Annual Report on Form 10-K also contains trademarks of third parties. Each trademark of another company appearing in this Annual Report on Form 10-K is the property of its owner.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 (the Exchange Act), are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) identify forward-looking statements.

Forward-looking statements are based on our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following:

- *failure to continue to successfully commercialize ARIKAYCE, our only approved product, in the United States (US), Europe or Japan (amikacin liposome inhalation suspension, Liposomal 590 mg Nebuliser Dispersion, and amikacin sulfate inhalation drug product, respectively), or to maintain US, European or Japanese approval for ARIKAYCE;*
- *uncertainties or changes in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community;*
- *our inability to obtain full approval of ARIKAYCE from the US Food and Drug Administration (FDA), including the risk that we will not successfully or in a timely manner validate a patient reported outcome (PRO) tool and complete the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE;*
- *inability of us, PARI Pharma GmbH (PARI) or our other third-party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira® Nebulizer System (Lamira);*
- *our inability to obtain and maintain adequate reimbursement from government or third-party payors for ARIKAYCE or acceptable prices for ARIKAYCE;*
- *development of unexpected safety or efficacy concerns related to ARIKAYCE, brensocatib, treprostinil palmitil inhalation powder (TPIP) or our other product candidates;*
- *inaccuracies in our estimates of the size of the potential markets for ARIKAYCE, brensocatib, TPIP or our other product candidates or in data we have used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates;*
- *the risks and uncertainties associated with, and the perceived benefits of, our secured senior loan with certain funds managed by Pharmakon Advisors, LP (Pharmakon) and our royalty financing with OrbiMed Royalty & Credit Opportunities IV, LP, (OrbiMed) including our ability to maintain compliance with the covenants in the agreements for the senior secured loan and royalty financing and the impact of the restrictions on our operations under these agreements;*
- *our inability to create or maintain an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE or any of our product candidates that are approved in the future;*
- *failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population;*
- *risk that brensocatib or TPIP does not prove to be effective or safe for patients in ongoing and future clinical studies, including, for brensocatib, the ASPEN study;*
- *risk that our competitors may obtain orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication;*
- *failure to successfully predict the time and cost of development, regulatory approval and commercialization for novel gene therapy products;*
- *failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib, TPIP and our other product candidates due to our limited experience in conducting preclinical development activities and clinical trials necessary for regulatory approval and our potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval of our product candidates or to permit the use of ARIKAYCE in the broader population of patients with MAC lung disease, among other things;*
- *risks that our clinical studies will be delayed, that serious side effects will be identified during drug development, or that any protocol amendments submitted will be rejected;*
- *risks that interim or partial data sets are not representative of a complete or larger data set or that blinded data will not be predictive of unblinded data;*

- *failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside the US, Europe or Japan, or for our product candidates in the US, Europe, Japan or other markets, including separate regulatory approval for Lamira in each market and for each usage;*
- *failure of third parties on which we are dependent to manufacture sufficient quantities of ARIKAYCE or our product candidates for commercial or clinical needs, to conduct our clinical trials, or to comply with our agreements or laws and regulations that impact our business or agreements with us;*
- *our inability to attract and retain key personnel or to effectively manage our growth;*
- *our inability to successfully integrate our recent acquisitions and appropriately manage the amount of management's time and attention devoted to integration activities;*
- *risks that our acquired technologies, products and product candidates are not commercially successful;*
- *inability to adapt to our highly competitive and changing environment;*
- *inability to access, upgrade or expand our technology systems or difficulties in updating our existing technology or developing or implementing new technology;*
- *risk that we are unable to maintain our significant customers;*
- *risk that government healthcare reform materially increases our costs and damages our financial condition;*
- *business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises;*
- *risk that our current and potential future use of artificial intelligence (AI) and machine learning may not be successful;*
- *deterioration in general economic conditions in the US, Europe, Japan and globally, including the effect of prolonged periods of inflation, affecting us, our suppliers, third-party service providers and potential partners;*
- *inability to adequately protect our intellectual property rights or prevent disclosure of our trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters;*
- *restrictions or other obligations imposed on us by agreements related to ARIKAYCE or our product candidates, including our license agreements with PARI and AstraZeneca AB (AstraZeneca), and failure to comply with our obligations under such agreements;*
- *the cost and potential reputational damage resulting from litigation to which we are or may become a party, including product liability claims;*
- *risk that our operations are subject to a material disruption in the event of a cybersecurity attack or issue;*
- *our limited experience operating internationally;*
- *changes in laws and regulations applicable to our business, including any pricing reform, and failure to comply with such laws and regulations;*
- *our history of operating losses, and the possibility that we never achieve or maintain profitability;*
- *goodwill impairment charges affecting our results of operations and financial condition;*
- *inability to repay our existing indebtedness and uncertainties with respect to our ability to access future capital; and*
- *delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities and unexpected expenses associated with those plans.*

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. Any forward-looking statement is based on information current as of the date of this Annual Report on Form 10-K and speaks only as of the date on which such statement is made. Actual events or results may differ materially from the results, plans, intentions or expectations anticipated in these forward-looking statements as a result of a variety of factors, many of which are beyond our control. More information on factors that could cause actual results to differ materially from those anticipated is included from time to time in our reports filed with the Securities and Exchange Commission (SEC), including, but not limited to, those described in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in this Annual Report on Form 10-K. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

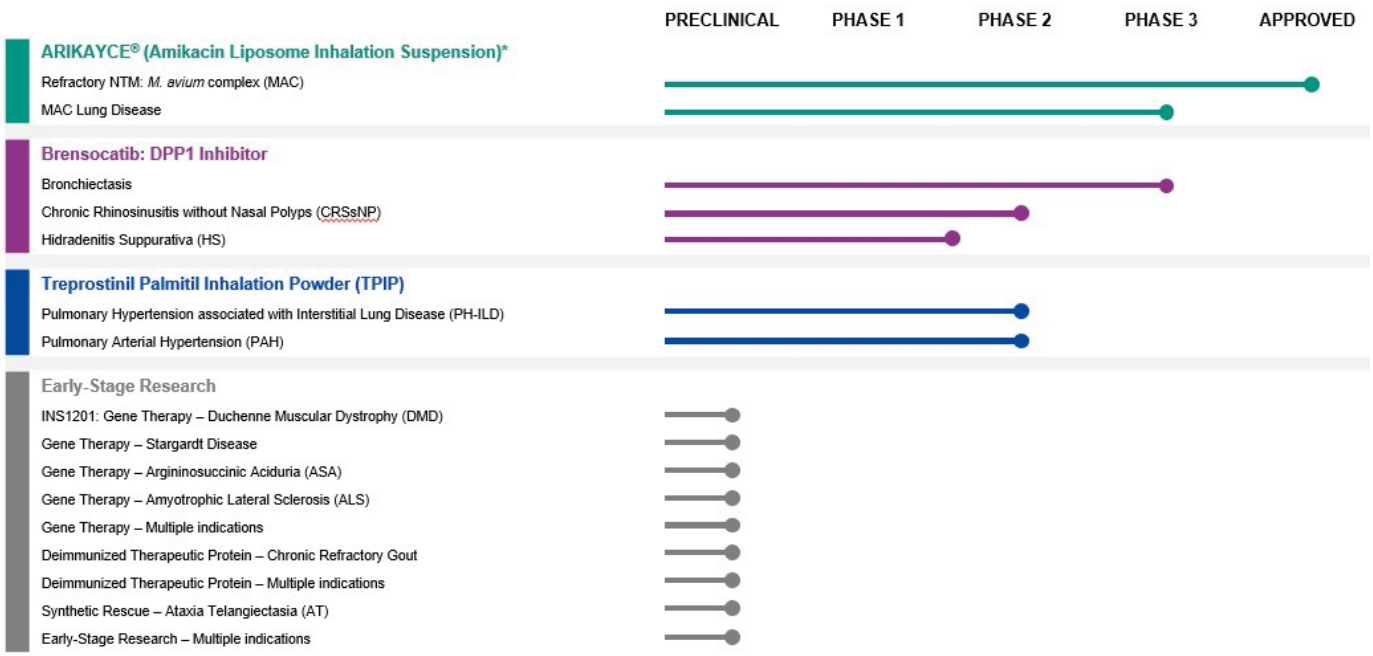
PART I

ITEM 1. BUSINESS

Business Overview

We are a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. Our first commercial product, ARIKAYCE, is approved in the US as ARIKAYCE® (amikacin liposome inhalation suspension), in Europe as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion and in Japan as ARIKAYCE inhalation 590mg (amikacin sulfate inhalation drug product). ARIKAYCE received accelerated approval in the US in September 2018 for the treatment of *Mycobacterium avium complex* (MAC) lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options in a refractory setting. In October 2020, the European Commission (EC) approved ARIKAYCE for the treatment of nontuberculous mycobacterial (NTM) lung infections caused by MAC in adults with limited treatment options who do not have cystic fibrosis (CF). In March 2021, Japan's Ministry of Health, Labour and Welfare (MHLW) approved ARIKAYCE for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen. NTM lung disease caused by MAC (which we refer to as MAC lung disease) is a rare and often chronic infection that can cause irreversible lung damage and can be fatal.

Our pipeline includes clinical-stage programs, brensocatib and TPIP, as well as other early-stage research programs. Brensocatib is a small molecule, oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1), which we are developing for the treatment of patients with bronchiectasis and other neutrophil-mediated diseases, including chronic rhinosinusitis without nasal polyps (CRSsNP). TPIP is an inhaled formulation of the treprostinil prodrug treprostinil palmitil which may offer a differentiated product profile for pulmonary hypertension associated with interstitial lung disease (PH-ILD) and pulmonary arterial hypertension (PAH). Our early-stage research programs encompass a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA-end joining, and synthetic rescue. A summary of our commercial and pipeline products is shown below:



The information below summarizes our achievements in 2023 and the anticipated near-term milestones for ARIKAYCE and our product candidates.

ARIKAYCE

- We announced positive topline results from the ARISE trial in the third quarter of 2023. Based on these results, we have proposed to the FDA that the change of the respiratory score derived from the Quality of Life – Bronchiectasis (QOL-B) respiratory domain PRO be the primary endpoint for the ENCORE study, the second trial in our post-marketing confirmatory clinical trial program for ARIKAYCE. We anticipate receiving FDA feedback on the PRO in the first half of 2024.
- In December 2023, we received written feedback from the FDA on the PRO data produced in the ARISE study. We expect to meet with the FDA in the coming months to gain additional insights and guidance, from which we will finalize our statistical plans for the ENCORE study, including an updated enrollment target for the study.
- In January 2024, we reached enrollment of 250 patients in the ENCORE trial. Enrollment in the study remains ongoing as we await feedback from the FDA on the finalization of our statistical plan. We anticipate reporting topline data from ENCORE in 2025.

Brensocatib

- In the first quarter of 2023, we completed enrollment of the Phase 3 ASPEN trial in adult patients with bronchiectasis, and we anticipate sharing topline data in the latter half of the second quarter of 2024.
- We plan to explore the potential of brensocatib in additional neutrophil-mediated diseases. We have initiated the Phase 2b BiRCh trial of brensocatib in patients with CRSsNP.
- We are advancing commercial readiness activities in preparation for a launch of brensocatib for patients with bronchiectasis, if approved. If successful, we anticipate a launch in the US in mid-2025, followed by launches in Europe and Japan in the first half of 2026.
- We expect to initiate a Phase 2 study of brensocatib in patients with hidradenitis suppurativa (HS) in the second half of 2024.

TPIP

- In November 2023, we completed enrollment in the Phase 2 PH-ILD study, with 39 patients enrolled. Topline data from the study are anticipated in the second quarter of 2024.
- Enrollment in the Phase 2 study of TPIP in PAH remains ongoing. The Company anticipates enrolling 99 patients in the study, 45 of whom had been enrolled by year-end 2023, with topline results expected in 2025.

Early-Stage Research

- We continue to progress our early-stage research programs across a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA end-joining, and synthetic rescue.

To complement our internal research and development, we also actively evaluate in-licensing and acquisition opportunities for products, product candidates and technologies, including those that address serious and rare diseases with significant unmet need.

Our Strategy

Our strategy focuses on the needs of patients with serious and rare diseases. Our first product, ARIKAYCE, is approved in the US as ARIKAYCE® (amikacin liposome inhalation suspension), in Europe as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion and in Japan as ARIKAYCE inhalation 590mg (amikacin sulfate inhalation drug product). We are not aware of any other approved inhaled therapies specifically indicated to treat MAC lung disease in North America, Europe or Japan. We believe that ARIKAYCE has the potential to prove beneficial in other patients with refractory MAC. Our product candidates are brensocatib, our Phase 3 product candidate which we are developing for patients with bronchiectasis and other neutrophil-mediated diseases, and TPIP, our Phase 2 product candidate that may offer a differentiated product profile for patients with PH-ILD and PAH. We are also advancing our early-stage research programs encompassing a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA-end joining, and synthetic rescue.

Our key priorities are as follows:

- Continue to provide ARIKAYCE to appropriate patients and expand our reliable revenue stream;
- Produce topline clinical data readouts in the near and long term;
- Advance commercial readiness activities to serve significantly more patients with serious and rare diseases; and
- Control spending, prudently deploying capital to support the best return-generating opportunities.

ARIKAYCE for Patients with MAC Lung Disease

ARIKAYCE is our first approved product. ARIKAYCE received accelerated approval in the US in September 2018 for the treatment of refractory MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options. In October 2020, ARIKAYCE received approval in Europe for the treatment of NTM lung infections caused by MAC in adults with limited treatment options who do not have CF. In March 2021, ARIKAYCE received approval in Japan for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen. MAC lung disease is a rare and often chronic infection that can cause irreversible lung damage and can be fatal. Amikacin solution for parenteral administration is an established drug that has activity against a variety of NTM; however, its use is limited by the need to administer it intravenously and by toxicity to hearing, balance, and kidney function. Unlike amikacin solution for intravenous administration, our proprietary Pulmovance™ technology uses charge-neutral liposomes to deliver amikacin directly to the lungs where liposomal amikacin is taken up by the lung macrophages where the MAC infection resides. This technology also prolongs the release of amikacin in the lungs, while minimizing systemic exposure, thereby offering the potential for decreased systemic toxicities. ARIKAYCE's ability to deliver high levels of amikacin directly to the lung and sites of MAC infection via the use of our Pulmovance technology distinguishes it from intravenous amikacin. ARIKAYCE is administered once-daily using Lamira, an inhalation device developed and manufactured by PARI. Lamira is a portable nebulizer that enables aerosolization of liquid medications via a vibrating, perforated membrane, and was designed specifically for ARIKAYCE delivery.

The FDA has designated ARIKAYCE as an orphan drug and a Qualified Infectious Disease Product (QIDP) for NTM lung disease. Orphan designated drugs are eligible for seven years of exclusivity for the orphan indication. QIDP designation provides an additional five years of exclusivity for the designated indication. The FDA granted a total of 12 years of exclusivity in the indication for which ARIKAYCE was approved.

ARIKAYCE also has been included in the international treatment guidelines for NTM lung disease. The evidence-based guidelines, issued by the American Thoracic Society (ATS), European Respiratory Society (ERS), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and Infectious Diseases Society of America (IDSA), strongly recommend the use of ARIKAYCE for MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options who have failed to convert to a negative sputum culture after at least six months of treatment.

In October 2020, the FDA approved a supplemental new drug application for ARIKAYCE, adding important efficacy data regarding the durability and sustainability of culture conversion to the ARIKAYCE label. The data, which are from the Phase 3 CONVERT study of ARIKAYCE, demonstrate that the addition of ARIKAYCE to guideline-based therapy (GBT) was associated with sustained culture conversion through the end of treatment as well as durable culture conversion three months post-treatment compared with GBT alone.

Accelerated Approval

In March 2018, we submitted a new drug application (NDA) for ARIKAYCE to the FDA to request accelerated approval. Accelerated approval allows drugs that (i) are being developed to treat a serious or life-threatening disease or condition and (ii) provide a meaningful therapeutic benefit over existing treatments to be approved substantially based on an intermediate endpoint or a surrogate endpoint that is reasonably likely to predict clinical benefit, rather than a clinical endpoint

such as survival or irreversible morbidity. In September 2018, the FDA granted accelerated approval for ARIKAYCE under the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) for the treatment of refractory MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options. LPAD, which was enacted as part of the 21st Century Cures Act, serves to advance the development of new antibacterial drugs to treat serious or life-threatening infections in limited populations of patients with unmet needs. As required for drugs approved under the LPAD pathway, labeling for ARIKAYCE includes certain statements to convey that the drug has been shown to be safe and effective only for use in a limited population.

As a condition of accelerated approval, we must conduct a post-marketing confirmatory clinical trial. In December 2020, we commenced the post-marketing confirmatory clinical trial program for ARIKAYCE in patients with MAC lung disease consisting of the ARISE trial, an interventional study designed to validate cross-sectional and longitudinal characteristics of a PRO tool in MAC lung disease, and the ENCORE trial, designed to establish the clinical benefits and evaluate the safety of ARIKAYCE in patients with newly diagnosed or recurrent MAC lung infection who have not started antibiotics using the PRO tool validated in the ARISE trial. In September 2023, we announced positive topline results from the ARISE trial. The study met its primary objective of demonstrating that the QOL-B respiratory domain works effectively as a PRO tool in patients with MAC lung disease. Based on these results, we have proposed to the FDA that the change of the respiratory score derived from the QOL-B respiratory domain PRO be the primary endpoint for the ENCORE study. We reached our original target enrollment of 250 patients in the ENCORE trial in patients with newly diagnosed or recurrent nontuberculous mycobacterial lung infection caused by MAC who had not started antibiotics. Enrollment in the study remains ongoing. We received written feedback from the FDA on the patient-reported outcome data produced in the Phase 3 ARISE study in December 2023. We expect to meet with the FDA in the coming months to gain additional insights and guidance, from which we will finalize our statistical plans for the Phase 3 ENCORE study, including an updated enrollment target for the study.

Regulatory Pathway Outside of the US

In October 2020, the EC granted marketing authorization for ARIKAYCE for the treatment of NTM lung infections caused by MAC in adults with limited treatment options who do not have CF. ARIKAYCE can now be prescribed for patients across the European Union (EU) countries as well as in the UK. ARIKAYCE is reimbursed nationally in France, Belgium, the Netherlands, the UK and Ireland. We have worked with the German National Association of Statutory Health Insurance Funds (GKV-SV) towards an agreement on the price of ARIKAYCE that would allow us to better serve the needs of patients in Germany; however, since we have been unable to reach an agreement, patient supply of ARIKAYCE in Germany was enabled by import from other EU countries in September 2022. We are working to ensure an uninterrupted supply of ARIKAYCE for patients in Germany and to provide physicians and pharmacists the information they need to obtain ARIKAYCE for their patients through the importation pathway. In January 2023, we agreed upon reimbursement terms with the French authorities. To date, we have been unable to reach an acceptable agreement of a nationally reimbursed price with the Italian Medicines Agency (AIFA); however, ARIKAYCE remains commercially available for physicians to prescribe in Italy under Class C, where we set the price and funding is agreed locally.

In March 2021, Japan's MHLW approved ARIKAYCE for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen. In July 2021, we launched ARIKAYCE in Japan.

The CONVERT Study and 312 Study

Accelerated approval of ARIKAYCE was supported by preliminary data from the CONVERT study, a global Phase 3 study evaluating the safety and efficacy of ARIKAYCE in adult patients with refractory MAC lung disease, using achievement of sputum culture conversion (defined as three consecutive negative monthly sputum cultures) by Month 6 as the primary endpoint. Patients who achieved sputum culture conversion by Month 6 continued in the CONVERT study for an additional 12 months of treatment following the first monthly negative sputum culture in order to assess the durability of culture conversion, as defined by patients that have completed treatment and continued in the CONVERT study off all therapy for three months. In May 2019, we presented at the American Thoracic Society meeting that 41/65 (63.1%) of patients on ARIKAYCE plus GBT who had achieved culture conversion by Month 6 had maintained durable culture conversion for three months off all therapy compared to 0/10 (0%) on GBT only ($p<0.0002$). Safety data for these patients were consistent with safety data previously reported for patients by Month 6 of the CONVERT study.

Patients who did not culture convert by Month 6 may have been eligible to enroll in the 312 study, an open-label extension study for these non-converting patients who completed six months of treatment in the CONVERT study. The primary objective of the 312 study was to evaluate the long-term safety and tolerability of ARIKAYCE in combination with a standard multi-drug regimen. The secondary objectives of the 312 study included evaluating the proportion of subjects achieving culture conversion (defined in the same way as the CONVERT study) by Month 6 and the proportion of subjects achieving culture conversion by Month 12, which was the end of treatment. We previously reported interim data as of December 2017 for patients in the 312 study, with 28.4% of patients who received GBT only in the CONVERT study (19/67) and 12.3% of patients

who had received ARIKAYCE plus GBT in the CONVERT study (7/57) achieving culture conversion by Month 6 of the 312 study. The 312 study has concluded and final efficacy data regarding culture conversion were consistent with these interim data. We have analyzed the safety and efficacy data from the 312 study, and we did not observe any new safety signals.

The ARISE Study

The ARISE trial was a global, randomized, double-blind, placebo-controlled Phase 3b study in adult patients with newly diagnosed or recurrent MAC infections that aimed to generate evidence demonstrating the domain specification, reliability, validity, and responsiveness of PRO-based scores, including a respiratory symptom score. The ARISE study met its primary objective of demonstrating that the QOL-B respiratory domain works effectively as a PRO tool in patients with MAC lung disease. Based on these results, we have proposed to the FDA that the change of the respiratory score derived from the QOL-B respiratory domain PRO be the primary endpoint for the ENCORE study.

Patients in ARISE (N=99) were randomized 1:1 to treatment with ARIKAYCE plus macrolide-based background regimen (ARIKAYCE arm) or placebo plus macrolide-based background regimen (comparator arm) once daily for six months, followed by one month off treatment. ARIKAYCE-treated patients performed better than those in the comparator arm as measured by the QOL-B instrument, with 43.8% of patients achieving an improvement in QOL-B respiratory score above the estimated meaningful within-subject score difference of 14.8, compared with 33.3% of patients in the comparator arm. While the study was not powered to show a statistically significant difference between treatment arms, a strong trend toward significance was observed for improvement from baseline at Month 7 (12.24 vs. 7.76, p=0.1073). Patients in the ARIKAYCE arm also achieved nominally statistically significantly higher culture conversion rates at Month 7 versus patients in the comparator arm (78.8% vs. 47.1%, p=0.0010), and culture conversion was faster and more likely to persist through Month 7 for the ARIKAYCE arm.

Based on the results of ARISE, we plan to explore accelerating the filing for approval of ARIKAYCE in newly infected patients with MAC lung disease with the FDA. Consistent with our expectations, the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan recently confirmed that it does not have an accelerated approval pathway and would therefore not consider a label expansion for ARIKAYCE based on data from the ARISE study alone.

ARISE Culture Conversion

Consistent with prior clinical studies, a higher proportion of patients in the ARIKAYCE arm achieved culture conversion by Month 6 (defined as negative cultures at Months 5 and 6) compared to patients in the comparator arm (80.6% vs. 63.9%, p=0.0712). Among patients who achieved culture conversion by Month 6, more patients in the ARIKAYCE arm achieved the first of their two required monthly negative cultures for clinical conversion at Month 1 versus the comparator arm (74.3% vs. 46.7%). As reported above, at Month 7 (one month following the cessation of treatment), 78.8% of patients in the ARIKAYCE arm vs. 47.1% of patients in the comparator arm were culture-converted, suggesting that ARIKAYCE-treated patients are more likely to remain negative.

Correlation Between ARISE Culture Conversion and QOL-B Performance

Patients in the ARIKAYCE arm who achieved culture conversion at both Month 6 and Month 7 had nominally statistically significantly greater improvements in QOL-B respiratory domain scores at Month 7 compared to patients in the ARIKAYCE arm who did not achieve culture conversion (15.74 vs. 3.53, p=0.0167 at Month 6 and 14.89 vs. 4.50, p=0.0416 at Month 7).

ARISE Safety and Tolerability

The discontinuation rate of ARIKAYCE or the placebo used in the comparator arm was 22.9% in the ARIKAYCE arm and 7.8% in the comparator arm. Study completion rates were 91.7% in the ARIKAYCE arm and 94.1% in the comparator arm. No new safety events were observed in the ARIKAYCE arm, and the safety profile in general was as expected in both treatment arms. Treatment-emergent adverse events (TEAEs) were reported by 91.7% of patients in the ARIKAYCE arm and 80.4% of patients in the comparator arm. The most common TEAEs were dysphonia (41.7% for the ARIKAYCE arm vs. 3.9% for the comparator arm), cough (27.1% vs. 7.8%), diarrhea (27.1% vs. 25.5%), and COVID-19 (12.5% vs. 9.8%). Of the treatment-emergent serious adverse events observed in the trial, none were determined to be related to ARIKAYCE by investigators.

Further Research and Lifecycle Management

We are currently exploring and supporting research and lifecycle management programs for ARIKAYCE beyond treatment of refractory MAC lung disease as part of a combination antibacterial regimen for adult patients who have limited or no treatment options. As noted above, we will continue to advance the post-marketing confirmatory MAC lung disease clinical trial program for ARIKAYCE, through the ARISE and ENCORE trials, which are intended to fulfill the FDA's post-marketing requirement to allow for the full approval of ARIKAYCE in the US, as well as to support the use of ARIKAYCE as a treatment for patients with MAC lung disease.

The ENCORE trial is a randomized, double-blind, placebo-controlled Phase 3b study to evaluate the efficacy and safety of an ARIKAYCE-based regimen in patients with newly diagnosed or recurrent MAC infection who have not started antibiotics. Patients are randomized 1:1 to receive ARIKAYCE plus background regimen or placebo plus background regimen once daily for 12 months. Patients will then discontinue all study treatments and remain in the trial for three months for the assessment of durability of culture conversion. The primary endpoint is change from baseline to Month 13 in respiratory symptom score. The key secondary endpoint is the proportion of subjects achieving durable culture conversion at Month 15. We completed our original target enrollment of 250 patients in the ENCORE trial. Enrollment is ongoing, and we anticipate reporting topline data from ENCORE in 2025.

Subsequent lifecycle management studies could also potentially enable us to reach more patients. These initiatives may include new clinical studies sponsored by us and may also include investigator-initiated studies, which are independent clinical studies initiated and sponsored by physicians or research institutions, with funding from us.

Market Opportunity for ARIKAYCE in MAC Lung Disease

NTM lung disease is associated with increased rates of morbidity and mortality, and MAC is the predominant pathogenic species in NTM lung disease in the US, Europe and Japan. The prevalence of NTM lung disease has increased over the past two decades, and we believe it is an emerging public health concern worldwide. Based on an analysis conducted in 2017, using information from external sources, including market research funded by us and third parties, and internal analyses and calculations, we estimated the potential patient populations in the US, the European 5 (comprised of France, Germany, Italy, Spain and the United Kingdom (UK)) and Japan in 2019 were as follows:

Potential Market	Estimated Number of Patients with Diagnosed NTM Lung Disease	Estimated Number of Patients Treated for MAC Lung Disease	Estimated Number of MAC lung disease Patients Refractory to Treatment
United States	95,000-115,000	48,000-55,000	12,000-17,000
European 5	14,000	4,400	1,400
Japan	125,000-145,000	60,000-70,000	15,000-18,000

We are not aware of any other approved inhaled therapies specifically indicated for NTM lung disease in North America, Europe or Japan. Based on a burden of illness study that we conducted in the US with a major medical benefits provider, we previously concluded that patients with NTM lung disease are costly to healthcare plans, while a claims-based study in the US has shown that patients with NTM lung disease have higher resource utilization and costs than their age and gender-matched controls. Accordingly, we believe that a significant market opportunity for ARIKAYCE in NTM lung disease exists in the US and internationally.

In October 2020, the EC approved ARIKAYCE for the treatment of NTM lung infections caused by MAC in adults with limited treatment options who do not have CF. The CONVERT study included a comprehensive pharmacokinetic sub-study in Japanese subjects in lieu of a separate local pharmacokinetic study in Japan, as agreed with the PMDA. In March 2021, Japan's MHLW approved ARIKAYCE for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen.

Product Pipeline

Brensocatib

Brensocatib is a small molecule, oral, reversible inhibitor of DPP1, which we licensed from AstraZeneca in October 2016. DPP1 is an enzyme responsible for activating neutrophil serine proteases (NSPs) in neutrophils when they are formed in the bone marrow. Neutrophils are the most common type of white blood cell and play an essential role in pathogen destruction and inflammatory mediation. Neutrophils contain the NSPs (including neutrophil elastase, proteinase 3, and cathepsin G) that have been implicated in a variety of inflammatory diseases. In chronic inflammatory lung diseases, neutrophils accumulate in the airways and result in excessive active NSPs that cause lung destruction and inflammation. Brensocatib may decrease the damaging effects of inflammatory diseases such as bronchiectasis by inhibiting DPP1 and its activation of NSPs.

Based on the positive results of the WILLOW study discussed below, in December 2020 we commenced our Phase 3 trial, ASPEN, which will investigate brensocatib in bronchiectasis. ASPEN is a global, randomized, double-blind, placebo-controlled Phase 3 study to assess the efficacy, safety, and tolerability of brensocatib in adult patients with bronchiectasis. Patients with bronchiectasis due to CF were not enrolled in the study. Patients will be randomized to receive brensocatib 10 mg, brensocatib 25 mg, or placebo once daily for 52 weeks. The primary endpoint is the rate of pulmonary exacerbations over the 52-week treatment period. Secondary endpoints include time to first pulmonary exacerbation, percentage of subjects who remain pulmonary exacerbation-free, change from baseline in post-bronchodilator FEV1, rate of severe pulmonary exacerbations, change from baseline in the Bronchiectasis QOL-B Respiratory Symptoms Domain Score, and incidence and

severity of TEAEs. This study completed enrollment of adult patients in the first quarter of 2023. The study enrolled 1,682 adult patients at approximately 460 sites in 40 countries. We anticipate sharing topline data in the latter half of the second quarter of 2024.

In March 2020, AstraZeneca exercised its first option pursuant to our October 2016 license agreement under which AstraZeneca can advance clinical development of brensocatib in the indications of chronic obstructive pulmonary disease (COPD) or asthma. Under the terms of the agreement, upon exercise of this option, AstraZeneca is solely responsible for all aspects of the development of brensocatib up to and including Phase 2b clinical trials in COPD or asthma. The agreement also includes a second and final option which, if exercised, would permit AstraZeneca to further develop brensocatib beyond Phase 2b clinical trials upon reaching agreement on commercial terms satisfactory to each party for the further development and commercialization of brensocatib in COPD or asthma. We retain full development and commercialization rights for brensocatib in all other indications and geographies.

In June 2020, the FDA granted breakthrough therapy designation for brensocatib for the treatment of adult patients with non-cystic fibrosis bronchiectasis (NCFBE) for reducing exacerbations. The FDA's breakthrough therapy designation is designed to expedite the development and review of therapies that are intended to treat serious or life-threatening diseases and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy. The benefits of breakthrough therapy designation include more frequent communication and meetings with the FDA, eligibility for rolling and priority review, intensive guidance on an efficient drug development program, and organizational commitment from the FDA involving senior managers. In November 2020, brensocatib was granted access to the PRIME scheme from the European Medicines Agency (EMA) for patients with NCFBE.

In October 2021, the EMA’s Paediatric Committee approved the brensocatib Pediatric Investigational Plan for the treatment of patients with NCFBE. Subsequently, the ASPEN trial will now include 41 adolescent patients between ages 12 to 17, which will fulfill the pediatric study requirements to support marketing applications in this patient population in the US, Europe and Japan.

The WILLOW Study

The WILLOW study was a randomized, double-blind, placebo-controlled, parallel-group, multi-center, multi-national, Phase 2 study to assess the efficacy, safety and tolerability, and pharmacokinetics of brensocatib administered once daily for 24 weeks in patients with NCFBE. The WILLOW study was conducted at 116 sites and enrolled 256 adult patients diagnosed with NCFBE who had at least two documented pulmonary exacerbations in the 12 months prior to screening. Patients were randomized 1:1:1 to receive either 10 mg or 25 mg of brensocatib or matching placebo. The primary efficacy endpoint was the time to first pulmonary exacerbation over the 24-week treatment period in the brensocatib arms compared to the placebo arm.

WILLOW Efficacy Data

We announced topline data for the WILLOW study in February 2020 and full data for the WILLOW study in June 2020. In September 2020, final results from the WILLOW study were published online in the New England Journal of Medicine. The data demonstrate that the WILLOW study met its primary endpoint of time to first pulmonary exacerbation over the 24-week treatment period for both the 10 mg and 25 mg dosage groups of brensocatib compared to placebo (p=0.027, p=0.044, respectively). The risk of exacerbation at any time during the trial was reduced by 42% for the 10 mg group versus placebo (HR 0.58, p=0.029) and by 38% for the 25 mg group versus placebo (HR 0.62, p=0.046). In addition, treatment with brensocatib 10 mg resulted in a significant reduction in the rate of pulmonary exacerbations, a key secondary endpoint, versus placebo. Specifically, patients treated with brensocatib experienced a 36% reduction in the 10 mg arm (p=0.041) and a 25% reduction in the 25 mg arm (p=0.167) versus placebo. Change in concentration of active neutrophil elastase in sputum versus placebo from baseline to the end of the treatment period was also statistically significant (p=0.034 for 10 mg, p=0.021 for 25 mg).

WILLOW Safety and Tolerability Data

Brensocatib was generally well-tolerated in the study. Rates of AEs leading to discontinuation in patients treated with placebo, brensocatib 10 mg, and brensocatib 25 mg were 10.6%, 7.4%, and 6.7%, respectively. The most common AEs in patients treated with brensocatib were cough, headache, sputum increase, dyspnea, fatigue, and upper respiratory tract infection. Rates of adverse events of special interest (AESIs) in patients treated with placebo, brensocatib 10 mg, and brensocatib 25 mg, respectively, were as follows: rates of skin events (including hyperkeratosis) were 11.8%, 14.8%, and 23.6%; rates of dental events were 3.5%, 16.0%, and 10.1%; and rates of infections that were considered AESIs were 17.6%, 13.6%, and 16.9%.

Further Research and Development

In August 2019, we received notice from the FDA that we were awarded a development grant of $1.8 million for specific work to be performed on a PRO tool. The grant funding is for the development of a novel PRO tool for use in clinical trials to measure symptoms in patients with NCFBE with and without NTM lung infection.

In January 2023, we reported topline data from the Phase 2, multiple-dose, pharmacokinetic/pharmacodynamic study of brensocatib in patients with CF. This Phase 2 study included both patients who were on background CFTR modulator drugs and patients who were not on CFTR modulator drugs. The study duration was approximately one month and dosed CF patients to placebo, 10 mg, 25 mg, and 40 mg of brensocatib. A clear dose-dependent and exposure-dependent inhibition of blood NSPs was observed in patients treated with brensocatib across all doses in this study, consistent with the mechanism of action of brensocatib. Safety and tolerability were consistent with what was observed during the Phase 2 WILLOW study, with no significant drug-related findings. We concluded that an additional cohort evaluating a 65 mg dose of brensocatib is not needed in this patient population. Upon the availability of the ASPEN study results, we will evaluate potential future developments in CF patients.

We also plan to explore the potential of brensocatib in additional neutrophil-mediated diseases, including CRSsNP. CRSsNP currently has no approved therapies and many patients do not respond to corticosteroids or endoscopic sinus surgery. We have initiated our Phase 2b BiRCh trial in patients with CRSsNP.

Market Opportunity for Brensocatib in Bronchiectasis

Bronchiectasis is a severe, chronic pulmonary disorder in which the bronchi become permanently dilated due to a cycle of infection, inflammation, and lung tissue damage. The condition is marked by frequent pulmonary exacerbations requiring antibiotic therapy and/or hospitalizations. Symptoms include chronic cough, excessive sputum production, shortness of breath, and repeated respiratory infections, which can worsen the underlying condition. Based on information from external sources, including market research funded by us and third parties, and internal analyses and calculations, we estimate the potential addressable market in bronchiectasis at launch in the US, the European 5 and Japan will be as follows (approximately):

Potential Market	Estimated Number of Patients Diagnosed with Bronchiectasis
United States	450,000
European 5	400,000
Japan	150,000

Today, there are no approved therapies in the US, Europe, or Japan for the treatment of patients with bronchiectasis.

Treprostinil Palmitil Inhalation Powder

TPIP is an investigational inhaled formulation of a treprostinil prodrug that has the potential to address certain of the current limitations of existing prostanoid therapies. We believe that TPIP prolongs duration of effect and may provide patients with greater consistency in pulmonary arterial pressure reduction over time. Current inhaled prostanoid therapies must be dosed four to nine times per day. Reducing dose frequency has the potential to ease treatment burden for patients and improve compliance. Additionally, we believe that TPIP may be associated with fewer side effects, including severity and/or frequency of cough, headache, throat irritation, nausea, flushing and dizziness that are associated with high initial drug levels and local upper airway exposure when using current inhaled prostanoid therapies. We believe TPIP may offer a differentiated product profile for PH-ILD and PAH.

In February 2021, we announced topline results from the Phase 1 study of TPIP in healthy volunteers. The objective of this first-in-human single ascending dose and multiple ascending dose study was to assess the pharmacokinetics and tolerability profile of TPIP. Data from the study demonstrated that TPIP was generally well tolerated, with a pharmacokinetic profile that supports continued development with once-daily dosing. The most common AEs across all cohorts in the study were cough, dizziness, headache, and nausea. Most AEs were mild in severity and consistent in nature with those typically seen with other inhaled prostanoid therapies. There were few moderate AEs and no severe or serious AEs. Subjects in the multiple dose panel that incorporated an up-titration approach beginning at 112.5 µg once-daily and progressing to 225 µg once-daily reported fewer AEs compared to the panel dosed with 225 µg once-daily from the first dose.

Overall pharmacokinetic results demonstrated that treprostinil exposure (AUC and Cmax) was dose-proportional, with low to moderate inter-subject variability. Treprostinil was detected in the plasma at 24 hours at all doses and throughout the 48-hour sampling period for the two highest doses. Compared with currently available inhaled treprostinil therapy, TPIP showed substantially lower Cmax and longer half-life. Data from this study were presented in an oral session at the European Society of Cardiology Congress in August 2021.

We are advancing the development of TPIP with two ongoing Phase 2 studies. The first study is designed to assess the safety and tolerability of TPIP in patients with PH-ILD over a 16-week treatment period using an up-titration, once-daily dosing schedule. The second study is designed to investigate the effect of TPIP in patients with PAH on changes in PVR and six-minute walk distance over a 16-week treatment period and will also employ an up-titration, once-daily dosing schedule. A third study, which was a Phase 2a study designed to study the immediate impact of a single dose of TPIP in PAH patients over a 24-hour period was discontinued primarily due to hospital and intensive care unit restrictions during the COVID-19 pandemic that

were necessary to conduct the study. One patient was dosed in this study at 112.5 µg. This patient went on to complete the 16-week extension period for the study and was titrated to a dose of 320 µg once daily, which was found to be safe and tolerable. We did not observe any safety concerns with TPIP, and the data suggested a trend toward improvement in various cardiac measures during the study period.

In October 2023, we shared certain blended and blinded dose titration and safety and tolerability data from both the PH-ILD and PAH studies. In the PAH study, of the 24 patients who had reached their Week 5 visit, which is the last point in the study at which the TPIP dose can be increased, 83% of patients were able to titrate up to the maximum dose level in the study, 640 µg, or matching placebo. In the PH-ILD study, of the 10 patients who had reached their Week 5 visit, 80% reached the maximum dose level in the study, 640 µg, or matching placebo.

Based on the blended and blinded review of 22 patients who had completed 16 weeks of treatment in the ongoing PAH study, including patients receiving placebo, the average reduction in PVR from baseline was 21.5%. Among the 64% of patients who experienced reductions in their PVR, the average rate of reduction was 47%, and several patients experienced PVR reductions in excess of 65%. No new or unexpected safety concerns have been observed in either study so far. AEs observed to date have been consistent with the events commonly seen in patients with PAH or PH-ILD and with the known effects of inhaled prostacyclin therapies. AEs related to cough were reported to be mostly mild and there have been no observed instances of throat irritation or pain, which are among the most common reasons for limiting the dose of inhaled treprostinil in clinical practice. Based on the blended and blinded data from these studies, we plan to seek to increase the maximum dose of TPIP from 640 µg to up to 1,280 µg, once a day, in the open label extension study for certain PAH patients based on investigator decision.

With respect to the observations from the ongoing studies noted above, the dose titration, efficacy, and safety analyses were based on data available as of August 28, September 12, and October 23, 2023, respectively. These findings may not be representative of results after the studies are completed and all data is collected and analyzed. As a result, later interim data readouts and final data from these studies may be materially different than the observations described above, including with respect to efficacy, safety and tolerability of TPIP.

We will continue to advance our Phase 2 development work in both PH-ILD and PAH. We expect topline results from the PH-ILD study to be shared in the second quarter of 2024.

Early-Stage Research

Our early-stage research efforts are comprised of our preclinical programs, advanced through internal research and development and augmented through business development activities. In March 2021, we acquired a proprietary protein deimmunization platform, called Deimmunized by Design, focused on the reengineering of therapeutic proteins to evade immune recognition and reaction. In August 2021, we acquired Motus Biosciences, Inc. (Motus) and AlgaeneX, Inc. (AlgaeneX), preclinical stage companies engaged in the research, development and manufacturing of gene therapies for rare genetic disorders. In January 2023, we acquired Vertuis Bio, Inc. (Vertuis), a privately held, preclinical stage company engaged in the research and development of gene therapies for rare genetic disorders. In June 2023, we acquired Adrestia Therapeutics Ltd. (Adrestia), a privately held, preclinical stage company using precision genetic models to search for therapeutic targets, precision diagnostics, novel drug compounds and new applications for existing drugs.

We continue to progress our early-stage research programs across a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA end-joining, and synthetic rescue.

Corporate Development

We plan to continue to develop, acquire, in-license or co-promote other products, product candidates and technologies, including those that address serious and rare diseases with significant unmet need. We are focused broadly on serious and rare disease therapeutics and prioritizing those areas that best align with our core competencies.

Manufacturing

We do not have any in-house manufacturing capability other than for small-scale preclinical development programs and we depend completely on a small number of third-party manufacturers and suppliers for the manufacture of our product candidates for use in clinical trials. We plan to rely primarily on third-party manufacturers and suppliers for the commercial manufacture and supply of most product candidates that we commercialize. ARIKAYCE is manufactured currently by Resilience Biotechnologies Inc. (Resilience) (formerly Therapure Biopharma Inc.) in Canada at a 200 kilogram (kg) scale. For additional information about our agreement with Resilience, see *License and Other Agreements—ARIKAYCE-related Agreements*.

In October 2017, we entered into certain agreements with Patheon UK Limited (Patheon), a wholly-owned subsidiary of Thermo Fisher Scientific, Inc. (Thermo Fisher), related to increasing our long-term production capacity for ARIKAYCE commercial inventory. The agreements provide for Patheon to manufacture and supply ARIKAYCE for our long-term

anticipated commercial needs. Under these agreements, we are required to deliver to Patheon the required raw materials, including active pharmaceutical ingredients, and certain fixed assets needed to manufacture ARIKAYCE. The aggregate investment to increase the long-term production capacity, including under these agreements, and related agreements or purchase orders with third parties for raw materials and fixed assets, is estimated to be approximately $104 million. In addition, we have a commercialization agreement with PARI, the manufacturer of our drug delivery nebulizer for ARIKAYCE, to address our commercial supply needs (the Commercialization Agreement).

We expect our future requirements for brensocatib and TPIP will be manufactured by contract manufacturing organizations (CMOs). Certain product candidates will be manufactured using future in-house manufacturing capabilities.

Intellectual Property

We own or license rights to more than 900 issued patents and pending patent applications in the US and in foreign countries, including more than 300 issued patents and pending patent applications related to ARIKAYCE. Our success depends in large part on our ability to maintain proprietary protection surrounding our product candidates, technology and know-how; to operate without infringing the proprietary rights of others; and to prevent others from infringing our proprietary rights. We actively seek patent protection by filing patent applications, including on inventions that are important to the development of our business in the US, Europe, Japan, Canada, and selected other foreign markets that we consider key for our product candidates. These international markets generally include Australia, China, India, Israel and Mexico.

Our patent strategy includes obtaining patent protection, where possible, on compositions of matter, methods of manufacture, methods of use, dosing and administration regimens and formulations. We also rely on trade secrets, know-how, continuing technological innovation, in-licensing and partnership opportunities to develop and maintain our proprietary position.

We monitor for activities that may infringe our proprietary rights, as well as the progression of third-party patent applications that may have the potential to create blocks to our products or otherwise interfere with the development of our business. We are aware, for example, of US patents, and corresponding international counterparts, owned by third parties that contain claims related to treating lung infections using inhaled antibiotics. If any of these patents were to be asserted against us, we do not believe that our marketed product or development candidates would be found to infringe any valid claim of these patents.

Reflecting our commitment to safeguarding proprietary information, we require our employees, consultants, advisors, collaborators and other third-party partners to sign confidentiality agreements to protect the exchange of proprietary materials and information. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

ARIKAYCE Patents

Of the patents and applications related to ARIKAYCE, there are 12 issued US patents that cover the ARIKAYCE composition and its use in treating NTM that are listed in the FDA Orange Book. These patents and their expiration dates are as follows:

- US Patent No. 7,718,189 (expires June 6, 2025)
- US Patent No. 8,226,975 (expires August 15, 2028)
- US Patent No. 8,632,804 (expires December 5, 2026)
- US Patent No. 8,802,137 (expires April 8, 2024)
- US Patent No. 8,679,532 (expires December 5, 2026)
- US Patent No. 8,642,075 (expires December 5, 2026)
- US Patent No. 9,566,234 (expires January 18, 2034)
- US Patent No. 9,827,317 (expires April 8, 2024)
- US Patent No. 9,895,385 (expires May 15, 2035)
- US Patent No. 10,251,900 (expires May 15, 2035)
- US Patent No. 10,751,355 (expires May 15, 2035)
- US Patent No. 11,446,318 (expires May 15, 2035)

In addition, we own five pending US patent applications that cover the ARIKAYCE composition and/or its use in treating NTM, including MAC infections. One or more of the patent applications, if issued as patents in their current form, may be eligible for listing in the FDA Orange Book for ARIKAYCE. We also own a pending US application that covers methods for making ARIKAYCE. We anticipate that in the US, we will have patent coverage for ARIKAYCE and its use in treating NTM lung disease, including NTM lung disease caused by MAC, through May 15, 2035.

Ten patents have been granted by the European Patent Office (EPO) (European Patent Nos. 1581236, 1909759, 1962805, 2823820, 2852391, 3067046, 3142643, 3427742, 3466432 and 3766501) that relate to ARIKAYCE and its use in treating NTM, including MAC infections. In addition, we have additional patent applications pending before the EPO that relate to ARIKAYCE and its use in treating NTM lung disease. European Patent No. 1909759 (the '759 patent), owned by us, was previously opposed by Generics (UK) Ltd. A hearing was held on October 19, 2015, during which we submitted amended claims. The European Patent Office Opposition Division (EPOOD) maintained the patent as amended and Generics (UK) Ltd appealed the decision. The EPO Technical Board of Appeals heard arguments related to the appeal on January 8, 2019 and the product claims of the patent were held invalid. The method of manufacture claims was remitted to the EPOOD for further consideration, and the EPO has since maintained the validity of these claims. European Patent Nos. 1962805 and 3067046, both of which expire approximately five months after the '759 patent (December 5, 2026 vs. July 19, 2026), also include claims related to ARIKAYCE and its use in treating NTM lung disease. European Patent No. 2852391 expires May 21, 2033 and includes claims related ARIKAYCE together with a vibrating mesh nebulizer having certain properties. European Patent Nos. 3142643, 3466432 and 3766501 each expires May 15, 2035 and include claims related to ARIKAYCE and its use for treating MAC lung infections.

More than 60 patents have also been issued in other major foreign markets, e.g., Japan, China, Korea, Australia, and India, that relate to ARIKAYCE and/or methods of using ARIKAYCE for treating various pulmonary disorders, including NTM lung disease. More than 30 foreign patent applications are pending that relate to the ARIKAYCE composition and/or its use in treating various pulmonary disorders, including NTM lung disease.

Through our agreements with PARI, we have license rights to US and foreign patents and applications that cover the Lamira medical device through January 18, 2034. We have entered into a commercial supply agreement with PARI and we also have rights to use the nebulizers in expanded access programs and clinical trials.

Brensocatib Patents

Through our agreement with AstraZeneca, we have licensed US Patent Nos. 9,522,894, 9,815,805, 10,287,258, 10,669,245, 11,655,221, 11,655,222, 11,655,223, 11,655,224, 11,673,871, 11,773,069, and 11,814,359, which have claims related to brensocatib and methods for using brensocatib in certain treatment methods, including the treatment of obstructive diseases of the airway such as bronchiectasis. US Patent No. 9,522,894 expires March 12, 2035 while the remaining US patents expire January 21, 2035 (not taking into account any potential patent term extension). Counterpart patents have issued in Australia, Canada, Europe, China, Japan, South Korea, India, Israel, and Mexico and expire January 21, 2035, not accounting for any potential patent term extension. In addition, patent applications related to brensocatib are pending in the US and throughout the world, including in Europe, China, and Japan.

TPIP Patents

We own US Patent Nos. 9,255,064, 9,469,600, 10,010,518, 10,526,274, 10,995,055 and 11,795,135, each expiring October 24, 2034 (not taking into account any potential patent term extensions or adjustments), each with claims covering treprostinil palmitil, the treprostinil prodrug component of TPIP, compositions comprising the same, and/or its use. US Patent No. 9,255,064 has claims reciting hexadecyl-treprostinil, and other treprostinil prodrugs. US Patent No. 9,469,600 has claims related to TPIP and other treprostinil prodrug formulations. US Patent No. 10,010,518 has claims directed to methods of treating pulmonary hypertension, including PAH, using compositions related to TPIP such as treprostinil prodrug formulations. US Patent No. 10,526,274 has claims directed to methods for treating pulmonary fibrosis with treprostinil palmitil. US Patent No. 10,995,055 has claims directed to compositions comprising treprostinil palmitil in the form of a dry powder, and methods for treating pulmonary hypertension with the same. US Patent No. 11,795,135 has claims directed to methods for treating PH-ILD, with treprostinil palmitil. Counterpart patent applications to these US Patents have issued in Europe, Japan and other foreign jurisdictions. Counterpart patent applications to these US Patents are also pending in select jurisdictions, including the US, Europe and Japan.

We own pending patent applications that relate to methods for using treprostinil prodrugs and formulations comprising the same, including TPIP in treating patients with PAH and other diseases, as well as methods for manufacturing such treprostinil prodrugs and formulations. Should the patent applications related to TPIP formulations and methods of using TPIP in pulmonary hypertension treatment methods issue, these patents would expire in October 2041.

Trademarks

In addition to our patents and trade secrets, we have filed applications to register certain trademarks in the US and/or abroad, including INSMED and ARIKAYCE. At present, we have received two registrations for the INSMED mark and one registration for the ARIKAYCE mark from the US Patent and Trademark Office (USPTO). We have also received notices of allowance or registrations in a number of countries abroad for the INSMED and ARIKAYCE marks, among others. The EMA has authorized the use of the name ARIKAYCE liposomal, and the FDA has approved our use of the name ARIKAYCE, as the trade name for amikacin liposome inhalation suspension. Our ability to obtain and maintain trademark registrations will in certain geographical locations depend on making use of the mark in commerce on or in connection with our products and approval of the trademarks for our products by regulatory authorities in each country.

License and Other Agreements

ARIKAYCE-related Agreements

We currently rely, and will continue to rely, on agreements with a number of third parties in connection with the development and manufacture of ARIKAYCE.

PARI

We have a licensing agreement with PARI for use of the optimized Lamira Nebulizer System for delivery of ARIKAYCE in treating patients with NTM lung infections, CF and bronchiectasis. Under the licensing agreement, we have rights under several US and foreign issued patents and patent applications involving improvements to the optimized Lamira Nebulizer System, to exploit the system with ARIKAYCE for the treatment of such indications, but we cannot manufacture the nebulizers except as permitted under our Commercialization Agreement with PARI, which is described in further detail below. Lamira has been approved for use in the US (in combination with ARIKAYCE) and EU and is authorized for use in Japan. We also currently have rights to use the nebulizers in expanded access programs and clinical trials. Lamira must receive regulatory approval before we can market ARIKAYCE outside the US, EU and Japan, and it is labeled as investigational for use in our clinical trials outside of these regions.

We have certain obligations under this licensing agreement in relation to specified licensed indications. With respect to NTM, we met all obligations to achieve certain commercial, developmental and regulatory milestones by the required deadlines. With respect to bronchiectasis, we have an obligation to use commercially reasonable efforts to initiate a Phase 3 trial for bronchiectasis by a set deadline. With respect to CF, we are obligated to use commercially reasonable efforts to develop, obtain regulatory and reimbursement approval, market and sell ARIKAYCE in two or more major European countries, as well as to achieve certain milestones specified in the licensing agreement. Termination of the licensing agreement or loss of exclusive rights may occur if we fail to meet our obligations, including payment of royalties to PARI.

Under the licensing agreement, we paid PARI an upfront license fee and milestone payments. Upon FDA acceptance of our NDA and the subsequent FDA and EMA approvals of ARIKAYCE, we made additional milestone payments of €1.0 million, €1.5 million and €0.5 million, respectively, to PARI. In October 2017, we exercised an option to buy-down the royalties payable to PARI. PARI is entitled to receive royalty payments in the mid-single digits on annual global net sales of ARIKAYCE pursuant to the licensing agreement, subject to certain specified annual minimum royalties.

This licensing agreement will remain in effect on a country-by-country basis until the final royalty payments have been made with respect to the last country in which ARIKAYCE is sold, or until the agreement is otherwise terminated by either party. We have the right to terminate this licensing agreement upon written notice for PARI's uncured material breach, if PARI is the subject of specified bankruptcy or liquidation events, or if PARI fails to reach certain specified obligations. PARI has the right to terminate this licensing agreement upon written notice for our uncured material breach, if we are the subject of specified bankruptcy or liquidation events, if we assign or otherwise transfer the agreement to a third-party that does not agree to assume all of our rights and obligations set forth in the agreement, or if we fail to reach certain specified milestones.

In July 2014, we entered into a Commercialization Agreement with PARI for the manufacture and supply of the Lamira Nebulizer Systems and related accessories (the Device) as optimized for use with ARIKAYCE. Under the Commercialization Agreement, PARI manufactures the Device except in the case of certain defined supply failures, when we will have the right to make the Device and have it made by third parties (but not certain third parties deemed under the Commercialization Agreement to compete with PARI). The Commercialization Agreement has an initial term of 15 years that began to run in October 2018 (the Initial Term). The term of the Commercialization Agreement may be extended by us for an additional five years by providing written notice to PARI at least one year prior to the expiration of the Initial Term.

Resilience

In February 2014, we entered into a contract manufacturing agreement with Therapure Biopharma Inc., which has been assumed by Resilience, for the manufacture of ARIKAYCE, on a non-exclusive basis, at a 200 kg scale. Pursuant to the agreement, we collaborated with Resilience to construct a production area for the manufacture of ARIKAYCE in Resilience's existing manufacturing facility in Mississauga, Ontario, Canada. The agreement has an initial term of five years, which began in

October 2018, and will renew automatically for successive periods of two years each, unless terminated by either party by providing the required two years' prior written notice to the other party. Notwithstanding the foregoing, the parties have rights and obligations under the agreement prior to the commencement of the initial term. Under the agreement, we are obligated to pay a minimum of $6 million for commercial ARIKAYCE batches produced and certain manufacturing activities each calendar year. The agreement allows for termination by either party upon the occurrence of certain events, including (i) the material breach by the other party of any provision of the agreement or the quality agreement expected to be entered into between the parties, and (ii) the default or bankruptcy of the other party. In addition, we may terminate the agreement for any reason upon no fewer than 180 days' advance notice.

Patheon (a wholly-owned subsidiary of Thermo Fisher) and related agreements

In October 2017, we entered into certain agreements with Patheon related to the increase of our long-term production capacity for ARIKAYCE. The agreements provide for Patheon to manufacture and supply ARIKAYCE for our anticipated commercial needs. Under these agreements, we are required to deliver to Patheon the required raw materials, including active pharmaceutical ingredients, and certain fixed assets needed to manufacture ARIKAYCE. Patheon's supply obligations will commence once certain technology transfer and construction services are completed. Our manufacturing and supply agreement with Patheon will remain in effect for a fixed initial term, after which it will continue for successive renewal terms unless either we or Patheon have given written notice of termination. The technology transfer agreement will expire when the parties agree that the technology transfer services have been completed. The agreements may also be terminated under certain other circumstances, including by either party due to a material uncured breach of the other party or the other party’s insolvency. These early termination clauses may reduce the amounts due to the relevant parties. The aggregate investment to increase our long-term production capacity, including under the Patheon agreements and related agreements or purchase orders with third parties for raw materials and fixed assets, is estimated to be approximately $104 million.

Cystic Fibrosis Foundation Therapeutics, Inc.

In 2004 and 2009, we entered into research funding agreements with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) whereby we received $1.7 million and $2.2 million in research funding for the development of ARIKAYCE. As a result of the US approval of ARIKAYCE and in accordance with the CFFT agreements, as amended, we owe milestone payments to CFFT of $13.4 million in the aggregate payable through 2025, of which $7.4 million has been paid as of December 31, 2023. Furthermore, if certain global sales milestones were met within five years of the commercialization of ARIKAYCE, we would have owed up to an additional $3.9 million. We met and paid $1.7 million of these additional global sales milestone payments.

PPD Development, L.P. (a wholly-owned subsidiary of Thermo Fisher)

In April 2020, we entered into a master services agreement with PPD Development, L.P. (PPD) pursuant to which we retained PPD to perform clinical development services in connection with certain of our clinical research programs. The master services agreement has an initial term of five years. Either party may terminate (i) any project addendum under the master services agreement for any reason and without cause upon 30 days’ written notice, (ii) any project addendum in the event of the other party’s breach of the master services agreement or such project addendum upon 30 days’ written notice, provided that such breach is not cured within such 30-day period, (iii) the master services agreement or any project addendum immediately upon the occurrence of an insolvency event with respect to the other party or (iv) any project addendum upon 30 days’ written notice if (a) the continuation of the services under such project addendum would post material ethical or safety risks to study participants, (b) any approval from a regulatory authority necessary to perform the applicable study is revoked, suspended or expires without renewal or (c) in the reasonable opinion of such party, continuation of the services provided under such project addendum would be in violation of applicable law. We have entered into project addenda with PPD to perform clinical development services over several years for, but not limited to, our ARISE, ENCORE, ASPEN studies and other brensocatib and TPIP studies. We currently expect to incur approximately $430.1 million of costs related to these project addenda.

Brensocatib-related Agreements

AstraZeneca

In October 2016, we entered into a license agreement with AstraZeneca (the AZ License Agreement), pursuant to which AstraZeneca granted us exclusive global rights for the purpose of developing and commercializing AZD7986 (renamed brensocatib). In consideration of the licenses and other rights granted by AstraZeneca, we made an upfront payment of $30.0 million in late October 2016. In December 2020, we incurred a $12.5 million milestone payment obligation upon the first dosing in a Phase 3 clinical trial of brensocatib. Upon the earlier of our notification to AstraZeneca that we intend to file an NDA or releasing an official public statement that we intend to file an NDA, we will owe AstraZeneca an additional $12.5 million. Subsequent to this milestone, we are also obligated to make a series of additional contingent milestone payments totaling up to an additional $60.0 million upon the achievement of regulatory filing milestones. If we elect to develop brensocatib for a second indication, we will be obligated to make an additional series of contingent milestone payments totaling up to $42.5 million, the first of which occurs at the initiation of a Phase 3 trial in the additional indication. We are not obligated

to make any additional milestone payments for additional indications. In addition, we have agreed to pay AstraZeneca tiered royalties ranging from a high single-digit to mid-teens on net sales of any approved product based on brensocatib and one additional payment of $35.0 million upon the first achievement of $1 billion in annual net sales. The AZ License Agreement provides AstraZeneca with the option to negotiate a future agreement with us for commercialization of brensocatib in chronic obstructive pulmonary disease or asthma. If we fail to comply with our obligations under our agreements with AstraZeneca (including, among other things, if we fail to use commercially reasonable efforts to develop and commercialize a product based on brensocatib, or we are subject to a bankruptcy or insolvency), AstraZeneca would have the right to terminate the license.

Competition

The biotechnology and pharmaceutical industries are highly competitive. We face potential competitors from many different areas including commercial pharmaceutical, biotechnology and device companies, academic institutions and scientists, other smaller or earlier stage companies and non-profit organizations developing anti-infective drugs and drugs for respiratory, inflammatory, immunology, oncology, and rare diseases. Many of these companies have greater human and financial resources and may have product candidates in more advanced stages of development and may reach the market before our product candidates. Competitors may develop products that are more effective, safer or less expensive or that have better tolerability or convenience. We also may face generic competitors where third-party payors will encourage use of the generic products. Although we believe that our formulation delivery technology, respiratory and anti-infective expertise, experience and knowledge in our specific areas of focus provide us with competitive advantages, these potential competitors could reduce our commercial opportunity. Additionally, there currently are, and in the future there may be, already-approved products for certain of the indications for which we are developing, or in the future may choose to develop, product candidates. For instance, PAH is a competitive indication with established products, including other formulations of treprostinil.

In the lung disease market, our major competitors include pharmaceutical and biotechnology companies that have approved therapies or therapies in development for the treatment of chronic lung infections. There are other companies that are currently conducting clinical trials for the treatment of lung disease. While there are currently no approved treatments for bronchiectasis, clinical studies in this disease state and specific endotypes (for instance, bronchiectasis with eosinophilic inflammation) have been initiated. Products developed by certain of our competitors may potentially be used in combination with brensocatib, if approved.

With regard to ARIKAYCE, we are not aware of any approved inhaled therapies specifically indicated for refractory NTM lung infections in North America, Europe or Japan, but there is a recommended treatment regimen that is utilized. The international treatment guidelines, which are issued by the ATS, ERS, ESCMID and IDSA, strongly recommend the use of ARIKAYCE for the treatment of patients with refractory NTM lung disease caused by MAC as a part of a combination antibacterial drug regiment for adult patients with limited or no alternative treatment options who have failed to convert to a negative sputum culture after at least six months of treatment.

The fields of gene therapy and protein engineering are rapidly advancing and highly competitive. While we believe our internal expertise provides a competitive advantage, we expect competition to intensify, including from other pharmaceutical companies, government agencies and public and private research institutions. If any of our gene therapy or protein engineering programs are approved for their indications, we expect to compete with other gene therapy products, protein engineering technologies and any other existing or new therapies or technologies that may become available in the future.

Government Regulation

Orphan Drug Designation

United States

Under the Orphan Drug Act (ODA), the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, defined as a disease or condition for which the drug is intended affects fewer than 200,000 people in the US or for which there is no reasonable expectation that the cost of developing and making available in the US a drug for such disease or condition will be recovered from US sales of such drug, if it meets certain criteria specified by the ODA and FDA. After the FDA grants orphan drug designation, the drug and the specific intended use(s) for which it has obtained designation are listed by the FDA in a publicly accessible database. The FDA designated ARIKAYCE as an orphan drug for treatment of NTM infections, bronchiectasis in patients with *Pseudomonas* aeruginosa or other susceptible microbial pathogens, and bronchopulmonary *Pseudomonas* aeruginosa infections in CF patients. However, the orphan drug designations for bronchiectasis in patients with *Pseudomonas* aeruginosa or other susceptible microbial pathogens and bronchopulmonary *Pseudomonas* aeruginosa infections in CF patients were withdrawn at our request in August 2023.

Orphan drug designation qualifies the sponsor for various development incentives of the ODA, including tax credits for qualified clinical testing, and a waiver of the PDUFA application fee (unless the application seeks approval for an indication not included in the orphan drug designation). Orphan drug designation also may afford the company a period of exclusivity for the orphan indication upon approval of the drug. Specifically, the first NDA or biologics license application (BLA) applicant

with an FDA orphan drug designation for a particular drug to receive FDA approval of the drug for an indication covered by the orphan designation is entitled to a seven-year exclusive marketing period, often referred to as orphan drug exclusivity, in the US for that drug in that indication. A product that has several separate orphan designations may have several separate exclusivities for separate orphan indications. During the orphan drug exclusivity period, the FDA may not approve any other applications to market the same drug for the same indication for use, except in limited circumstances, such as a showing of clinical superiority to the product that has orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition or the same drug for a different disease or condition, and it does not alter the timing or scope of the regulatory review and approval process; the sponsor must still submit evidence from clinical and non-clinical studies sufficient to demonstrate the safety and effectiveness of the drug.

In a decision issued in September 2021 (*Catalyst Pharmaceuticals, Inc. v. Becerra*), the US Court of Appeals for the Eleventh Circuit held that the FDA had erred by limiting the scope of orphan drug exclusivity for FIRDAPSE® (amifampridine) to the product's approved indication, an action that the FDA taken in accordance with its regulations interpreting the ODA. The court held that under the ODA, FIRDAPSE's orphan drug exclusivity instead protected the broader rare disease or condition that received orphan drug designation. Notwithstanding the Eleventh Circuit's decision in *Catalyst*, the FDA announced in January 2023 that it would continue to apply the FDA's regulations tying the scope of orphan drug exclusivity to a product's approved uses or indications. In light of the FDA's announcement, the scope of orphan drug exclusivity and other issues relating to the FDA's implementation of the ODA with respect to previously approved and future products may be the subject of further litigation or legislative action.

European Union

The EMA grants orphan drug designation to promote the development of drugs or biologics (1) for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the EU, or (2) for life threatening, seriously debilitating or serious and chronic condition in the EU where, without incentives, sales of the drug in the European Economic Area (the EU plus Iceland, Lichtenstein and Norway) (EEA) are unlikely to be sufficient to justify its development. Orphan drug designation is available either if no other satisfactory method of diagnosing, preventing or treating the condition is approved in the EEA or if such a method does exist but the proposed orphan drug will be of significant benefit to patients.

If a drug with an orphan drug designation subsequently receives an orphan drug marketing authorization from the EC for a therapeutic indication which is covered by such designation, the drug is entitled to orphan exclusivity. The EC has granted an orphan drug marketing authorization for ARIKAYCE for the treatment of NTM lung infections caused by MAC in adults with limited treatment options who do not have CF. Orphan exclusivity means that the EMA or a national medicines agency may not accept another application for authorization, or grant an authorization, for a same or similar drug for the same therapeutic indication. Competitors may receive such a marketing authorization despite orphan exclusivity, provided that they demonstrate that the existing orphan product is not supplied in sufficient quantities or that the 'second' drug or biologic is clinically superior to the existing orphan product. The 'second' drug may but need not have an orphan designation as well. The period of orphan exclusivity is 10 years, which can be extended by two years where an agreed pediatric investigation plan has been implemented. The exclusivity period may also be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Each orphan designated marketing authorization carries the potential for one market exclusivity for all the therapeutic indications that are covered by the designation. Market exclusivity is an orphan incentive awarded by the EC to a specific clinical indication with an orphan designation. Each indication with an orphan designation confers ten years of market exclusivity for the particular indication. A medicine that has multiple orphan designations for different conditions may benefit from separate market exclusivity periods pertaining to its different orphan designations.

Orphan drug designation also provides opportunities for free protocol assistance and fee reductions for access to the centralized regulatory procedure or fee exemptions for companies with a small and medium enterprises status. In addition, EU Member States may provide national benefits to orphan drugs, such as early access to the reimbursement procedure or exemption from any turnover tax imposed on pharmaceutical companies.

The orphan designation may be applied for at any time during the development of the drug but before the application for marketing authorization. At the time of marketing authorization, the criteria for orphan designation are examined again, and the EC decides on the maintenance of the orphan designation in granting an orphan drug marketing authorization. The non-maintenance of the orphan designation means that the drug loses its orphan status and thus no longer benefits from orphan exclusivity, fee reductions or exemptions, and national benefits.

Japan

The MHLW may, after hearing the opinion of the Pharmaceutical Affairs and Food Sanitation Council, grant orphan drug designation to a drug intended to treat a rare disease or condition if the drug meets the following conditions: (i) the number of target patients is less than 50,000 in Japan; (ii) the necessity of orphan drug designation is high from a medical point of view; (iii) there are sufficient theoretical grounds to use the drug for the target disease; and (iv) the plan for development of the drug

is appropriate. Even if a drug is granted orphan drug designation, however, it does not always receive the manufacturing and marketing approval that is necessary for the drug to be sold or marketed in Japan. ARIKAYCE did not qualify for orphan drug designation in Japan due to the estimated number of NTM patients in Japan exceeding 50,000.

Drug Approval

United States

In the US, pharmaceutical products are subject to extensive regulation by the FDA and other government bodies. The US Federal Food, Drug, and Cosmetic Act (FDCA), the Public Health Services Act (PHSA) (in the case of biological products), and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable US requirements at any time during product development, approval, or after approval may subject a company to a variety of administrative or judicial sanctions, such as imposition of clinical holds, FDA refusal to file or approve NDAs or BLAs, warning letters, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, civil penalties, and criminal prosecution. The description below summarizes the current approval process in the US for our product and product candidates.

Preclinical Studies

Preclinical studies may include laboratory evaluation of product chemistry, formulation and toxicity, and pharmacology, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including the FDA's good laboratory practice (GLP) regulations and the US Department of Agriculture's regulations implementing the Animal Welfare Act. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature, and a proposed clinical trial protocol, among other things, to the FDA as part of an IND. Certain non-clinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND might not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects (healthy volunteers or patients) under the supervision of a qualified investigator. Clinical trials must be conducted (i) in compliance with all applicable federal regulations and guidance, including those pertaining to good clinical practice (GCP) standards that are meant to protect the rights, safety, and welfare of human subjects and to define the roles of clinical trial sponsors, investigators, and monitors as well as (ii) under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing of a new drug in the US (whether in patients or healthy volunteers) must be included as a submission to the IND, and the FDA must be notified of subsequent protocol amendments, including new protocols. In addition, the protocol must be reviewed and approved by an institutional review board (IRB), and all study subjects must provide informed consent. Typically, before any clinical trial, each institution participating in the trial will require review of the protocol before the trial commences at that institution. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and there are additional, more frequent reporting requirements for certain AEs.

A study sponsor might choose to discontinue a clinical trial or a clinical development program for a variety of reasons. The FDA may impose a temporary or permanent clinical hold, or other sanctions, if it believes that the clinical trial either is not being conducted in accordance with the FDA requirements or presents an unacceptable risk to the clinical trial subjects. An IRB also may require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs or BLAs for marketing approval are typically conducted in three sequential pre-approval phases, but the phases may overlap or be combined. In Phase 1, short term (typically less than a few months) testing is conducted in a small group of subjects (typically 20-100), who may be patients with the target disease or condition or healthy volunteers, to evaluate its safety, determine a safe dosage range, and identify side effects. In Phase 2, the drug is given to a larger group of subjects (typically up to several hundred) with the target condition to further evaluate its safety and gather preliminary evidence of efficacy. Phase 3 studies typically last between several months and two years. In Phase 3, the drug is given to a large group of subjects with the target disease or condition (typically several hundred to several thousand), often at multiple geographical sites, to confirm its effectiveness, monitor side effects, and collect data to support drug approval. Only a small percentage of investigational drugs complete all three phases of development and obtain marketing approval.

NDAs and BLAs

After completion of the required clinical testing, an NDA or BLA can be prepared and submitted to the FDA. FDA approval of the NDA or BLA is required before marketing of the product may begin in the US. The NDA or BLA is a large submission that must include, among other things, the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The application also includes representative samples, copies of the proposed product labeling, patent information, and a financial certification or disclosure statement. The cost of preparing and submitting an NDA or BLA is substantial. Additionally, under federal law (as amended by the most recent reauthorization of the Prescription Drug User Fee Act (PDUFA VII) in the FDA User Fee Reauthorization Act of 2022), most NDAs and BLAs are subject to a substantial application fee and, upon approval, the applicant will be assessed an annual prescription drug program fee, both of which are adjusted annually. NDAs and BLAs for orphan drugs are not subject to an application fee, unless the application includes an indication other than an orphan-designated indication. The FDA also has the authority to grant waivers of certain user fees, pursuant to the FDCA.

The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application is accepted for filing based on the FDA's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins a substantive review. The FDA may refer applications for novel drug or biological products or drug or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes outside clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will typically inspect the facility or the facilities at which the drug or biological product is manufactured. The FDA will not approve the product unless, among other requirements, compliance with current good manufacturing practice (cGMP) is satisfactory and the NDA or BLA contains data that provide substantial evidence of effectiveness for the proposed indication, generally consisting of adequate and well-controlled clinical investigations, and that the drug is safe for use under the conditions of use in the proposed labeling. The FDA also reviews the proposed labeling submitted with the NDA or BLA and typically requires changes in the labeling text.

After the FDA evaluates the NDA or BLA and the manufacturing and testing facilities, it issues either an approval letter or a complete response letter. Complete response letters generally outline the deficiencies in the submission and delineate the additional testing or information needed in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA or BLA, the FDA will issue an approval letter. An approval letter, which may specify post approval requirements, authorizes commercial marketing of the drug or biological product for the approved indication or indications and the other conditions of use set out in the approved prescribing information. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. The FDA sets a goal date by which the FDA expects to issue either an approval letter or a complete response letter, unless the review period is adjusted by mutual agreement between the FDA and the applicant or as a result of the applicant submitting a major amendment. The FDA's current performance goals call for the FDA to complete review of 90 percent of standard (non-priority) NDAs and BLAs within 10 months of the end of the 60-day filing review period and priority NDAs and BLAs within six months of the end of the 60-day filing review period (in the case of new molecular entity (NME) NDA and original BLA submissions). For non-NME NDA/BLAs the FDA's current performance goals call for the FDA to complete review of 90 percent of standard (non-priority) NDAs and BLAs within 10 months of receipt and priority NDAs and BLAs within 6 months of receipt.

As a condition of NDA or BLA approval, the FDA may require substantial post-approval testing, known as Phase 4 studies, to be conducted in order to gather additional information on the drug's effect in various populations and any side effects. Beyond routine post marketing safety surveillance, the FDA may require specific additional surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling restrictions that can materially affect the potential market and profitability of the drug. As a condition of approval, or after approval, the FDA also may require submission of a risk evaluation and mitigation strategy (REMS) or a REMS with elements to assure safe use to mitigate any identified or suspected serious risks. The REMS may include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools. Further post-approval requirements are discussed below.

Expedited Review and Approval of Eligible Drugs

Under the FDA's accelerated approval program, the FDA may approve certain drugs for serious or life-threatening conditions on the basis of a surrogate or intermediate endpoint that is reasonably likely to predict clinical benefit, which can substantially reduce time to approval. A surrogate endpoint used for accelerated approval is a marker—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 irreversible morbidity and mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint.

As a condition of accelerated approval, the FDA typically requires certain post-marketing clinical studies to verify and describe clinical benefit of the product, and may impose restrictions on distribution to assure safe use. Post marketing studies would usually be required to be studies already underway at the time of the accelerated approval. In addition, promotional materials for an accelerated approval drug to be used in the first 120 days post-approval must be submitted to the FDA prior to approval, and materials to be used after that 120-day period must be submitted 30 days prior to first use. If the required post-marketing studies fail to verify the clinical benefit of the drug, or if the applicant fails to perform the required post-marketing studies with due diligence, the FDA may withdraw approval of the drug under streamlined procedures in accordance with the FDCA, as amended by the Food and Drug Omnibus Reform Act of 2022. The agency may also withdraw approval of a drug if, among other things, the promotional materials for the product are false or misleading, or other evidence demonstrates that the drug product is not shown to be safe or effective under its conditions of use.

The FDA also has various programs—fast track designation, priority review and breakthrough designation—that are intended to expedite or streamline the process for the development and FDA review of drugs that meet certain qualifications. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. The programs each have different eligibility criteria and provide different benefits, and can be applied either alone or in combination depending on an applicant's circumstances.

Fast track designation applies to a drug that is intended to treat a serious condition and for which nonclinical or clinical data demonstrate the potential to address unmet medical need. It should be requested at the time of IND submission or ideally no later than the pre-NDA or pre-BLA meeting. The FDA must respond to requests for fast track designation within 60 days of receipt of the request. If granted, the applicant is eligible for actions to expedite development and review, such as frequent interaction with the review team, as well as rolling review, meaning that the applicant may submit sections of the application as they are available. The timing of the FDA's review of these sections depends on a number of factors, and the review clock does not start running until the agency has received a complete NDA or BLA submission. The FDA may withdraw fast track designation if the agency determines that the designation is no longer supported by data emerging in the drug development process.

Priority review applies to an application (both original and efficacy supplement) for a drug that treats a serious condition and that, if approved, would provide a significant improvement in safety or effectiveness. It also applies to any supplement that proposes a labeling change pursuant to a report on a pediatric study conducted pursuant to section 505A of the FDCA. A request for priority review is submitted at the time of submission of an NDA or BLA, or supplemental NDA or BLA. The FDA must respond within 60 days of receipt of the request. If granted, the review time is shortened from the standard 10 months to 6 months, beginning either after the 60-day filing review period (in the case of NME NDA and original NDA submissions) or the date of receipt (in the case of non-NME original NDA submissions).

Breakthrough therapy designation applies to a drug that is intended to treat a serious condition and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. It can be requested with the IND submission and ideally no later than the end-of-Phase 2 meeting. The FDA must respond within 60 days of receipt of the request. If granted, the applicant receives intensive guidance on efficient drug development, intensive involvement of senior managers and experienced review and regulatory health project management staff in a proactive, collaborative, cross-disciplinary review, rolling review, and other actions to expedite review. Designation may be rescinded if the product no longer meets the criteria for breakthrough therapy designation.

Drugs that are designated as QIDPs may be eligible for priority review and will receive fast track designation upon the request of the sponsor, and also may be eligible for market exclusivity. A product is eligible for QIDP designation if it is an antibacterial or anti-fungal drug for human use that is intended to treat serious or life-threatening infections, including: those caused by an anti-bacterial or anti-fungal resistant pathogen, including novel or emerging infectious pathogens; or caused by qualifying pathogens listed by the FDA. A drug sponsor may request that the FDA designate its product as a QIDP at any time prior to NDA submission. The FDA must make a QIDP determination within 60 days of receiving the designation request. ARIKAYCE has been designated as a QIDP for NTM lung disease.

Additionally, the FDA may approve eligible drugs under the LPAD. A product is eligible if it is intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs, the drug otherwise meets the standards of approval, and the FDA receives a written request from the sponsor to approve the drug under this pathway. An antibacterial or anti-fungal drug approved through this pathway may follow a streamlined clinical development program involving smaller, shorter, or fewer clinical trials. Approval is based on a benefit-risk assessment in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative

treatment for the patient population. Such drugs might not have favorable benefit-risk profiles in a broader population. Drugs approved under LPAD are subject to additional regulatory requirements, including labeling and advertising statements regarding the limited population and submission of promotional materials to the FDA at least 30 days prior to dissemination. The FDA may remove these additional requirements if the agency approves the drug for a broader population.

Exclusivities

In the US, after NDA or BLA approval of a drug not previously approved, owners of relevant drug patents may obtain up to a five-year patent term extension on a single patent. The allowable patent term extension is generally calculated as half of the drug's testing phase (the time between the date the IND becomes effective and the NDA or BLA submission date) and all of the review phase (the time between the NDA or BLA submission date and the approval date) up to a maximum of five years, to the extent such testing phase and approval phase occur after the issue date of the patent. The total post-NDA or BLA approval patent term including the extension may not exceed 14 years. The extension also can be shortened if the FDA determines that the NDA/BLA applicant did not pursue approval with due diligence. For patents that might expire while a patent term extension application is pending, the patent owner may request an interim patent term extension. The Director of the USPTO shall extend, until a final determination is made, the term of the patent for periods of up to one year if the Director determines that the patent is eligible for extension. An interim patent term extension may be renewed up to four times until a final determination is made, and up to the amount of time for which the patent might be eligible for extension. For each interim patent term extension granted, the final patent term extension is reduced by a corresponding amount. Interim patent extensions may also be available for a patent that will expire before a drug is expected to be approved, but the NDA or BLA for the drug must have been submitted.

A variety of non-patent exclusivity periods are available under the FDCA that can delay the submission or approval of certain applications for competing products.

A five-year period of non-patent exclusivity within the US is granted to the first applicant to gain approval of an NDA for a new chemical entity (NCE). An NCE is a drug that contains no active moiety (the molecule or ion responsible for the action of the drug substance) that has been approved by the FDA in any other application submitted under section 505(b) of the FDCA. During the exclusivity period for an NCE, the FDA may not accept for review an abbreviated NDA, or ANDA, or a 505(b)(2) NDA submitted by another company that references (i.e., relies on the FDA's prior approval of) the NCE drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a patent certification for each patent listed with the FDA for the NCE drug (e.g., a certification of patent invalidity or non-infringement with respect to a patent listed with the FDA for the NCE drug).

A three-year period of non-patent exclusivity is granted for a drug product that contains an active moiety that has been previously approved, when the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the application, for example, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations, which means that the FDA may approve ANDAs and 505(b)(2) NDAs for other versions of the original, unmodified drug product. Where this form of exclusivity applies, it prevents FDA approval of an ANDA or 505(b)(2) NDA that is subject to the exclusivity for the three-year period; however, the FDA may accept and review ANDAs or 505(b)(2) NDAs during the three-year period.

These exclusivities also do not preclude FDA approval of a 505(b)(1) NDA for a duplicate version of the approved drug during the period of exclusivity, provided that the follow-on applicant conducts or obtains a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Products with QIDP designation may receive a five-year extension of other non-patent exclusivities for which the drug is also eligible, subject to certain limitations. Depending upon the scope of the non-patent exclusivity that is extended, the five-year extension might not prevent the FDA from approving a subsequent application for a change to the QIDP-designated drug that results in, for example, a new indication, route of administration, dosing, schedule, dosage form, delivery system, delivery device, or strength. A drug that has been designated as both an orphan drug and a QIDP for the same indication, like ARIKAYCE, might be eligible for a combined 12 years of exclusivity for that indication.

Under the PHSA, the FDA recognizes reference product exclusivity starting from the first licensure of a biological product. Reference product exclusivity affects the timing of submission and approval of a BLA for a biosimilar product. Under section 351(k) of the PHSA, a BLA for a biosimilar product may be approved based upon a showing that the proposed product is highly similar to a previously licensed product, known as the reference product, notwithstanding minor differences in clinically inactive components; and there are no clinically meaningful differences between the proposed biosimilar product and the reference product in terms of safety, purity, and potency. Reference product exclusivity prevents the FDA from accepting a BLA submitted under section 351(k) of the PHSA for a proposed biosimilar product for 4 years after the date of first licensure of the reference product, and prevents the FDA from approving such BLA for a proposed biosimilar product for 12 years after such date of first licensure. An additional period of reference product exclusivity is not available upon approval of a

supplemental BLA. Moreover, the PHSA limits the availability of reference product exclusivity for a subsequent BLA filed by the same sponsor or manufacturer of a biological product (or a licensor, predecessor in interest, or other related entity).

Medical Device Regulation

Medical devices, such as Lamira, may be marketed as stand-alone devices, or in some cases, as constituent parts of a combination product. In either case, the product will need to satisfy and comply with FDA requirements. Unless an exemption applies, each medical device commercially distributed in the US requires either FDA clearance of a 510(k) premarket notification, approval of a premarket approval application (PMA), or issuance of a de novo classification order. Medical devices are classified into one of three classes -- Class I, Class II or Class III -- depending on the degree of risk and the level of control necessary to assure the safety and effectiveness of each medical device. Medical devices deemed to pose lower risks are generally placed in either Class I or II.

While most Class I devices are exempt from the 510(k) premarket notification requirement, manufacturers of most Class II devices are required to submit to the FDA a pre-market notification. The FDA's permission to commercially distribute a device subject to a 510(k) premarket notification is generally known as 510(k) clearance. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting, or many implantable devices, or devices that have been found not substantially equivalent to a legally marketed Class I or Class II predicate device, are placed in Class III, requiring approval of a PMA. De novo classification is a risk-based classification process to classify novel medical devices into Class I or Class II.

Medical devices are also subject to certain postmarket requirements. Those requirements include, for example, establishment registration and device listing; compliance with the requirements of the Quality System Regulation (QSR); medical device reporting regulations; correction and removal reporting regulations; compliance with requirements for Unique Device Identification; and post-market surveillance activities and obligations. Device manufacturers must also comply with FDA requirements regarding promotion, which require that promotion is truthful, not misleading, fairly balanced, and that all claims are substantiated, and prohibit the promotion of products for unapproved or "off-label" uses.

Medical device manufacturers must demonstrate and maintain compliance with the FDA's QSR. The QSR is a complex regulatory scheme that covers the methods and documentation of the design, testing, control, manufacturing, labeling, quality assurance, packaging, storage and shipping of medical devices. The FDA enforces the QSR through periodic inspections and unannounced "for cause" inspections.

The FDCA permits medical devices intended for investigational use to be shipped to clinical sites if such devices comply with prescribed procedures and conditions. All clinical investigations of devices to determine safety and effectiveness must be conducted in accordance with the FDA's investigational device exemption, or IDE, regulations that govern investigational device labeling, prohibit promotion of the investigational device, and specify an array of study review and approval, informed consent, recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators.

Failure to comply with applicable regulations could result in enforcement actions such as: warning letters; fines; injunctions; civil penalties; inability to distribute products; recalls or seizures of products; delays in the introduction of products into the market; total or partial suspension of production; FDA refusal to grant, or delay in obtaining, marketing authorizations; and in the most serious cases, criminal penalties.

Combination Products

A combination product is a product comprising two or more regulated components (e.g., a drug and device) that are combined into a single product, co-packaged, or sold separately but intended for co-administration, as evidenced by the labeling for the products. Drugs that are administered using a nebulizer or another device, such as ARIKAYCE or TPIP, are examples of drug/device combination products.

The FDA is divided into various Centers, which each have authority over a specific type of product. NDAs are reviewed by personnel within the Center for Drug Evaluation and Research, while device applications, premarket notifications, and de novo authorization requests are reviewed by the Center for Devices and Radiological Health. Combination products, such as drug/device combinations, are typically reviewed through a marketing submission that corresponds to the constituent part which provides the product's primary mode of action (PMOA), i.e., is the single mode of action that provides the most important therapeutic action of the combination product. If the PMOA is unclear or in dispute, a sponsor may file a Request for Designation with the FDA's Office of Combination Products (OCP), which will render a determination and assign a lead Center. OCP generally assigns jurisdiction based on PMOA. If it is not possible to determine which one mode of action will provide a greater contribution than any other mode of action to the overall therapeutic effects of the combination product, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions. When there are no other combination products that present similar questions of safety and effectiveness with regard to the combination product as a whole, the agency will assign the combination product to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product.

When evaluating an application or other marketing submission for a combination product, a lead Center may consult other Centers, or it may assign review of a specific section of the application to another Center, delegating its review authority for that section. Depending on the type of combination product, approval or clearance could be obtained through submission of a single marketing application or through separate applications for the individual constituent parts (e.g., an NDA for the drug and a premarket notification for the device). The FDCA directs the FDA to conduct a review of a combination product under a single marketing application whenever appropriate. Applicants may choose to submit separate applications for constituent parts of a combination product (unless the FDA determines one application is necessary), and in limited situations, the FDA may determine an application for each constituent part is warranted. One reason to submit multiple applications is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each application is generally reviewed by the Center with authority over each application type. For combination products that contain an approved constituent part (such as a drug-device combination product in which the device has previously received clearance), the FDA may require that the application(s) include only such information as is necessary to meet the standard for clearance or approval, using a risk-based approach and taking into account any prior finding of safety or effectiveness for the approved constituent part.

Like their constituent products—e.g., drugs and devices—combination products are highly regulated and subject to a broad range of post marketing requirements including cGMP, adverse event reporting, periodic reports, labeling and advertising and promotion requirements and restrictions. Failure to comply with applicable requirements could result in enforcement actions.

Disclosure of Clinical Trial Information

Under US and certain foreign laws intended to improve clinical trial transparency, sponsors of clinical trials may be required to register and disclose certain information about their clinical trials. This can include information related to the investigational drug, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial. This information is then made publicly available. Under US regulations, sponsors are obligated to disclose the results of these trials after completion. In the US, disclosure of the results of these trials can be delayed for up to two years if the sponsor is seeking initial approval of the product or approval of a new indication. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Other Post-approval Regulatory Requirements

Once an NDA or BLA is approved, a product will be subject to certain post-approval requirements, including those relating to advertising, promotion, adverse event reporting, recordkeeping, and cGMP, as well as registration, listing, and inspection. There also are continuing, annual user fee requirements.

The FDA regulates the content and format of prescription drug labeling, advertising, and promotion, including direct-to-consumer advertising and promotional Internet communications. The FDA also establishes parameters for permissible non-promotional communications between industry and the medical community, including industry-supported scientific and educational activities. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion for uses not consistent with the approved labeling, and a company that is found to have improperly promoted off-label uses or otherwise not to have met applicable promotion rules may be subject to significant liability under the FDCA, the PHSA, and other statutes, including the False Claims Act.

Manufacturers are subject to requirements for adverse event reporting and submission of periodic reports following FDA approval of an NDA or BLA.

All aspects of pharmaceutical manufacture must conform to cGMP after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the FDA inspects manufacturing facilities to assess compliance with cGMP. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP.

Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, product formulation, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or BLA or NDA or BLA supplement, in some cases before the change may be implemented. An NDA or BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs or BLAs.

As previously mentioned, the FDA also may require Phase 4 studies and may require a REMS, which could restrict the distribution or use of the product.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA), which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

European Union

Marketing Authorization Application

To obtain approval of a drug under the EU regulatory system, an application for a marketing authorization may be submitted under a centralized, a decentralized or a national procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes or for orphan drugs, provides for the grant of a single marketing authorization that is valid for all EU member states, which grants the same rights and obligations in each member state as a national marketing authorization. As a general rule, only one marketing authorization may be granted for drugs approved through the centralized procedure and the marketing authorization is also relevant for the EEA countries.

Under the centralized procedure, the Committee for Medicinal Products for Human Use (CHMP) is required to adopt an opinion on a valid application within 210 days, excluding clock stops when additional information is to be provided by the applicant in response to questions. More specifically, on day 80 of the procedure, the Rapporteur and Co-Rapporteur generate their draft assessment report. This is followed at day 120 by issuing to the applicant their formal report and a list questions. Applicants then have up to three months to respond to the questions (and can request a three-month extension). The Rapporteur, Co-Rapporteur and CHMP assess the applicant's replies and at day 150 generate their Joint Assessment Report. At day 180, the Joint Assessment Report along with a list of outstanding issues for unresolved matters (as needed) is provided to the applicant. Applicants then have one month to respond to the CHMP (and can request a one or two-month extension). At day 180 the CHMP can also request the involvement of a Scientific Advisory Group (SAG), where the applicant is given the opportunity to present data supporting the application and addressing the specific questions addressed by the CHMP to the SAG. If the outstanding issues remain, an oral explanation may be requested by the EMA, where the applicant must attend the CHMP plenary session and address the Major Objections related to approval of the marketing authorization application (MAA). The CHMP members can then question the applicant on the key issues. At day 210, once its scientific evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the marketing authorization. After the adoption of the CHMP opinion, a decision must be adopted by the EC, after consulting the Standing Committee of the Member States. The EC prepares a draft decision and circulates it to the member states; if the draft decision differs from the CHMP opinion, the Commission must provide detailed explanations. The EC adopts a decision within 15 days of the end of the consultation procedure.

Accelerated Procedure, Conditional Approval and Approval Under Exceptional Circumstances

Various programs, including accelerated assessment, conditional approval and approval under exceptional circumstances, are intended to expedite or simplify the approval of drugs that meet certain qualifications. The purpose of these programs is to provide important new drugs to patients earlier than under standard approval procedures.

For drugs which are of major interest from the point of view of public health, in particular from the viewpoint of therapeutic innovation, applicants may submit a substantiated request for accelerated assessment. If the CHMP accepts the request, the review time is reduced from 210 to 150 days.

Furthermore, for certain categories of medicinal products, marketing authorizations may be granted on the basis of less complete data than is normally required in order to meet unmet medical needs of patients or in the interest of public health. In such cases, the company may request, or the CHMP may recommend, the granting of a marketing authorization, subject to certain specific obligations; such marketing authorization may be conditional or under exceptional circumstances. The timelines for the centralized procedure described above also apply with respect to applications for a conditional marketing authorization or marketing authorization under exceptional circumstances.

Conditional marketing authorizations may be granted for products designated as orphan medicinal products, if all of the following conditions are met: (1) the risk-benefit balance of the product is positive, (2) the applicant will likely be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs, and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required.

Conditional marketing authorizations are valid for one year, on a renewable basis until the holder provides a comprehensive data package. The granting of conditional marketing authorization depends on the applicant's ability to fulfill the conditions imposed within the agreed upon deadline. They are subject to "conditions", i.e., the holder is required to complete ongoing studies or to conduct new studies with a view to confirming that the benefit-risk balance is positive or to

fulfill specific obligations in relation to pharmacovigilance. Once the holder has provided a comprehensive data package, the conditional marketing authorization is replaced by a 'regular' marketing authorization.

Marketing authorizations under exceptional circumstances may be granted where the applicant demonstrates that, for objective and verifiable reasons, they are unable to provide comprehensive data on the efficacy and safety of the drug under normal conditions of use. Such marketing authorizations are subject to certain conditions, in particular relating to safety of the drug, notification of incidents relating to its use or actions to be taken. They are valid for an indefinite period of time, but the conditions upon which they are based are subject to an annual reassessment in order to ensure that the risk-benefit balance remains positive.

Exclusivities

If an approved drug contains a new active substance, it is protected by data exclusivity for eight years from the notification of the Commission decision granting the marketing authorization and then by marketing protection for an additional two or three years. Overall, the drug is protected for ten or eleven years against generic competition, and no additional exclusivity protection is granted for any new development of the active substance it contains.

During the eight-year period of data exclusivity, competitors may not refer to the marketing authorization dossier of the approved drug for regulatory purposes. During the period of marketing protection, competitors may not market their generic drugs. The period of marketing protection is normally two years but may become three years if, during the eight-year data exclusivity period, a new therapeutic indication is approved that is considered as bringing a significant clinical benefit over existing therapies.

Medical Devices Regulations

In May 2017, the EU adopted a new Medical Devices Regulation (EU) 2017/745 (MDR), which repealed and replaced Directive 93/42/EEC on Medical Devices (Directive 93/42) on May 26, 2021. The MDR and its associated guidance documents and harmonized standards, govern, among other things, device design and development, preclinical and clinical or performance testing, premarket conformity assessment, registration and listing, manufacturing, labeling, storage, claims, sales and distribution, export and import and post-market surveillance, vigilance, and market surveillance.

As of May 26, 2021, before a device can be placed on the market in the EU, compliance with the MDR requirements (i.e., the General Safety and Performance Requirements, or GSPRs, set out in Annex I of the MDR) must be demonstrated in order to affix the Conformité Européene mark, or CE Mark, to the product. The MDR provides recourse to harmonized European standards in order to facilitate compliance with the GSPRs. Harmonized standards provide a presumption of conformity with the GSPRs (although there are a limited number of standards harmonized currently). However, under transitional provisions provided for in the MDR, medical devices with Notified Body certificates issued under Directive 93/42 prior to May 26, 2021 may continue to be placed on the market for the remaining validity of the certificate, until December 31, 2027 at the latest for higher risk medical devices and until December 31, 2028 for other medical devices, in each case, so long as there is no significant changes in the design or intended purpose. After the expiry of any applicable transitional period, only devices that have been CE marked under the MDR may be placed on the market in the EU.

To demonstrate compliance with these requirements, a conformity assessment procedure is required. The MDR provides for several conformity assessment procedures, which depends on the type of medical device and the risks involved. Devices are divided in four groups based on risk: Class I, Class IIa, Class IIb, and Class III. Class I devices present the lowest level of risk so that, for most of these devices (other than those that are sterile and/or have measuring functionality) the manufacturer can self-certify the product plus affix the CE mark. For the other classes, the conformity assessment is carried out by an organization designated and supervised by a member state of the EEA to conduct conformity assessments, known as a Notified Body. The manufacturer initially classifies every device. However, when a device undergoes a conformity assessment with a Notified Body, the Notified Body may dispute the classification and assert that the device should be included in a class requiring stricter conformity assessment procedures. Specific rules apply to custom-made medical devices, medical devices that are used in clinical trials, and medical devices that incorporate a medicinal ingredient.

For classes of devices other than Class I, the Notified Body carries out the conformity assessment and issues a certificate of conformity, which entitles the manufacturer to affix the CE mark to its devices after having prepared and signed a related EU Declaration of Conformity. Affixing a CE mark allows the product to move freely within the EU and thus prevents EU Member States from restricting sales and marketing of the devices, unless such measure is justified on the basis of evidence of non-compliance. Ultimately, the manufacturer is responsible for the conformity of the device with the GSPRs and for the affixing of the CE mark. Lamira is CE marked by PARI, i.e., its manufacturer, in the EU.

Clinical evidence is required for most medium and high risk devices. In some cases, a clinical study may be required to support a CE marking application. A manufacturer that wishes to conduct a clinical study involving the device is subject to the clinical investigation requirements of the MDR, EU member state requirements, and current good clinical practices defined in harmonized standards and guidance documents.

After a device is placed on the market, it remains subject to significant regulatory requirements. The MDR prohibits misleading claims about devices and so devices may be marketed only for the uses and indications for which they are approved (although more detailed rules on marketing may be contained in national legislation). For CE marked devices, certain modifications to the device or quality system depending on the conformity assessment procedure used must be submitted to and approved by the Notified Body before placing the modified device on the market.

Economic Operators, include device manufactures, must register their establishments and devices in the EUDAMED database once available. Manufacturers of medical devices are subject to vigilance obligations that require reporting of incidents and are required to implement a post-marketing surveillance system (for monitoring data about the device and confirming the benefits of the device outweigh the risks). The vigilance obligations require that manufacturers must report serious incidents involving the device made available in the EU and any field safety corrective actions in respect of the device made available in the EU (including actions taken outside the EU) to relevant competent authorities. In addition, Notified Bodies regularly reassess the conformity of a medical device to the GSPRs and may from time to time audit the manufacturer and may, where needed, suspend or withdraw the manufacturer's certificate of conformity.

Japan

Under the Japanese regulatory system administered by the MHLW and the PMDA (which is responsible for product review and evaluations under the supervision of the MHLW), in principle, pre-marketing approval and clinical studies are required for all pharmaceutical products. The Law on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960) requires a license for marketing authorization when importing to Japan and selling pharmaceutical products manufactured in other countries, a holder of such license is referred to as a marketing authorization holder. It also requires a foreign manufacturer to get each of its manufacturing sites certified as a manufacturing site of pharmaceutical products to be marketed in Japan. To receive a license for marketing authorization, the manufacturer or seller must, at the very least, employ certain manufacturing marketing, quality and safety personnel. A license for marketing authorization may not be granted if the quality management methods and post marketing safety management methods applied with respect to the pharmaceutical product fail to conform to the standards stipulated in the ordinances promulgated by the MHLW. To obtain manufacturing/marketing approval for a new product, a Company must submit an application for approval to the MHLW with results of CMC, nonclinical and clinical studies to show the quality, efficacy and safety of the product candidate. A data compliance review, on-site inspection for good clinical practice, audit and detailed data review for compliance with current good manufacturing practices are undertaken by the PMDA. The application is then discussed by the committees of the Pharmaceutical Affairs and Food Sanitation Council. Based on the results of these reviews, the final decision on approval is made by the MHLW. The time required for the approval process varies depending on the product. PMDA's target review period (submission to approval) is one year (standard review) and nine months (priority review), although this is not a commitment. The product also needs approval for pricing in order to be eligible for reimbursement under Japan's National Health Insurance system. The medical products which, once they are approved and marketed, are subject to the continuing standards of Good Manufacturing Practice and Good Quality Practice and are also subject to regular post-marketing vigilance of safety and quality under the standards of Good Vigilance Practice and Good Post-marketing Study Practice. In Japan, the National Health Insurance system maintains a Drug Price List specifying which pharmaceutical products are eligible for reimbursement, and the MHLW sets the prices of the products on this list. After receipt of marketing approval, negotiations regarding the reimbursement price with the MHLW would begin. Price would be determined within 60 to 90 days following receipt of marketing approval unless the applicant disagrees, which may result in extended pricing negotiations. The government is currently introducing price cut rounds every year and mandates price decreases for specific products. New products judged innovative or useful, that are indicated for pediatric use, or that target orphan or small population diseases, however, may be eligible for a pricing premium. The government has also promoted the use of generics, where available.

Pediatric Information

United States

Under the Pediatric Research Equity Act of 2003 (PREA), as amended, certain NDAs, BLAs, and supplements must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of an applicant, grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, and subject to an exception for certain oncology drugs, PREA does not apply to any drug for an indication for which orphan designation has been granted. Under the Best Pharmaceuticals for Children Act (BPCA), pediatric research is incentivized by the possibility of six months of pediatric exclusivity, which if granted, is added to existing statutory and patent-based exclusivity periods listed for the applicable drug in the FDA's Orange Book at the time the FDA determines that the sponsor has satisfied the FDA's "written request" for pediatric research, provided that the FDA makes such determination at least nine months before the expiration of such exclusivity period. Sponsors may seek to negotiate the terms of a written request during drug development. While the sponsor of an orphan-designated drug may

not be required to perform pediatric studies under PREA unless one of the above exceptions applies, they are eligible to participate in the incentives under the BPCA if the FDA issues a written request.

European Union

In the EU, new drugs (i.e., drugs containing a new active substance) for adults must also be tested in children. This can also include pediatric pharmaceutical forms, in all subsets of the pediatric population. The mandatory pediatric testing is carried out through the implementation of a pediatric investigation plan (PIP), which is proposed by the applicant and approved by the EMA. A PIP contains all the studies to be conducted and measures to be taken in order to support the approval of the new drug, including pediatric pharmaceutical forms, in all subsets of the pediatric population. Implementation of a PIP is a pre-requisite to validation of an MAA. Following granting of the marketing authorization, post approval compliance is also reviewed through the life cycle of the product until the PIP is completed. A PIP may allow for one or more waivers or deferral for one or more of the studies or measures included therein in order not to delay the approval of the drug in adults, and, on another hand, the EMA may grant either a product-specific waiver for the (adult) disease/condition or one or more pediatric subsets or a class waiver for the disease/condition. PIPs are subject to potential modifications from time to time, when they no longer are workable, if approved by EMA. Any new indication as a variation to an existing marketing authorization requires a new PIP for that indication. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the market exclusivity period from ten to twelve years. To benefit from the additional exclusivity the PIP must be completed and content from the PIP must be included in the approved summary of product characteristics.

Japan

In Japan, there is no statutory rule which imposes any different obligation on pharmaceutical manufacturers engaging in pediatric drug development than on other pharmaceutical manufacturers. However, the guidelines of the MHLW (Handling of Pharmaceuticals during the Reexamination Interval Period (Issue No. 107, February 1, 1999) and Enforcement of the Ministerial Ordinance Partially Revising the Ministerial Ordinance on Standards for Post-marketing Surveillance of Pharmaceutical Products and Review of Post-marketing Surveillance for the Reexamination of Pharmaceutical Products (No. 1324, December 27, 2000)) state as follows: (i) since information on pediatric patients obtained in clinical trials may be limited, the MHLW recommends that pharmaceutical manufacturers conduct adequate post-marketing surveillance during the reexamination interval period and collect as much information as possible for proper use of drugs for pediatric patients; and (ii) if a pharmaceutical manufacturer plans to conduct a clinical trial to set the dose of a pediatric drug to prepare application for manufacturing/marketing approval or after receiving the same approval, the reexamination interval period may be extended up to ten years. In addition, since February 2010 the MHLW has convened a study group composed of physicians on a regular basis to discuss and promote the development of children's drugs that have been approved for use in Europe and the US but are not yet approved in Japan, so that they can be used as early as possible in Japan as well.

Regulation Outside the US, Europe and Japan

In addition to regulations in the US, Europe and Japan, we will be subject to a variety of regulations in other jurisdictions governing clinical studies of our candidate products, including medical devices. Regardless of whether we obtain FDA approval for a product candidate, we must obtain approval by the comparable regulatory authorities of countries outside the US before we can commence clinical studies or marketing of the product candidate in those countries. The requirements for approval and the approval process vary from country to country, and the time may be longer or shorter than that required for FDA approval. Under certain harmonized medical device approval/clearance regulations outside the US, reference to US clearance permits fast-tracking of market clearance. Other regions are harmonized with EU standards, and therefore recognize the CE mark as a declaration of conformity to applicable standards. Furthermore, we must obtain any required pricing approvals in addition to regulatory approval prior to launching a product candidate in the approving country. Although the UK is no longer part of the EU, its medicinal product and medical device regulations remain broadly aligned with the EU requirements.

Early Access Programs (EAPs)

Certain countries allow the supply or use of non-authorized medicinal products within strictly regulated EAPs. Some may also provide reimbursement for drugs provided in the context of EAPs. Under EU law, member states are authorized to adopt national legal regimes for the supply or use of non-authorized drugs in case of therapeutic needs. The most common national legal regimes are compassionate use programs and named patient sales, but other national regimes for early access may be available, depending on the member state. For drugs that must be approved through the centralized procedure, such as orphan drugs, compassionate use programs are also regulated at the European level. ARIKAYCE is available in certain countries under these early access programs.

Special programs can be set up to make available to patients with an unmet medical need a promising drug which has not yet been authorized for their condition (compassionate use). As a general rule, compassionate use programs can only be put in place for drugs or biologics that are expected to help patients with life-threatening, long-lasting or seriously disabling illnesses who currently cannot be treated satisfactorily with authorized medicines, or who have a disease for which no medicine

has yet been authorized. The compassionate use route may be a way for patients who cannot enroll in an ongoing clinical trial to obtain treatment with a potentially life-saving medicine. Compassionate use programs are coordinated and implemented by the EU member states, which decide independently how and when to open such programs according to national rules and legislation. Generally, doctors who wish to obtain a promising drug for their seriously ill patients will need to contact the relevant national authority in their respective country and follow the procedure that has been set up. Typically, the national authority keeps a register of the patients treated with the drug within the compassionate use program, and a system is in place to record any side effects reported by the patients or their doctors. Orphan drugs very often are subject to compassionate use programs due to their very nature (rare diseases are life-threatening, long-lasting or seriously disabling diseases) and the long time required for both their approval and effective marketing.

Doctors can also obtain certain drugs for their patients by requesting a supply of a drug from the manufacturer or a pharmacist located in another country, to be used for an individual patient under their direct responsibility. This is often called treatment on a 'named-patient basis' and is distinct from compassionate use programs. In this case, the doctor responsible for the treatment will either contact the manufacturer directly or issue a prescription to be fulfilled by a pharmacist. While manufacturers or pharmacists do record what they supply, there is no central register of the patients that are being treated in this way.

Reimbursement of Pharmaceutical Products

In the US, many independent third-party payors, as well as the Medicare and state Medicaid programs, reimburse dispensers of pharmaceutical products. Medicare is the federal program that provides healthcare benefits to senior citizens and certain disabled and chronically ill persons. Medicaid is the need-based federal and state program administered by the states to provide healthcare benefits to certain persons.

As one of the conditions for obtaining Medicaid and, if applicable, Medicare Part B coverage for our marketed pharmaceutical products, we will need to agree to pay a rebate to state Medicaid agencies that provide reimbursement for those products. We will also have to agree to sell our commercial products under contracts with the Department of Veterans Affairs, Department of Defense, Public Health Service, and numerous other federal agencies as well as certain hospitals that are designated by federal statutes to receive drugs at prices that are significantly below the price we charge to commercial pharmaceutical distributors. These programs and contracts are highly regulated and will impose restrictions on our business. Failure to comply with these regulations and restrictions could result in adverse consequences such as civil money penalties, imposition of a Corporate Integrity Agreement and/or a loss of Medicare and Medicaid reimbursement for our drugs.

Private healthcare payors also attempt to control costs and influence drug pricing through a variety of mechanisms, including through negotiating discounts with the manufacturers and through the use of tiered formularies and other mechanisms that provide preferential access to certain drugs over others within a therapeutic class. Payors also set other criteria to govern the uses of a drug that will be deemed medically appropriate and therefore reimbursed or otherwise covered.

Members of Congress have indicated an interest in legislative measures designed to lower drug costs. The Biden Administration has also indicated that lowering prescription drug prices is a priority. In August 2022, President Biden signed the Inflation Reduction Act (IRA) of 2022 (P.L. 117-169) into law. This law will, for the first time, allow Medicare to negotiate the price of certain high expenditure, single source Medicare Part B or Part D drugs. The Centers for Medicare & Medicaid Services is in the process of implementing a Medicare Drug Price Negotiation Program, and this program may affect future Medicare reimbursement for our drugs. The IRA also requires manufacturers of certain Part B and Part D drugs to issue to the US Department of Health and Human Services (HHS) rebates based on certain calculations and triggers (i.e., when drug prices increase and outpace the rate of inflation). Drug pricing is an active area for regulatory reform at both the federal and state levels, and additional significant changes to current drug pricing and reimbursement structures in the US could be forthcoming.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of drugs through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to patients. Some jurisdictions operate positive and negative list systems under which drugs may only be marketed once a reimbursement price has been agreed. 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 candidate to currently available therapies. Other member states allow companies to fix their own prices for drugs, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new drugs. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drugs will allow favorable reimbursement and pricing arrangements for any of our products.

In Japan, drugs can be sold on the market if they undergo the PMDA’s review of quality, efficacy and safety and receive manufacturing/marketing approval. However, in order for drugs to be covered by the National Health Insurance, they must be included in a Drug Price List. The "Drug Pricing Organization," which is a division of the Central Social Insurance

Medical Council (CSIMC), calculates the price of drugs, the general meeting of the CSIMC approves the calculated price, and the MHLW includes the drugs and the calculated price in the Drug Price List. After receiving manufacturing/marketing approval, drugs are included in the Drug Price List within 60 to 90 days unless the applicant disagrees, which may result in extended pricing negotiations. The MHLW updates the Drug Price List annually after taking into account the survey result of the actual sales price of drugs and hearing the opinion of the CSIMC.

Fraud and Abuse and Other Laws

Physicians and other healthcare providers and third-party payors (government or private) often play a primary role in the recommendation and prescription of healthcare products. In the US and most other jurisdictions, numerous detailed requirements apply to government and private healthcare programs, and a broad range of fraud and abuse laws, transparency laws, and other laws are relevant to pharmaceutical companies. US federal and state healthcare laws and regulations in these areas include the following:

- The federal Anti-kickback Statute;
- The federal civil False Claims Act;
- The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act;
- The federal criminal false statements statute;
- The price reporting requirements under the Medicaid Drug Rebate Program and the Veterans Health Care Act of 1992;
- The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program; and
- Analogous and similar state laws and regulations.

Similar restrictions apply in the member states of the EU and Japan, which have been set out by laws or industry codes of conduct.

Employees

As of December 31, 2023, we had a total of 912 full-time employees: 442 in research, clinical, regulatory, medical affairs and quality assurance; 70 in technical operations, manufacturing and quality control; 173 in general and administrative functions; and 227 in commercial activities. We had 703 full-time employees in the US, 124 employees in Europe and 85 employees in Japan. We anticipate increasing our headcount in 2024.

None of our employees are represented by a labor union and we believe that our relations with our employees are generally good. Generally, our US employees are at-will employees; however, we have entered into employment agreements with certain of our executive officers.

Human Capital

Employee Attraction, Retention and Development

We are dedicated to attracting and retaining the best possible talent. Our compensation program, including short- and long-term incentives and benefits, is designed to allow us to attract and retain individuals whose skills are critical to our current and long-term success. Total compensation is generally positioned within a competitive range of the peer market median, with differentiation based on tenure, skills, proficiency, and performance to attract and retain key talent. With our compensation program, we also aim to align the interests of our employees with those of our stockholders.

We believe that continued growth and development are essential to the professional well-being of our team. We seek to develop our employee talent within the organization through access to training, continuous learning programs and other development initiatives. As our organization and capabilities grow, we aim to ensure we have provided our team members with the guidance and resources they need to develop as professionals and to support our business.

Core Values

Five core values—collaboration, accountability, passion, respect, and integrity—set the tone for our culture and guide the actions we take each day. We strive to ensure that these values drive all of our human capital endeavors, including our annual employee feedback process, our Leadership Competencies, our Recognition Program, and our new employee onboarding initiatives.

Diversity and Inclusion

We are focused on maintaining an inclusive work environment that best supports the diverse needs of the patient communities we serve. Among other factors in hiring, we consider geographic, gender, age, racial and ethnic diversity. As of December 31, 2023, women represent 38% of our executive team, 28% of our leadership team (vice president and above), 33% of our board of directors and 53% of our workforce. We continue to grow our list of employee resource groups and expand our

sourcing for new talent to foster increased diversity in our talent pipeline. We are also committed to equitable pay for all employees. We use industry benchmarks and annual internal equity reviews to make salary adjustments as needed in efforts to ensure a fair and bias-free compensation system. As we grow, we are continuing to implement initiatives to advance the development of diverse talent and ensure diverse succession plans both in our employee workforce and our board of directors, and to support equity and inclusion for all. To further our initiatives, in the fourth quarter of 2023, we hired a director of inclusion and culture.

Environmental, Social and Governance (ESG)

As of 2021, we have a cross-functional group of employees that, together with members of our executive leadership, updates our Nominations and Governance Committee and Board of Directors on ESG considerations and strategy. We are cognizant of our environmental impact, currently support several green measures and community service programs, and continue to explore options to improve and build upon our sustainability efforts. We are committed to ensuring the health and well-being of our employees and promoting patient advocacy and safety. Finally, we are driven by integrity and believe good corporate governance is important and necessary to maintain ethical and compliant business practices. In 2023, we published our inaugural Responsibility Report.

Available Information

We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (Exchange Act). We make available on our website at http://www.insmed.com, free of charge, copies of these reports as soon as reasonably practicable after filing, or furnishing them to, the SEC. The public can also obtain materials that we file with the SEC through the SEC's website at http://www.sec.gov.

Also available through our website's "Investors-Corporate Governance" page are charters for the Audit, Compensation, Nominations and Governance and Science and Technology Committees of our board of directors, our Corporate Governance Guidelines, and our Code of Business Conduct and Ethics. We intend to satisfy the disclosure requirements regarding any amendment to, or waiver from, a provision of the Code of Business Conduct and Ethics by making disclosures concerning such matters available on our website.

The references to our website and the SEC's website are intended to be inactive textual references only. Neither the information in or that can be accessed through our website, nor the contents of the SEC's website, are incorporated by reference in this Annual Report on Form 10-K.

Financial Information

The financial information required under this Item 1 is incorporated herein by reference to Item 8 of this Annual Report on Form 10-K.

ITEM 1A. RISK FACTORS

Our business is subject to substantial risks and uncertainties. Any of the risks and uncertainties described below, either alone or taken together, could materially and adversely affect our business, financial condition, results of operations, prospects for growth, and the value of an investment in our common stock. In addition, these risks and uncertainties could cause actual results to differ materially from those expressed or implied by forward-looking statements contained in this Annual Report on Form 10-K (please read the Cautionary Note Regarding Forward-Looking Statements appearing at the beginning of this Annual Report on Form 10-K).

Risk Factor Summary

An investment in our securities is subject to various risks, the most significant of which are summarized below.

- Our prospects are highly dependent on the success of our only approved product, ARIKAYCE. If we are unable to successfully market and commercialize or maintain approval for ARIKAYCE, our business, financial condition, results of operations and prospects and the value of our common stock will be materially adversely affected.
- The commercial success of ARIKAYCE will depend on continued market acceptance by physicians, patients, third-party payors and others in the healthcare community.
- We obtained regulatory approval of ARIKAYCE in the US through an accelerated approval process, and full approval will be contingent on successful and timely completion of a confirmatory post-marketing clinical trial.
- We may not be able to obtain regulatory approvals for brensocatib, or for our other product candidates, and we may not be able to receive approval for ARIKAYCE in new markets. Any such failure to obtain regulatory approvals, particularly for brensocatib in the US, may materially adversely affect us.
- We remain subject to substantial, ongoing regulatory requirements related to ARIKAYCE, and failure to comply with these requirements could lead to enforcement action or otherwise materially harm our business.
- If we are unable to obtain or maintain adequate reimbursement from government or third-party payors for ARIKAYCE or if we are unable to obtain or maintain acceptable prices for ARIKAYCE, our prospects for generating revenue and achieving profitability will be materially adversely affected.
- ARIKAYCE could develop unexpected safety or efficacy concerns, which would have a material adverse effect on us.
- If estimates of the size of the potential markets for ARIKAYCE, brensocatib, TPIP, or our other product candidates are overstated or data we have used to identify physicians is inaccurate, our ability to earn revenue to support our business could be materially adversely affected.
- We may not be successful in clinical trials or in obtaining regulatory approvals required to expand the indications for ARIKAYCE, which may materially adversely affect our prospects and the value of our common stock.
- Pharmaceutical research and development is very costly and highly uncertain, and we may not succeed in developing product candidates in the future.
- 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, may be interpreted differently if additional data are disclosed, and are subject to audit and verification procedures that could result in material changes in the final data.
- Failure to obtain or maintain regulatory approval or clearance of our product devices, including Lamira, as a delivery system for ARIKAYCE and the delivery system for TPIP, could materially harm our business.
- If our clinical studies do not produce positive results or our clinical trials are delayed, or if serious side effects are identified during drug development, we may experience delays, incur additional costs and ultimately be unable to obtain regulatory approval for and commercialize our product candidates in the US, Europe, Japan or other markets.
- We may not be able to enroll enough patients to conduct and complete our clinical trials or retain a sufficient number of patients in our clinical trials to generate the data necessary for regulatory approval of our product candidates or to permit the use of ARIKAYCE in the broader population of patients with MAC lung disease.
- If another party obtains orphan drug exclusivity for a product essentially the same as a product we are developing for a particular indication, we may be precluded or delayed from commercializing the product in that indication.
- Our early-stage research activities include the research and development of novel gene therapy product candidates. It will be difficult to predict the time and cost of development and of subsequently obtaining regulatory approval for any such product candidates, or how long it will take to commercialize any gene therapy product candidates.
- If we are unable to form and sustain relationships with third-party service providers that are critical to our business, or if any third-party arrangements that we may enter into are unsuccessful, our ability to develop and commercialize our products may be materially adversely affected.
- We may not have, or may be unable to obtain, sufficient quantities of ARIKAYCE, Lamira or our product candidates to meet our required supply for commercialization or clinical studies, which would materially harm our business.
- Adverse consequences to our business could result if we and our manufacturing partners fail to comply with applicable regulations or maintain required approvals.
- We are dependent upon retaining and attracting key personnel, the loss of whose services could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

- We expect to continue to expand our development, regulatory and sales and marketing capabilities, and as a result, may encounter difficulties in managing our growth, which could disrupt our operations.
- Any acquisitions we make, or collaborative relationships we enter into, may not be clinically or commercially successful, and may require financing or a significant amount of cash, which could adversely affect our business.
- Our business and operations, including our drug development and commercialization programs, could be materially disrupted in the event of system failures, security breaches, cyber-attacks, deficiencies in our cybersecurity, violations of data protection laws or data loss or damage by us or third parties.
- We are subject to data privacy laws and regulations that govern how we can collect, process, store and transfer personal data.
- We have limited experience operating internationally, are subject to a number of risks associated with our international activities and operations and may not be successful in any efforts to further expand internationally.
- We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully.
- We have a limited number of significant customers and losing any of them could have an adverse effect on our financial condition and results of operations.
- Deterioration in general economic conditions in the US, Europe, Japan and globally, including the effect of prolonged periods of inflation on our suppliers, third-party service providers and potential partners, could harm our business and results of operations.
- If we are unable to adequately protect our intellectual property rights, the value of ARIKAYCE and our product candidates could be materially diminished.
- If we fail to comply with obligations in our third-party agreements, our business could be adversely affected, including as a result of the loss of license rights that are important to our business.
- Government healthcare reform could materially increase our costs, which could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.
- If we fail to comply with applicable laws, including "fraud and abuse" laws, anti-corruption laws and trade control laws, we could be subject to negative publicity, civil or criminal penalties, other remedial measures, and legal expenses, which could adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.
- We have a history of operating losses, expect to incur operating losses for the foreseeable future and may never achieve or maintain profitability.
- We may need to raise additional funds to continue our operations, but we face uncertainties with respect to our ability to access capital.
- We have outstanding indebtedness in the form of convertible senior notes, a term loan and a royalty financing arrangement and may incur additional indebtedness in the future, which could adversely affect our financial position, prevent us from implementing our strategy, and dilute the ownership interest of our existing shareholders.
- We may be unable to use certain of our net operating losses and other tax assets.
- Goodwill impairment charges in the future could have a material adverse effect on our business, results of operations and financial condition.
- Our shareholders may experience dilution of their ownership interests because of the future issuance of additional shares of our common stock for general corporate purposes and upon the conversion of the Convertible Notes.
- The market price of our stock has been and may continue to be highly volatile, which could lead to shareholder litigation against us.
- Certain provisions of Virginia law, our articles of incorporation and amended and restated bylaws and arrangements between us and our employees could hamper a third party’s acquisition of us or discourage a third party from attempting to acquire control of us.

Risks Related to the Commercialization and Continued Approval of ARIKAYCE

Our prospects are highly dependent on the continued success of our only approved product, ARIKAYCE, which was approved in the United States as ARIKAYCE (amikacin liposome inhalation suspension), in Europe as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion and in Japan as ARIKAYCE inhalation 590mg (amikacin sulfate inhalation drug product). If we are unable to successfully market and commercialize or maintain approval for ARIKAYCE, our business, financial condition, results of operations and prospects and the value of our common stock will be materially adversely affected.

Our long-term viability and growth depend on the continued successful commercialization of ARIKAYCE, our only approved product. ARIKAYCE was approved in the US for the treatment of MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options in a refractory setting, as defined by patients who do not achieve negative sputum cultures after a minimum of six consecutive months of a multidrug background regimen therapy. Subsequently, ARIKAYCE was approved in Europe for the treatment of NTM lung infections caused by

MAC in adults with limited treatment options who do not have CF, and in Japan for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatments with a multidrug regimen. We refer to NTM lung disease caused by MAC as MAC lung disease. We have invested and continue to invest significant efforts and financial resources in the commercialization of ARIKAYCE, and our ability to continue to generate revenue from ARIKAYCE will depend heavily on successfully commercializing and obtaining full regulatory approval for ARIKAYCE from the FDA by conducting an appropriate confirmatory post-marketing study. ARIKAYCE was our first commercial launch, and its successful commercialization and our receipt of full regulatory approval for ARIKAYCE in the US are subject to many risks.

In order to commercialize ARIKAYCE, we must establish and maintain marketing, market access, sales and distribution capabilities on our own or make arrangements with third parties for its marketing, sale and distribution. We are commercializing ARIKAYCE in the US, Europe and Japan using our sales force, but we may not continue to be successful in these efforts. The establishment, development and maintenance of our own sales force is and will continue to be expensive and time-consuming. As a result, we may seek one or more partners to handle some or all of the sales and marketing of ARIKAYCE in certain markets following approval by the relevant regulatory authority in those markets. In that case, we will be reliant on third parties to successfully commercialize ARIKAYCE and will have less control over commercialization efforts than if we handled commercialization with our own sales force. However, we may not be able to enter into arrangements with third parties to sell ARIKAYCE on favorable terms or at all. In the event that either our own marketing, market access, sales force or third-party marketing, and sales organizations are not effective, our ability to generate revenue would be adversely affected.

The commercial success of ARIKAYCE depends on continued market acceptance by physicians, patients, third-party payors and others in the healthcare community.

Despite receiving FDA, EC and Japan's MHLW approval of ARIKAYCE, market acceptance may vary among physicians, patients, third-party payors or others in the healthcare community. ARIKAYCE was the first product approved in the US via the LPAD pathway, and its approval under this pathway may impact market acceptance of the product. If ARIKAYCE does not achieve and maintain an adequate level of acceptance, it is not likely that we will generate significant revenue or become profitable. The degree of market acceptance of ARIKAYCE, which we launched in the US early in the fourth quarter of 2018, in Europe in the fourth quarter of 2020, and in Japan in the second quarter of 2021, is also dependent on a number of additional factors, including the following:

- The willingness of the target patient populations to use, and of physicians to prescribe, ARIKAYCE;
- The efficacy and potential advantages of ARIKAYCE over alternative treatments;
- The risk and safety profile of ARIKAYCE, including, among other things, physician and patient concern regarding the US boxed warning and other safety precautions resulting from its association with an increased risk of respiratory adverse reactions, and any adverse safety information that becomes available as a result of longer-term use of ARIKAYCE;
- Relative convenience and ease of administration, including any requirements for hospital administration of ARIKAYCE;
- The ability of the patient to tolerate ARIKAYCE;
- The pricing of ARIKAYCE;
- The ability and willingness of the patient to pay out of pocket costs for ARIKAYCE (for example co-payments);
- Sufficient third-party insurance coverage and reimbursement;
- The strength of marketing and distribution support and timing of market introduction of competitive products and treatments; and
- Publicity concerning ARIKAYCE or any potential competitive products and treatments.

Our efforts to educate physicians, patients, third-party payors and others in the healthcare community on the benefits of ARIKAYCE have required and will continue to require significant resources, which may be greater than those required to commercialize more established technologies and these efforts may never be successful.

We obtained regulatory approval of ARIKAYCE in the US through an accelerated approval process, and full approval will be contingent on successful and timely completion of a confirmatory post-marketing clinical trial. Failure to obtain full approval or otherwise meet our post-marketing requirements and commitments would have a material adverse effect on our business.

The FDA approved ARIKAYCE under the LPAD and accelerated approval pathways, and full approval will be based on results from a post-marketing confirmatory clinical trial. Accelerated approval allows drugs that (i) are being developed to treat a serious or life-threatening disease or condition and (ii) provide a meaningful therapeutic benefit over existing treatments to be approved substantially based on an intermediate endpoint or a surrogate endpoint that is reasonably likely to predict

clinical benefit, rather than a clinical endpoint such as survival or irreversible morbidity. Accelerated approval of ARIKAYCE was supported by preliminary data from the Phase 3 CONVERT study, which evaluated the safety and efficacy of ARIKAYCE in adult patients with refractory MAC lung disease, using achievement of sputum culture conversion (defined as three consecutive negative monthly sputum cultures) by Month 6 as the primary endpoint.

As a condition of accelerated approval, we must conduct a post-marketing confirmatory clinical trial. Additionally, we are required to submit periodic reports on the progress of this clinical trial. In the fourth quarter of 2020, we commenced the post-marketing confirmatory clinical trial program for ARIKAYCE in patients with MAC lung disease. The confirmatory clinical trial program consists of the ARISE trial, an interventional study designed to validate cross-sectional and longitudinal characteristics of a PRO tool in MAC lung disease, and the ENCORE trial, designed to establish the clinical benefits and evaluate the safety of ARIKAYCE in patients with newly diagnosed or recurrent MAC lung disease using the PRO tool validated in the ARISE trial. The confirmatory clinical program is intended to fulfill the FDA's post-marketing requirement to allow for full approval of ARIKAYCE by the FDA, and verification and description of clinical benefit in the ENCORE trial will be necessary for full approval of ARIKAYCE. The trial completion timetable agreed upon with the FDA when the approval letter for ARIKAYCE was received has been delayed. We remain engaged with the FDA regarding the timeline, status and execution of the ARISE and ENCORE trials. There is little precedent for clinical development and regulatory expectations for agents to treat MAC lung disease. In September 2023, we announced positive topline results from the ARISE trial. The study met its primary objective of demonstrating that the QOL-B respiratory domain works effectively as a PRO tool in patients with MAC lung disease. Based on these results, we have proposed to the FDA that the change of the respiratory score derived from the QOL-B respiratory domain PRO be the primary endpoint for the ENCORE study. If our PRO tool is not approved as the primary endpoint for the ENCORE study or if modifications are required, we would need to develop a new clinical endpoint for the ENCORE trial. We may also encounter substantial delays in completing enrollment for the ENCORE trial, including due to any increase to the enrollment target based on pending discussions with the FDA, and in conducting the trial, and we may not be able to enroll and conduct the trial in a manner satisfactory to the FDA or within the time period required by the FDA. The FDA could, among other things, withdraw its approval of ARIKAYCE using expedited procedures if the ENCORE trial is not successful or if the FDA concludes that we failed to conduct the ENCORE trial with due diligence, that other evidence demonstrates that ARIKAYCE is not shown to be safe and effective, or that we disseminated false or misleading promotional materials with respect to ARIKAYCE. Additionally, under the amendments to the FDCA made by the Food and Drug Omnibus Reform Act of 2022, the FDA could pursue administrative and judicial remedies for a violation of the FDCA if we were to fail to conduct the ENCORE trial with due diligence or not timely submit the required reports on the progress of the ENCORE trial. Separate from the confirmatory trial, additional results from ongoing and recently completed studies may affect the FDA's benefit-risk analysis for the product. Failure to meet all post-marketing commitments may raise additional regulatory challenges.

We remain subject to substantial, ongoing regulatory requirements, and failure to comply with these requirements could lead to enforcement action or otherwise materially harm our business.

We are subject to a variety of manufacturing, packaging, storage, labeling, advertising, promotion, and record-keeping requirements in the US, Europe, and Japan including requirements to:

- Conduct sales, marketing and promotion, scientific exchange, speaker programs, charitable donations and educational grant programs in compliance with federal and state laws;
- Disclose clinical trial information and payments to healthcare professionals and healthcare organizations on publicly available databases;
- Monitor and report complaints, AEs and instances of failure to meet product specifications;
- Comply with cGMP and quality systems requirements for devices;
- Acquire licenses for marketing authorization and certifications for our third-party manufacturers when importing and selling pharmaceutical products manufactured in other countries into Japan;
- Negotiate with national governments and other counterparties on pricing and reimbursement status;
- Carry out post-approval confirmatory clinical trials;
- Comply with ongoing pharmacovigilance requirements; and
- Disclose payments to healthcare professionals and healthcare organizations to national regulatory authorities and/or on publicly available websites.

If we ultimately receive approval for ARIKAYCE in jurisdictions other than the US, EU, and Japan, we expect to be subject to similar ongoing regulatory oversight by the relevant foreign regulatory authorities, including the requirement to negotiate with national governments and other counterparties on pricing and reimbursement prices for each new jurisdiction.

Failure to comply with these ongoing regulatory obligations could have significant negative consequences, including:

- Issuance of warning letters or untitled letters by the FDA asserting that we are in violation of the law;

- Imposition of injunctions or civil monetary penalties or pursuit by regulators of civil or criminal prosecutions and fines against us or our responsible officers;
- Suspension or withdrawal of regulatory approval;
- Suspension or termination of ongoing clinical trials or refusal by regulators to approve pending marketing applications or supplements to approved applications;
- Seizure of products, required product recalls or refusal to allow us to enter into supply contracts, including government contracts, or to import or export products;
- Enforcement actions, such as a product recalls, or product shortages due to failure to meet certain manufacturing or regulatory requirements, including the successful completion and results of quality control or release testing;
- Suspension of, or imposition of restrictions on, our operations, including costly new manufacturing requirements with respect to ARIKAYCE, brensocatib, TPIP, or any of our other product candidates; and
- Negative publicity, including communications issued by regulatory authorities, which could negatively impact the perception of us or ARIKAYCE, brensocatib, TPIP, or any of our other product candidates by patients, physicians, third-party payors or the healthcare community.

We provide financial assistance with out-of-pocket costs to patients enrolled in commercial health insurance plans. In addition, independent foundations may assist with out-of-pocket financial obligations. The ability of these organizations to provide assistance to patients is dependent on funding from external sources, and we cannot guarantee that such funding will be available at adequate levels, if at all. Patient assistance programs, whether provided directly by manufacturers or charitable foundations, have come under recent government scrutiny. If we are deemed to fail to comply with relevant laws, regulations or government guidance with respect to these programs, we could be subject to significant fines or penalties.

If we are unable to obtain adequate reimbursement from government or third-party payors for ARIKAYCE or if we are unable to obtain acceptable prices for ARIKAYCE, our prospects for generating revenue and achieving profitability will be materially adversely affected.

Our prospects for generating revenue and achieving profitability depend heavily upon the availability of adequate reimbursement for the use of ARIKAYCE from governmental and other third-party payors, both in the US and in other markets. A portion of our current ARIKAYCE revenue in the US comes from Medicare reimbursement, and we expect that trend to continue. Reimbursement by a third-party payor depends upon a number of factors, including the third-party payor's determination that use of a product is:

- A covered benefit under its health plan;
- Safe, effective and medically necessary;
- Appropriate for the specific patient;
- Cost-effective; and
- Neither experimental nor investigational.

Obtaining a determination of coverage and reimbursement for a product from each relevant governmental or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor. Payors in the US have evaluated ARIKAYCE for inclusion on formularies. Going forward, we may not be able to provide data sufficient to gain positive coverage and reimbursement determinations or we might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of ARIKAYCE to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources.

Even when a payor determines that a product is eligible for reimbursement, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA or non-US regulatory authorities and/or may set a reimbursement rate that is too low to support a profitable sales price for the product. For example, in France we agreed with the French authorities to a reimbursed price which was lower than the price in our temporary authorization for use (Autorisation Temporaire d'Utilisation or ATU) and are required to refund the difference. As a result, we recorded a revenue reversal in the fourth quarter of 2022, related to revenue recorded in prior periods. In addition, in 2023, we experienced a one-time, prospective price decrease for ARIKAYCE in Japan of 9.4%. In the US, payors have restricted and continue to restrict coverage of ARIKAYCE by using a variable co-payment structure that imposes higher costs on patients for drugs that are not preferred by the payor and by imposing requirements for prior authorization or step edits. Subsequent approvals of competitive products could result in a detrimental change to the reimbursement of our products. The occurrence of any of these events likely would adversely impact market acceptance and demand for ARIKAYCE, which, in turn, could affect our ability to successfully commercialize ARIKAYCE and adversely impact our business, financial condition, results of operations and prospects and the value of our common stock.

There is a significant focus in the US healthcare industry and elsewhere on drug prices and value, and public and private payors are taking increasingly aggressive steps to control their expenditures for pharmaceuticals by, among other things, negotiating manufacturer discounts and placing restrictions on reimbursement for, and patient access to, medications. These pressures could negatively affect our business. We expect changes in the Medicare program and state Medicaid programs, as well as managed care organizations and other third-party payors, to continue to put pressure on pharmaceutical product pricing. One significant example of recent legislative action is the IRA, which was signed into law on August 16, 2022. While the IRA is still subject to rulemaking (with more information to come via guidance documents from the responsible federal agencies), the IRA purports to give the HHS the ability and authority to directly negotiate with manufacturers the price that Medicare will pay for certain high-priced drugs and set caps on the negotiated price of such drugs, among other changes. The IRA also requires manufacturers of certain Part B and Part D drugs to issue to HHS rebates based on certain calculations and triggers (i.e., when drug prices increase and outpace the rate of inflation). At this time, while we believe that ARIKAYCE will be excluded from negotiation due to its orphan drug designation, we cannot predict other potential implications the IRA provisions will have on our business or the pricing of any future products. These types of laws may have a significant impact on our ability to set a product price we believe is fair and may adversely affect our ability to generate revenue and achieve or maintain profitability. We expect further federal and state proposals and healthcare reforms to continue to be proposed, which could limit the prices that can be charged for the products we develop or may otherwise limit our commercial opportunity. See Reimbursement of Pharmaceutical Products in Item 1 of Part I of this Annual Report on Form 10-K for more information. In addition, in connection with various government programs, we are required to report certain pricing information to the government, and the failure to do so may subject us to penalties.

In markets outside the US, including countries in Europe, Japan and Canada, pricing of pharmaceutical products is subject to governmental control. Evaluation criteria used by many government agencies in European countries for the purposes of pricing and reimbursement typically focus on a product's degree of innovation and its ability to meet a clinical need unfulfilled by currently available therapies. The Patient Protection and Affordable Care Act (ACA) created a similar entity, the Patient-Centered Outcomes Research Institute, designed to review the effectiveness of treatments and medications in federally-funded healthcare programs. An adverse result could lead to a treatment or product being removed from Medicare or Medicare coverage. The decisions of such governmental agencies could affect our ability to sell our products profitably.

We continue to have discussions with third-party payors regarding our price for ARIKAYCE, and our pricing may meet resistance from them and the public generally. If we are unable to maintain adequate reimbursement for ARIKAYCE in the US, Europe and Japan, the adoption of ARIKAYCE by physicians and patients may be limited. If we are unable to negotiate acceptable prices for ARIKAYCE, we may be unable to generate sufficient revenue to achieve profitability. Both of these risks, in turn, could affect our ability to successfully commercialize ARIKAYCE and adversely impact our business, financial condition, results of operations and prospects and the value of our common stock.

ARIKAYCE could develop unexpected safety or efficacy concerns, which would likely have a material adverse effect on us.

ARIKAYCE is now being used by larger numbers of patients, for longer periods of time than during our clinical trials (including in the CONVERT study), and we and others (including regulatory agencies and private payors) are collecting extensive information on the efficacy and safety of ARIKAYCE by monitoring its use in the marketplace. In addition, we are conducting a confirmatory trial to assess and describe the clinical benefit of ARIKAYCE in patients with MAC lung disease and may conduct additional trials in connection with lifecycle management programs for ARIKAYCE. New safety or efficacy data from both market surveillance and our clinical trials may result in negative consequences including the following:

- Modification to product labeling or promotional statements, such as additional boxed or other warnings or contraindications, or the issuance of additional "Dear Doctor Letters" or similar communications to healthcare professionals;
- Required changes in the administration of ARIKAYCE;
- Imposition of additional post-marketing surveillance, post-marketing clinical trial requirements, distribution restrictions or other risk management measures, such as a risk evaluation and mitigation strategy (REMS) or a REMS with elements to assure safe use;
- Suspension or withdrawal of regulatory approval;
- Suspension or termination of ongoing clinical trials or refusal by regulators to approve pending marketing applications or supplements to approved applications;
- Suspension of, or imposition of restrictions on, our operations, including costly new manufacturing requirements with respect to ARIKAYCE; and
- Voluntary or mandatory product recalls or withdrawals from the market and costly product liability claims.

Any of these circumstances could reduce ARIKAYCE's market acceptance and would be likely to materially adversely affect our business.

If estimates of the size of the potential markets for ARIKAYCE, brensocatib, TPIP, or our other product candidates are overstated or data we have used to identify physicians is inaccurate, our ability to earn revenue to support our business could be materially adversely affected.

We have relied on external sources, including market research funded by us and third parties, and internal analyses and calculations to estimate the potential market opportunities for ARIKAYCE, brensocatib, TPIP, or any of our other product candidates. The externally sourced information used to develop these estimates has been obtained from sources we believe to be reliable, but we have not verified the data from such sources, and their accuracy and completeness cannot be assured. With respect to ARIKAYCE, our internal analyses and calculations are based upon management's understanding and assessment of numerous inputs and market conditions, including, but not limited to, the projected increase in prevalence of MAC lung disease, Medicare patient population growth and ongoing population shifts to geographies with increased rates of MAC lung disease. These understandings and assessments necessarily require assumptions subject to significant judgment and may prove to be inaccurate. As a result, our estimates of the size of these potential markets for ARIKAYCE could prove to be overstated, perhaps materially.

In addition, we are relying on third-party data to identify the physicians who treat the majority of MAC lung disease patients in the US and to determine how to deploy our resources to market to those physicians; however, we may not be marketing to the appropriate physicians and may therefore be limiting our market opportunity.

With regards to brensocatib, our estimated number of total diagnosed bronchiectasis patients in the US was derived from an external source. A similar per capita prevalence was used to calculate the estimated prevalence in the European 5. However, studies indicate a lack of consensus on prevalence rates.

In the future, we may develop additional estimates with respect to market opportunities for our other product candidates, and such estimates are subject to similar risks. In addition, a potential market opportunity could be reduced if a regulator limits the proposed treatment population for one of our product candidates, similar to the limited population for which ARIKAYCE was approved. In either circumstance, even if we obtain regulatory approval, we may be unable to commercialize the product on a scale sufficient to generate significant revenue from such product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

We may not be successful in clinical trials or in obtaining regulatory approvals required to expand the indications for ARIKAYCE, which may materially adversely affect our prospects and the value of our common stock.

The FDA granted accelerated approval of ARIKAYCE for the treatment of MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options in a refractory setting, as defined by patients who do not achieve negative sputum culture after a minimum of six consecutive months of a multidrug background regimen therapy. Our CONVERT study and 312 study focused on this refractory population, and we do not anticipate obtaining an indication for a broader population of patients with MAC lung disease or any other illnesses or infections without additional clinical data. Additional clinical trials will require additional time and expense. While we reported positive topline results from our ARISE trial, we are continuing to conduct our confirmatory clinical trial program for full approval of ARIKAYCE in the broader population of patients with MAC lung disease through our ENCORE trial, but this trial program, along with any other clinical trials of ARIKAYCE, may not be successful. Additional results from ongoing and recently completed studies may affect the FDA's benefit-risk analysis for the product. If we are unable to expand the indication for use of ARIKAYCE, our prospects and the value of our common stock may be materially adversely affected.

Risks Related to the Development and Regulatory Approval of Our Product Candidates Generally

Pharmaceutical research and development is very costly and highly uncertain, and we may not succeed in developing product candidates in the future.

Product development in the pharmaceutical industry is an expensive, high-risk, lengthy, complicated, resource intensive process. In order to develop a product successfully, we must, among other things:

- Identify potential product candidates;
- Submit for and receive regulatory approval to perform clinical trials;
- Design and conduct appropriate preclinical and clinical trials, including confirmatory clinical trials, according to good laboratory practices and good clinical practices and disease-specific expectations of the FDA and other regulatory bodies;
- Select and recruit clinical investigators and subjects for our clinical trials;
- Obtain and correctly interpret data establishing adequate safety of our product candidates and demonstrating with statistical significance that our product candidates are effective for their proposed indications, as indicated by satisfaction of pre-established endpoints;

- Submit for and receive regulatory approvals for marketing; and
- Manufacture the product candidates and device constituent parts according to cGMP and other applicable standards and regulations.

There is a high rate of failure inherent in this process, and potential products that appear promising at early stages of development may fail for a number of reasons. Importantly, positive results from preclinical studies of a product candidate may not be predictive of similar results in human clinical trials, promising results from earlier clinical trials of a product candidate may not be replicated in later clinical trials, and observations from ongoing trials, including observations based on interim, preliminary, or blinded data, may not be representative of results after the trials are completed and all data is collected and analyzed. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving positive results in earlier stages of development and have abandoned development efforts or sought partnerships in order to continue development.

In addition, there are many other difficulties and uncertainties inherent in pharmaceutical research and development that could significantly delay or otherwise materially impair our ability to develop future product candidates, including the following:

- Conditions imposed by regulators, ethics committees or institutional review boards for preclinical testing and clinical trials relating to the scope or design of our clinical trials, including selection of endpoints and number of required patients or clinical sites;
- Challenges in designing our clinical trials to support potential claims of superiority over current standard of care or future competitive therapies;
- Restrictions placed upon, or other difficulties with respect to, clinical trials and clinical trial sites, including with respect to potential clinical holds or suspension or termination of clinical trials due to, among other things, potential safety or ethical concerns or noncompliance with regulatory requirements;
- Delayed or reduced enrollment in clinical trials, high discontinuation rates or overly concentrated patient enrollment in specific geographic regions;
- Failure by third-party contractors, contract research organizations (CROs), clinical investigators, clinical laboratories, or suppliers to comply with regulatory requirements or meet their contractual obligations in a timely manner;
- Greater than anticipated cost of our clinical trials; and
- Insufficient product supply or inadequate product quality.

We cannot state with certainty when or whether our product candidates now under development will be approved or launched; whether, if initially granted, such approval will be maintained; whether we will be able to develop, license, or otherwise acquire additional products or product candidates; or whether our products, once launched, will be commercially successful. Failure to successfully develop future product candidates for any of these reasons may materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

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, may be interpreted differently if additional data are disclosed, 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 clinical trials, which may be based on a preliminary analysis of then-available data in a summary or topline format, and the results and related findings may change as more patient data become available, may be interpreted differently if additional data are disclosed at a later time and are subject to audit and verification procedures that could result in material changes in the final data. For example, in September 2023, we announced topline data for the ARISE trial and we expect to announce topline data for the ASPEN trial in the latter half of the second quarter of 2024. If additional results from our clinical trials are not viewed favorably, our ability to obtain approval for and commercialize our approved drug and drug candidates, our business, operating results, prospects, or financial condition may be harmed and our stock price may decrease.

We also make assumptions, estimates, 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 preliminary or topline results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been disclosed and/or are received and fully evaluated. Such 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. As a result, preliminary and topline data should be viewed with caution until the final data are available. We may also disclose interim data from our clinical trials. 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. Differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, other parties, 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 business in general. In addition, in regards to the information we publicly disclose regarding a particular study or clinical trial, such as topline data, you or others may not agree with what we determine is the material or otherwise appropriate information to include in such disclosure, and any information we determine not to disclose, or to disclose at a later date, such as at a medical meeting may ultimately be deemed significant with respect to future decisions, conclusions, views, activities, or otherwise regarding a particular drug, drug candidate, or our business. If the topline data that we report differ from actual results or are interpreted differently once additional data are disclosed at a later date, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our drug candidates, our business, operating results, prospects, or financial condition may be harmed or our stock price may decline.

We may not be able to obtain regulatory approvals for brensocatib, or for our other product candidates and we may not be able to receive approval for ARIKAYCE in new markets. Any such failure to obtain regulatory approvals, particularly for brensocatib, may materially adversely affect us.

We are required to obtain various regulatory approvals prior to studying our products in humans and then again before we market and distribute our products, and the failure to obtain such approvals will prevent us from commercializing our products, which would materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock. While we have obtained accelerated approval for ARIKAYCE in the US and approval in the EU and Japan, seeking regulatory approvals for brensocatib or our other product candidates as well as approval for ARIKAYCE in other jurisdictions presents significant obstacles. Approval processes in the US, Europe, Japan and other markets require the submission of extensive preclinical and clinical data, manufacturing and quality information regarding the process and facility, scientific data characterizing our product and other supporting data in order to establish safety and effectiveness. These processes are complex, lengthy, expensive, resource intensive and uncertain. Regulators will also conduct a rigorous review of any trade name we intend to use for our products. Even after they approve a trade name, these regulators may request that we adopt an alternative name for the product if adverse event reports indicate a potential for confusion with other trade names and medication error. If we are required to adopt an alternative name, potential commercialization of brensocatib or our other product candidates or commercialization of ARIKAYCE could be delayed or interrupted. We have limited experience in submitting and pursuing applications necessary to obtain these regulatory approvals.

Data submitted to regulators are subject to varying interpretations that could delay, limit or prevent regulatory agency approval. Even if we believe our clinical trial results are promising, regulators may disagree with our interpretation of data, study design or execution and may refuse to accept our application for review or decline to grant approval.

In addition, the grant of a designation by the FDA or EMA or approval by the FDA, EC or MHLW does not ensure a similar decision by the regulatory authorities of other countries, and a decision by one foreign regulatory authority does not ensure regulatory authorities in other foreign countries or the FDA will agree with the decision. For instance, although ARIKAYCE received orphan drug designation in the US, ARIKAYCE did not qualify for orphan drug designation in Japan due to the estimated number of NTM patients in Japan exceeding 50,000. Similarly, clinical studies conducted in one country may not be accepted by regulatory authorities in other countries. Approval procedures vary among countries and can involve additional product testing, including additional preclinical studies or clinical trials, and administrative review periods. The time required to obtain approval in these other territories might differ from that required to obtain FDA approval. We may never obtain approval for brensocatib or for our other product candidates in the US or other jurisdictions, or for ARIKAYCE outside of the US, Europe and Japan, which would limit our market opportunities and materially adversely affect our business. Even if brensocatib or another product candidate is approved, or if ARIKAYCE is approved outside of the US, Europe and Japan, regulators may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval.

We may also encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a product and the period required for review of any application for regulatory agency approval of a particular product. Resolving such delays could force us or third parties to incur significant costs, limit our allowed activities or the allowed activities of third parties, diminish any competitive advantages that we or our third parties may attain or adversely affect our ability to receive royalties, any of which could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

We will need to secure regulatory approval in each market for Lamira as a delivery system for ARIKAYCE. Any failures to secure separate regulatory approvals for Lamira as a delivery system will limit our ability to successfully commercialize ARIKAYCE. Additionally, we plan to submit an NDA for TPIP as a drug/device combination product or as a stand-alone marketing application, as dictated by local regulations. Failure to obtain or maintain regulatory approval or clearance of our product devices could materially harm our business.

Lamira must receive separate regulatory approval or clearance in connection with each approved product or product candidate it will be used to administer. The FDA granted accelerated approval of Lamira with ARIKAYCE as part of the approval of the drug/device combination product, and Lamira is CE marked by PARI in Europe and authorized for use by MHLW in Japan. However, outside the US, Europe and Japan, Lamira is labeled as investigational for use in our clinical trials, including in Canada and Australia, and is not approved for commercial use in Canada or certain other markets in which we may seek to commercialize ARIKAYCE in the future.

In addition, we plan to submit a marketing application for TPIP as a drug/device combination product or as a stand-alone application, as dictated by local regulations, and we will need to seek additional approvals in connection with the delivery device for TPIP in certain markets before we can market and commercialize TPIP in them.

We will continue to work closely with PARI to coordinate efforts regarding regulatory requirements, including our proposed filings. If we and PARI are not successful in obtaining approval for each usage of Lamira in each market, our ability to commercialize ARIKAYCE in those markets would be materially impaired. In addition, failure to maintain regulatory approval or clearance of Lamira could result in increased development costs, withdrawal of regulatory approval, delays or other material harm our business. Finally, failure to obtain regulatory approval or clearance of the delivery device for TPIP would affect our ability to develop and commercialize TPIP.

If our clinical studies do not produce positive results or our clinical trials are delayed, or if serious side effects are identified during drug development, we may experience delays, incur additional costs and ultimately be unable to obtain regulatory approval for and successfully commercialize our product candidates in the US, Europe, Japan or other markets.

Before obtaining regulatory approval for the sale of our product candidates, we must conduct, at our own expense, extensive preclinical tests to demonstrate the safety of our product candidates in animals, and clinical trials to demonstrate the safety and efficacy of our product candidates in humans. If we experience delays in our clinical trials or other testing or the results of these trials or tests are not positive or are only modestly positive, including with respect to safety, we may:

- Experience increased product development costs;
- Be delayed in obtaining, or be unable to obtain, regulatory approval for one or more of our product candidates;
- Obtain approval for indications or patient populations that are not as broad as intended or entirely different than those indications for which we sought approval or with labeling with boxed warnings or other warnings or contraindications;
- Need to change the way the product is administered;
- Be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- Have regulatory authorities withdraw, or suspend, their approval of the product or impose risk mitigation strategies such as restrictions on distribution or other REMS;
- Face a shortened patent protection period during which we may have the exclusive right to commercialize our products;
- Have competitors that are able to bring similar products to market before us;
- Be sued for alleged injuries caused to patients using our products; or
- Suffer reputational damage.

Such circumstances would impair our ability to commercialize our products and harm our business and results of operations.

We may not be able to enroll enough patients to conduct and complete our clinical trials or retain a sufficient number of patients in our clinical trials to generate the data necessary for regulatory approval of our product candidates or to permit the use of ARIKAYCE in the broader population of patients with MAC lung disease.

The completion rate of our clinical trials is dependent on, among other factors, the patient enrollment rate. Patient enrollment is a function of many factors, including:

- Investigator identification and recruitment;
- Regulatory approvals to initiate study sites;
- Patient population size;
- The nature of the protocol to be used in the trial;
- Patient proximity to clinical sites;
- Eligibility criteria for the trial;
- Patient willingness to participate in the trial;

- Discontinuation rates; and
- Competition from other companies' potential clinical trials for the same patient population.

Delays in patient enrollment for our clinical trials could increase costs and delay commercialization and sales, if any, of our products and, with respect to our ENCORE trial, delay or restrict our ability to commercialize ARIKAYCE in the broader population of patients with MAC lung disease. Once enrolled, patients may elect to discontinue participation in a clinical trial at any time. If patients elect to discontinue participation in our clinical trials at a higher rate than expected, we may be unable to generate the data required by regulators for approval of our product candidates.

If another party obtains orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication, we may be precluded or delayed from commercializing the product in that indication.

Under the ODA, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition. In the EU, the EMA Committee for Orphan Medicinal Products grants orphan drug designation to products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating disease or condition affecting not more than five in 10,000 people in the EU. The company that obtains the first regulatory approval from the FDA for a designated orphan drug for an indication within the designated rare disease or condition generally receives marketing exclusivity for use of that drug for that indication for a period of seven years. Similar laws exist in the EU with a term of 10 years. See Business — Government Regulation — Orphan Drug Designation in Item 1 of Part I of this Annual Report on Form 10-K for additional information. If a competitor obtains approval of the same drug for the same indication before us, and the FDA grants such orphan drug exclusivity, we would be prohibited from obtaining approval for our product for seven or more years, unless our product can be shown to be clinically superior. In addition, even if we obtain orphan exclusivity, the FDA may approve another product during our orphan exclusivity period for the same indication under certain circumstances.

Our early-stage research activities include the research and development of novel gene therapy product candidates. It will be difficult to predict the time and cost of development and of subsequently obtaining regulatory approval for any such product candidates, or how long it will take to commercialize any gene therapy product candidates.

We intend to identify and develop novel gene therapy product candidates as part of our early-stage research efforts. We have limited experience with gene therapy programs and cannot be certain that any gene therapy product candidates that we develop will successfully complete preclinical studies and clinical trials, or that they will not cause significant adverse events or toxicities. Any such results could impact our ability to develop a product candidate, including our ability to enroll patients in our clinical trials. Furthermore, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material, which could adversely affect our ability to obtain and maintain regulatory approvals for and commercialize any gene therapy products we may develop.

In addition, only a small number of gene therapy products have been approved in the US, Europe or elsewhere, and regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. We may seek regulatory approval in territories outside the US and Europe, which may have their own regulatory authorities along with frequently changing requirements or guidelines. The regulatory review committees and advisory groups in the US, Europe and elsewhere, and any new guidelines they promulgate, may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Within the FDA, the Center for Biologics Evaluation and Research (CBER) regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Therapeutic Products, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. CBER works closely with the National Institutes of Health (the NIH) to accelerate the development of gene therapy. The FDA has published guidance documents with respect to the development and approval of gene therapy products. For example, in January 2020, the FDA issued final guidance documents that updated draft guidance documents that were originally released in July 2018 to reflect recent advances in the field, and to set forth the framework for the development, review and approval of gene therapies. These final guidance documents pertain to the development of gene therapies for the treatment of specific disease categories, including rare diseases, and to manufacturing and long-term follow-up issues relevant to gene therapy, among other topics. The FDA also issued a final guidance document in September 2021 describing the FDA's approach for determining whether two gene therapy products are the same or different for the purpose of orphan-drug designation and orphan-drug exclusivity. In addition, the FDA can put an IND for a gene therapy study on clinical hold for several reasons, including if the information in an IND is not sufficient to assess the risks in study subjects.

As we advance gene therapy product candidates, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate product revenue.

Due to these factors, it is more difficult for us to predict the time and cost of gene therapy product candidate development, and we cannot predict whether the application of our approach to gene therapy, or any similar or competitive programs, will result in the identification, development and regulatory approval of any product candidates, or that the gene therapy programs of our competitors will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to gene therapy product candidates will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays and challenges in achieving sustainable, reproducible and scalable production. Any of these factors may prevent us from completing our preclinical studies or clinical trials or commercializing any gene therapy product candidates we may develop on a timely or profitable basis, if at all.

Risks Related to Our Reliance on Third Parties

We rely on third parties including collaborators, CROs, clinical and analytical laboratories, CMOs and other providers for many services that are critical to our business. If we are unable to form and sustain these relationships, or if any third-party arrangements that we may enter into are unsuccessful, including due to non-compliance by such third parties with our agreements or applicable law, our ability to develop and commercialize our products may be materially adversely affected.

We currently rely, and expect to continue to rely, on third parties for significant research, analytical services, preclinical development, clinical development and manufacturing of our product candidates and commercial scale manufacturing of ARIKAYCE and Lamira. For example, we do not own facilities for clinical-scale or commercial manufacturing of our product candidates, and we expect that our future supply requirements for brensocatib and TPIP will be manufactured by CMOs. We currently rely on Resilience to provide our clinical and commercial supply of ARIKAYCE, and intend to also rely on Patheon in the future. We currently primarily rely on Esteve Pharmaceuticals, S.A. (Esteve) and Thermo Fisher to provide our clinical supply for brensocatib. Additionally, almost all of our clinical trial work is done by CROs, such as PPD, our CRO for the ARISE, ENCORE, ASPEN, BiRCh, and TPIP trials, and clinical laboratories. In addition, we rely on third parties to manufacture clinical materials for our early-stage research programs. Reliance on these third parties poses a number of risks, including the following:

- The diversion of management time and cost of third-party advisers associated with the negotiation, documentation and implementation of agreements with third parties in the pharmaceutical industry;
- The inability to control whether third parties devote sufficient resources to our programs or products, including with respect to meeting contractual deadlines;
- The inability to control the regulatory and contractual compliance of third parties, including their quality systems, processes and procedures, systems utilized to collect and analyze data, and equipment used to test drug product and/or clinical supplies;
- The inability to establish and implement collaborations or other alternative arrangements on favorable terms;
- Disputes with third parties, including CROs, leading to loss of intellectual property rights, delay or termination of research, development, or commercialization of product candidates or litigation or arbitration;
- Contracts with our collaborators fail to provide sufficient protection of our intellectual property; and
- Difficulty enforcing our contractual rights if one of these third parties fails to perform.

We also rely on third parties to select and enter into agreements with clinical investigators to conduct clinical trials to support approval of our product candidates, and the failure of these third parties to appropriately carry out such evaluation and selection can adversely affect the quality of the data from these studies and, potentially, the approval of our products. In particular, as part of future drug approval submissions to the FDA, we must disclose certain financial interests of investigators who participated in any of the clinical studies being submitted in support of approval, or must certify to the absence of such financial interests. The FDA evaluates the information contained in such disclosures to determine whether disclosed interests may have an impact on the reliability of a study. If the FDA determines that financial interests of any clinical investigator raise serious questions of data integrity, the FDA can institute a data audit, request that we submit further data analyses, conduct additional independent studies to confirm the results of the questioned study, or refuse to use the data from the questioned study as a basis for approval. A finding by the FDA that a financial relationship of an investigator raises serious questions of data integrity could delay or otherwise adversely affect approval of our products.

These risks could materially harm our business, financial condition, results of operations and prospects and the value of our common stock.

We may not have, or may be unable to obtain, sufficient quantities of ARIKAYCE, Lamira or our product candidates to meet our required supply for commercialization or clinical studies, which would materially harm our business.

We do not have any in-house manufacturing capability other than for small-scale preclinical development programs and depend completely on a small number of third-party manufacturers and suppliers for the manufacture of our product

candidates on a clinical or commercial scale. For instance, we are and expect to remain dependent upon Resilience and eventually Patheon to supply ARIKAYCE both for our clinical trials and commercial sale. Resilience manufactures placebo for our clinical trials and our current supply of ARIKAYCE. If approved, we expect Patheon to significantly increase our ARIKAYCE manufacturing capacity. However, we may not be able to maintain adequate quantities to meet future demand, including as a result of manufacturing and/or quality issues experienced by our third-party manufacturers or higher customer demands than expected. If we encounter delays or difficulties in the manufacturing process that disrupt our ability to supply our distributors and others with ARIKAYCE or our product candidates, we may experience product stock-outs, which would likely have a material adverse effect on our business and reputation.

In addition, we have entered into certain agreements with Patheon related to increasing our long-term production capacity for ARIKAYCE commercial inventory, although Patheon's supply obligations will commence only after certain technology transfer and construction services are completed. Any delay in the commencement of Patheon's supply obligations, whether due to delays in technology transfer and construction or from adding Patheon to our NDA as a CMO, would increase the risks associated with Resilience being unable to provide us with an adequate supply of ARIKAYCE.

We are also dependent upon PARI being able to provide an adequate supply of nebulizers for commercial sale of ARIKAYCE, any ongoing clinical trials, and future commercial sales of our product candidates that use Lamira as their delivery mechanism, as PARI is the sole manufacturer of Lamira. We have no alternative supplier for the nebulizer, and because significant effort and time were expended in the optimization of the nebulizer for use with ARIKAYCE, we do not intend to seek an alternative or secondary supplier. In the event PARI cannot provide us with sufficient quantities of the nebulizer, replication of the optimized device by another party would likely require considerable time and additional regulatory approval. In the case of certain specified supply failures, we have the right under our commercialization agreement with PARI to make the nebulizer and have it made by certain third parties, but not those deemed under the commercialization agreement to compete with PARI.

We also anticipate that we will be reliant on CMOs to manufacture supply of brensocatib and TPIP for our future requirements. Esteve and Thermo Fisher manufacture our current clinical supply of brensocatib. We plan to enter into commercial agreements with CMOs for brensocatib and TPIP, and cannot guarantee that we will be able to locate adequate partners or enter into favorable agreements with them.

We are in the process of developing in-house clinical manufacturing capability for our gene therapy product candidates, but we expect to rely on third-party CMOs for manufacturing of all testing materials for the foreseeable future. Products intended for use in gene therapies are novel, complex and difficult to manufacture. As we shift towards in-house clinical manufacturing capability for our gene therapy product candidates, we may encounter delays in obtaining regulatory approval of our manufacturing processes or in complying with ongoing manufacturing regulatory requirements and applicable cGMP, including challenges related to producing adequate quantities of clinical grade materials that meet FDA, EMA, MHLW or other applicable standards or specifications with consistent and acceptable production yields and costs.

We do not have long-term commercial agreements with all of our suppliers and if any of our suppliers are unable or unwilling to perform for any reason, we may not be able to locate suppliers or enter into favorable agreements with them.

An inadequate supply of ARIKAYCE, Lamira, brensocatib or our other product candidates would likely harm our commercial efforts or delay or impair clinical trials of ARIKAYCE or our product candidates and adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

The manufacturing facilities of our third-party manufacturers are subject to significant government regulations and approvals, which are often costly and could result in adverse consequences to our business if we and our manufacturing partners fail to comply with the regulations or maintain the approvals.

Manufacturers of ARIKAYCE, Lamira and our product candidates are subject to cGMP, Quality System Regulations and similar standards. While we have policies and procedures in place to select third-party manufacturers for our product and product candidates that adhere, and monitor their adherence to, such standards, they may nonetheless fail to do so. Similarly, while we have entered into a Commercialization Agreement with PARI for the manufacture of Lamira for use with ARIKAYCE, PARI may fail to adhere to applicable standards. These manufacturers and their facilities will be subject to periodic review and inspections by the FDA and other regulatory authorities following regulatory approval of our products, as with ARIKAYCE. For instance, to monitor compliance with applicable regulations, the FDA routinely conducts inspections of facilities and may identify potential deficiencies. The FDA issues what are referred to as "Form 483s" that set forth observations and concerns identified during its inspections. Failure to satisfactorily address the concerns or potential deficiencies identified in a Form 483 could result in the issuance of a warning letter, which is a notice of the issues that the FDA believes to be significant regulatory violations requiring prompt corrective actions. Failure to respond adequately to a warning letter, or to otherwise fail to comply with applicable regulatory requirements could result in enforcement, remedial and/or punitive actions by the FDA or other regulatory authorities.

If one of these manufacturers fails to maintain compliance with regulatory requirements or experiences supply problems, including in the scale-up of commercial production, the production of ARIKAYCE, Lamira, brensocatib and our other product candidates could be interrupted, resulting in delays, additional costs or restrictions on the marketing or sale of our products. An alternative manufacturer would need to be qualified, through regulatory filings, which could result in further delay. The regulatory authorities may also require additional testing if a new manufacturer is relied upon for commercial production. In addition, with respect to our product candidates, our manufacturers and their facilities are subject to pre-approval cGMP inspection by the FDA and other regulatory authorities, and the findings of the cGMP inspection could result in a failure to obtain, or a delay in obtaining, regulatory approval for future product candidates.

Risks Related to the Operation of our Business

We are dependent upon retaining and attracting key personnel, the loss of whose services could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

We depend heavily on our management team and our principal clinical and commercial personnel, the loss of whose services might significantly delay or prevent the achievement of our research, development or commercialization objectives. Our success depends, in large part, on our ability to attract and retain qualified management, clinical and commercial personnel, including those who join us through our business development activities, and on our ability to develop and maintain important relationships with commercial partners, leading research institutions and key distributors.

Competition for skilled personnel in our industry and market is intense because of the numerous pharmaceutical and biotechnology companies that seek similar personnel. These companies may have greater financial and other resources, offer a greater opportunity for career advancement and have a longer history in the industry than we do. We also experience competition for the hiring of our clinical and commercial personnel from universities, research institutions, and other third parties. We cannot assure that we will attract and retain such persons or maintain such relationships. Our inability to retain and attract qualified employees would materially harm our business, financial condition, results of operations and prospects and the value of our common stock.

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

In connection with our commercialization of ARIKAYCE in the US, Europe and Japan, our continued international expansion efforts, and our ongoing development and planned commercialization of brensocatib, TPIP and other product candidates, we expect to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, quality, commercial compliance, medical affairs, and sales and marketing. For example, we plan to continue to hire additional personnel to support ARIKAYCE, the continued development and anticipated commercialization of brensocatib and the advancement of our other pipeline programs. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to the limited experience of our management team in managing a company with this anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. We may not be able to effectively manage the expansion of our operations, which could delay the execution of our business plans or disrupt our operations.

Any acquisitions we make, or collaborative relationships we enter into, may not be clinically or commercially successful, and may require financing or a significant amount of cash, which could adversely affect our business.

As part of our business strategy, we may effect acquisitions to obtain additional businesses, products, technologies, capabilities and personnel. For example, we acquired Motus and AlgaeneX in August 2021, Vertuis in January 2023, and Adrestia in June 2023, each a privately-held, preclinical stage company. Acquisitions involve a number of operational risks, including:

- Failure to achieve expected synergies;
- The possibility that our acquired technologies, products and product candidates may not be commercially successful;
- Difficulty and expense of assimilating the operations, technology and personnel of any acquired business;
- The inability to retain the management, key personnel and other employees of any acquired business;
- The inability to maintain any acquired company’s relationship with key third parties, such as alliance partners;
- Exposure to legal claims or other liabilities for activities of any acquired business prior to acquisition;
- Diversion of our management’s attention from our core business; and
- Potential impairment of intangible assets, adversely affecting our reported results of operations and financial condition.

We also may enter into collaborative relationships that would involve our collaborators conducting proprietary development programs. Disagreements with collaborators may develop over the rights to our intellectual property, and any conflict with our collaborators could limit our ability to obtain future collaboration agreements and negatively influence our relationship with existing collaborators.

If we make one or more significant acquisitions or enter into a significant collaboration in which the consideration includes cash, we may be required to use a substantial portion of our available cash and/or need to raise additional capital, which could adversely affect our financial condition.

We may be subject to product liability claims, and we have only limited product liability insurance.

The manufacture and sale of human therapeutic products involve an inherent risk of product liability claims, particularly as we now commercialize ARIKAYCE in the US, Europe and Japan. Regardless of merit or eventual outcome, liability claims may result in:

- Decreased demand for ARIKAYCE and any other products that we may commercialize, and a corresponding loss of revenue;
- Substantial monetary awards to patients or trial participants;
- Significant time and costs to defend the related litigation;
- Withdrawal or reduced enrollment of clinical trial participants; and
- Reputational harm and significant negative media attention.

We currently have only limited product liability insurance for our products. We do not know if we will be able to maintain existing, or obtain additional, product liability insurance on acceptable terms or with adequate coverage against potential liabilities. This type of insurance is expensive and may not be available on acceptable terms. If we are unable to obtain or maintain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to commercialize our products. A successful product liability claim brought against us in excess of our insurance coverage, if any, may require us to pay substantial amounts and may materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our business and operations, including our drug development and commercialization programs, could be materially disrupted in the event of system failures, security breaches, cyber-attacks, deficiencies in cybersecurity, violations of data protection laws or data loss or damage by us or third parties.

We are dependent upon information technology systems, infrastructure, and data to operate our business. In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers, as well as personally identifiable information of clinical trial participants, patients and employees. Despite the implementation of security measures, our internal computer systems and those of our CROs, CMOs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such an event could have a material adverse effect on our business operations, including a material disruption of our drug development and commercialization programs.

It is critical that we maintain such confidential information in a manner that preserves its confidentiality and integrity. Unauthorized disclosure of sensitive or confidential patient or employee data, including personally identifiable information, whether through breach of computer systems, systems failure, employee negligence, fraud or misappropriation, or otherwise, or unauthorized access to or through our information systems and networks, whether by our employees or third parties, could result in negative publicity, legal liability and damage to our reputation. Unauthorized disclosure of personally identifiable information could also expose us to sanctions for violations of data privacy laws and regulations around the world. In addition, the loss of clinical trial data for our product candidates could result in delays in our regulatory submission and approval efforts and significantly increase our costs to recover or reproduce the data, if possible. To the extent that any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed. For example, the loss of or damage to clinical trial data, such as from completed or ongoing clinical trials, for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our drug candidates or any future drug candidates and to conduct clinical trials, and similar events relating to their systems and operations could also have a material adverse effect on our business and lead to regulatory agency actions.

We have previously been, and expect to remain, the target of cyber-attacks. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist

organizations, or hostile foreign governments or agencies. Notifications and follow-up actions related to a security incident could impact our reputation or cause us to incur substantial costs, including legal and remediation costs, in connection with these measures and otherwise in connection with any actual or suspected security breach. Although we have general liability insurance coverage, including coverage for errors and omissions and potential cyber security breaches, our insurance may not cover all claims, continue to be available on reasonable terms or be sufficient in amount to cover one or more large claims; additionally, the insurer may disclaim coverage as to any claim. The successful assertion of one or more large claims against us that exceed or are not covered by our insurance coverage or changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

We are subject to data privacy laws and regulations that govern how we can collect, process, store, and transfer personal data.

Laws and regulations governing personal data continue to develop at a rapid pace, and jurisdictions around the world continue to propose new legislation and rules. For example, a number of US states have passed consumer privacy laws or consumer health data laws. Other jurisdictions outside of the US either have data protection laws in place or continue to advance proposals for similar legislation and regulation. These laws place restrictions on how we collect, use, and transfer personal data, and they result in increased compliance and operational costs. Noncompliance with data protection laws and regulations can result in meaningful penalties, enforcement, and/or reputational harm and have a significant impact on our operations.

Our inability to access, upgrade or expand our technology systems or difficulties in updating our existing technology or developing or implementing new technology could have a material adverse effect on our business or results of operations.

We have and will continue to expand, upgrade and develop our information technology capabilities, including our enterprise resource planning system, which was implemented through Oracle software in 2022, and a new enterprise-wide human capital management system, Workday, expected to be implemented in 2024. If we are unable to successfully continue upgrading or expanding our technological capabilities to support our growth or if there are deficiencies in the design or implementation of such capabilities, we may not be able to take advantage of market opportunities, manage our costs effectively, manage our inventory, maintain a secure data environment, file timely reports with the SEC, or otherwise efficiently manage our internal controls. In addition, costs, potential problems and interruptions associated with the implementation of new or upgraded systems and technology, or with maintenance or adequate support of existing systems, could also disrupt or reduce the efficiency of our operations. Moreover, many of our vendors provide their services to us via a cloud-based model instead of software that is installed on our premises. As a result, we depend upon our vendors to provide us with services that are always available and are free of errors or defects that could cause disruptions in our business processes. Any failure by such vendors to do so, or any disruption in our ability to access the Internet, could materially and adversely affect our ability to manage our operations.

We have limited experience operating internationally, are subject to a number of risks associated with our international activities and operations and may not be successful in our efforts to expand internationally.

We currently have limited operations outside of the US. As of December 31, 2023, we had 124 employees located in Europe and 85 employees located in Japan, although we have clinical trial sites and suppliers located around the world. In order to meet our long-term goals, we expect to grow our international operations over the next several years, including in Europe and Japan, and continue to source material used in the manufacture of our product candidates from abroad. Consequently, we are and will continue to be subject to risks related to operating in foreign countries, including:

- Limited experience with international regulatory requirements;
- An inability to achieve optimal pricing and reimbursement for ARIKAYCE, if approved in another jurisdiction, or subsequent changes in reimbursement, pricing and other regulatory requirements;
- Any implementation of, or changes to, tariffs, trade barriers and other import-export regulations in the US or other countries in which we, or our third-party partners, operate;
- Unexpected AEs related to ARIKAYCE or our product candidates occurring in foreign markets that we have not experienced in the US, Europe or Japan;
- Scrutiny from customers, regulators, investors and other stakeholders related to environmental, health and safety, diversity, labor conditions, human rights and other concerns in the countries in which we, or our third-party partners, operate;
- Economic and political conditions, including foreign currency fluctuations and inflation, could result in reduced revenue, increased or unpredictable operating expenses and other obligations incident to doing business in, or with a company located in, another country;
- Geopolitical events, such as conflicts, war and terrorism, could cause disruptions in our international operations, including planned or ongoing clinical studies; and

- Compliance with foreign or US laws, rules and regulations, including data privacy requirements, labor relations laws, tax laws, anti-competition regulations, import, export and trade restrictions, anti-bribery/anti-corruption laws, regulations or rules, which could lead to actions by us or our distributors, manufacturers, other third parties who act on our behalf or with whom we do business in foreign countries or our employees who are working abroad that could subject us to investigation or prosecution under such foreign or US laws.

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

We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully.

Biotechnology and related pharmaceutical technology have undergone and are likely to continue to experience rapid and significant change. Our future success will depend in large part on our ability to maintain a competitive position with respect to these technologies and to obtain and maintain protection for our intellectual property. Compounds, products or processes that we develop may become obsolete before we recover any expenses incurred in connection with their development. We face substantial competition from pharmaceutical, biotechnology and other companies, universities and research institutions with respect to NTM lung disease, bronchiectasis, PAH and PH-ILD, and will face substantial competition with respect to future product candidates we may develop in these and other disease areas. Relative to us, most of these entities have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical studies, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products. Many of our competitors may achieve product commercialization or obtain patent protection earlier than us. Furthermore, we believe that our competitors have used, and may continue to use, litigation to gain a competitive advantage. Our competitors may also use different technologies or approaches to develop products similar to ARIKAYCE, brensocatib, TPIP and our preclinical product candidates.

We expect that competing successfully will depend on, among other things, the relative speed with which we can develop products, complete the clinical testing and regulatory approval processes and supply commercial quantities of the product to the market, as well as product efficacy, safety, reliability, availability, timing and scope of regulatory approval and price. We expect competition to increase as technological advances are made and commercial applications broaden. There are potential competitive products, both approved and in development, which include oral, systemic, or inhaled antibiotic products to treat chronic respiratory infections. For instance, certain entities have expressed interest in studying their products for lung disease and are seeking to advance studies in lung disease, including NTM lung disease caused by mycobacterial species other than MAC. We are not aware of any entities currently conducting clinical trials for the treatment of refractory MAC lung disease or of any other approved inhaled therapies specifically indicated for NTM lung disease in North America, Europe or Japan. If any of our competitors develops a product that is more effective, safe, tolerable or convenient, or less expensive than ARIKAYCE or our product candidates, it would likely materially adversely affect our ability to generate revenue. We also may face lower priced generic competitors if third-party payors encourage use of generic or lower-priced versions of our product or if competing products are imported into the US or other countries where we may sell ARIKAYCE. In addition, in an effort to put downward pressure on drug pricing, Congress and the FDA are working to facilitate generic competition, which could result in our experiencing competition earlier than otherwise would be the case.

There are also other amikacin products that have been approved by the FDA, MHLW and other regulatory agencies for use in other indications, and physicians may elect to prescribe those products rather than ARIKAYCE to treat the indications for which ARIKAYCE has received approval, which is commonly referred to as off-label use. Although regulations prohibit a drug company from promoting off-label use of its product, the FDA and other regulatory agencies do not regulate the practice of medicine and cannot direct physicians as to what product to prescribe to their patients. As a result, we would have limited ability to prevent any off-label use of a competitor's product to treat diseases for which we have received FDA or other regulatory agency approval, even if this use violates our patents or any statutory exclusivities that the FDA may grant for the use of amikacin to treat such diseases.

In addition, based in part on our successful phase 2 Willow trial in bronchiectasis, certain entities have expressed interest in studying other DPP1 inhibitors for the treatment of bronchiectasis. We are aware of at least two entities currently conducting clinical trials for the treatment of bronchiectasis with a DPP1 inhibitor. If any of these competitors develops a DPP1 inhibitor product that is more effective, safe, tolerable or convenient, it would likely materially adversely affect our ability to generate revenue, should brensocatib ultimately be approved. If we are unable to compete successfully, it will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

We have a limited number of significant customers and losing any of them could have an adverse effect on our financial condition and results of operations.

Our three largest customers as of December 31, 2023 accounted for 88% and 90% of our total gross product revenue for the years ended December 31, 2023 and 2022, respectively. The degree to which a limited number of customers make up a

significant portion of our gross product revenue may change as we continue to commercialize ARIKAYCE and, if approved, our product candidates in additional markets. There can be no guarantee that we will be able to sustain our accounts receivable or gross sales levels from our key customers. If, for any reason, we were to lose, or experience a decrease in the amount of business with our largest customers, whether directly or through our distributor relationships, our financial condition and results of operations could be negatively affected.

Deterioration in general economic conditions in the United States, Europe, Japan and globally, including the effect of prolonged periods of inflation on our suppliers, third-party service providers and potential partners, could harm our business and results of operations.

Our business and results of operations could be adversely affected by changes in national or global economic conditions. These conditions include but are not limited to inflation, rising interest rates, limited availability of financing, energy availability and costs, the negative impacts caused by the COVID-19 pandemic and other public health crises, negative impacts resulting from the military conflict between Russia and the Ukraine or the ongoing conflict in the Middle East, relations between the US and China, and the effects of governmental initiatives to manage economic conditions. Impacts of such conditions could be passed on to our business in the form of higher costs for labor and materials, possible reductions in pharmaceutical industry-wide spending on research and development and acquisitions and higher costs of capital.

The resurgence of the COVID-19 pandemic or emergence of another pandemic, and efforts to reduce its spread, could negatively impact our business and operations.

Our global operations expose us to risks associated with public health crises and pandemics, including COVID-19, particularly as the patients we seek to treat suffer from serious and rare diseases that may make them especially vulnerable. A pandemic, including a resurgence of COVID-19, may also have an adverse impact on our operations and supply chain as a result of (i) our or our third-party manufacturers' employees or other key personnel becoming infected, (ii) preventive and precautionary measures that governments and we and other businesses, including our third-party manufacturers, are taking, such as border closures, prolonged quarantines and other travel restrictions, (iii) shortages of supplies necessary for the manufacture of ARIKAYCE, including as a result of government orders providing for the requisition of personal protective equipment and other medical supplies and equipment, and (iv) cold-chain storage and shipping limitations resulting from the need to prioritize delivery of one or more COVID-19 vaccines, which could cause disruptions or delays in our ability to distribute ARIKAYCE due to lack of sufficient cold-chain storage and shipping capacity. Any of these circumstances could impact the ability of third parties on which we rely to manufacture ARIKAYCE or its components and our ability to perform critical functions, which could significantly hamper our ability to supply ARIKAYCE to patients. While we have experienced no disruption to date in our supply chain due to the COVID-19 pandemic, if we encounter delays or difficulties in the manufacturing process that disrupt our ability to supply ARIKAYCE, we may not be able to satisfy patient demand or we may experience a product stock-out, which would likely have a material adverse effect on our business.

A resurgence of the COVID-19 pandemic or another pandemic could also require us to delay the start of new clinical trials or otherwise impair our ability to complete those trials. For instance, our ability to enroll patients and retain principal investigators and site staff could be impaired due to an outbreak in their geography or prioritization of hospital resources toward the outbreak, or as a result of quarantines and other travel restrictions that interrupt healthcare services. Furthermore, patients, investigators, or site staff may be unwilling or unable to comply with clinical trial protocols due to illness, concerns about a pandemic, or quarantines or other travel restrictions that impede their movement. Additionally, any interruption in the supply of the study drug might delay our ability to start or complete clinical trials. Significant delays in the timing and completion of our clinical trials are costly and could adversely affect our ability to satisfy our post-marketing requirements for ARIKAYCE and to obtain regulatory approval for and to commercialize our product candidates.

Our current and potential future use of artificial intelligence (AI) and machine learning may not be successful and presents new risks and challenges to our business.

We currently integrate AI and machine learning in certain of our research and development activities, including identification of potential product candidates, and are seeking to further integrate AI and machine learning throughout our business. We are exploring additional opportunities to incorporate AI and machine learning into our processes for drug discovery, drug development, drug commercialization, and in connection with our enabling functions. For example, we are currently evaluating the use of AI to produce initial drafts of documents like clinical study reports. Such efforts may not be successful. Issues relating to the use of new and evolving technologies such as AI and machine learning may cause us to experience brand or reputational harm, competitive harm, legal liability, and new or enhanced governmental or regulatory scrutiny, and we may incur additional costs to resolve such issues.

As with many innovations, AI presents risks and challenges that could undermine or slow its adoption, and therefore harm our business. Developing, testing and deploying AI systems may also increase our operating costs due to the nature of the computing costs involved in such systems, which could adversely affect our business, financial condition and results of

operation. The use of AI by us and our business partners may lead to novel and urgent cybersecurity risks, which could have a material adverse effect on our operations and reputation as well as the operations of any of our business partners. We may also face increased competition from other companies that are using AI, some of whom may develop more effective methods than we and any of our business partners have, which could have a material adverse effect on our business, results of operations, or financial condition. In addition, our efforts to develop, acquire or integrate these technologies will involve significant time, costs, and other resources, and may divert our management team's attention and focus from executing on other elements of our strategy. Furthermore, uncertainties regarding developing legal and regulatory requirements and standards may require significant resources to modify and maintain business practices to comply with US and non-US laws concerning the use of AI, the nature of which cannot be determined at this time.

Risks Related to Our Intellectual Property

If we are unable to protect our intellectual property rights adequately, the value of ARIKAYCE and our product candidates could be materially diminished.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal, technical, scientific and factual questions, and our success depends in large part on our ability to protect our proprietary technology and to obtain and maintain patent protection for our products, prevent third parties from infringing our patents, both domestically and internationally. We have sought to protect our proprietary position by filing patent applications in the US and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing products and technologies.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection or otherwise provide us with any competitive advantage. Any conclusions we may reach regarding non-infringement, inapplicability or invalidity of a third party's intellectual property vis-à-vis our proprietary rights, or those of a licensor, are based in significant part on a review of publicly available databases and other information. There may be information not available to us or otherwise not reviewed by us that could render these conclusions inaccurate. Our competitors may also be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

Additionally, patents issued to us or our licensors may be challenged, narrowed, invalidated, held to be unenforceable or circumvented through litigation, either in district court, the US international trade commission (ITC) or US patent office (USPTO), or in analogous foreign courts and patent offices, which could limit our ability to stop competitors from marketing similar products or reduce the term of patent protection for ARIKAYCE or our product candidates. US patents and patent applications may also be subject to interference or derivation proceedings, and US patents may be subject to re-examination proceedings, reissue, post-grant review and/or *inter partes* review in the USPTO. Our foreign patents have been and may be in the future subject to opposition or comparable proceedings in the corresponding foreign patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. See *Intellectual Property—ARIKAYCE Patents* in Item 1 of Part I of this Annual Report on Form 10-K for more information on our European patents that have been previously opposed.

Changes in either patent laws or in interpretations of patent laws in the US and other countries may also diminish the value of our intellectual property or narrow the scope of our patent protection, including making it easier for competitors to challenge our patents. For example, the America Invents Act included a number of changes to established practices, including the transition to a first-inventor-to-file system and new procedures for challenging patents and implementation of different methods for invalidating patents.

If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of ARIKAYCE and our product candidates could be materially diminished.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality and restrictive covenant agreements with our employees, consultants, advisors, collaborators, and other third parties and partners to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information or may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, third parties may independently develop or discover our trade secrets and proprietary information. Regulators also may disclose information we consider to be proprietary to third parties under certain circumstances, including in response to third-party requests for such disclosure under the Freedom of Information Act or comparable laws. Additionally, the FDA, as part of its Transparency Initiative, continues to consider whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the

present time whether and how the FDA's disclosure policies may change in the future. Further, several states have limited or prohibited the use of post-employment non-compete agreements and the Federal Trade Commission is evaluating a federal-level prohibition on such agreements, which could increase the difficulty of protecting trade secrets and other proprietary information. There are similar risks outside the US, such as the risk that a foreign regulatory agency would make available information we consider to be proprietary to third parties or the public, and the risks arising from other factors making it difficult to protect trade secrets, such as prohibitions or restrictions on post-employment non-compete agreements and other rules and regulations.

We may not be able to enforce our intellectual property rights throughout the world, which could harm our business.

The legal systems of some foreign countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. Many companies have encountered significant problems in protecting and defending intellectual property rights in such foreign jurisdictions. For example, certain foreign countries have compulsory licensing laws under which a patent owner may be required to grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. This legal environment could make it difficult for us to stop the infringement of our patents or in-licensed patents or the misappropriation of our other intellectual property rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, and our efforts to protect our intellectual property rights in such countries may be inadequate.

The drug research and development industry has a history of intellectual property litigation, and we could become involved in costly intellectual property disputes, which could delay or impair our product development efforts or prevent us from, or increase the cost of, commercializing ARIKAYCE or any other approved product candidate.

Third parties may claim that we have infringed upon or misappropriated their proprietary rights. Any existing third-party patents, or patents that may later issue to third parties, could negatively affect our commercialization of ARIKAYCE, brensocatib, TPIP, or any other product candidate that receives regulatory approval. For instance, PAH is a competitive indication with established products, including other formulations of treprostinil. Our supply of treprostinil palmitil, the treprostinil prodrug present in TPIP, is dependent upon a single supplier. The supplier owns patents on its manufacturing process and crystalline drug product, and we have filed patent applications for TPIP; however, a competitor in the PAH indication may claim that we or our supplier have infringed upon or misappropriated its proprietary rights. Moreover, in the event that we pursue approval of TPIP, or any other product candidate, via the 505(b)(2) regulatory pathway, we will be required to file a certification of non-infringement or invalidity against any unexpired patents listed in the Orange Book for the third-party drug we reference as part of our regulatory submission. This certification process may lead to litigation and could also delay launch of a product candidate, if approved by regulators.

In the event of successful litigation or settlement of claims against us for infringement or misappropriation of a third party's proprietary rights, we may be required to take actions including but not limited to the following:

- Paying damages, including up to treble damages, royalties, and the other party's attorneys' fees, which may be substantial;
- Ceasing development, manufacture, marketing and sale of products or use of processes that infringe the proprietary rights of others;
- Expending significant resources to redesign our products or our processes so that they do not infringe the proprietary rights of others, which may not be possible, or may result in significant regulatory delays associated with conducting additional clinical trials or other steps to obtain regulatory approval; and/or
- Acquiring one or more licenses from third parties, which may not be available to us on acceptable terms or at all.

We may also have to undertake costly litigation or engage in other proceedings, such as interference or *inter partes* review, to enforce or defend the validity of any patents issued or licensed to us, to confirm the scope and validity of our or a licensor's proprietary rights or to defend against allegations that we have infringed a third party's intellectual property rights. Any proceedings regarding our intellectual property rights are likely to be time consuming and may divert management attention from operation of our business, and could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

Certain of the agreements to which we are, or may become, a party relating to ARIKAYCE and our product candidates impose, or may in the future impose, restrictions on our business or other material obligations on us. If we fail to comply with these obligations, our business could be adversely affected, including as a result of the loss of license rights that are important to our business.

We are a party to various agreements related to ARIKAYCE and our product candidates, including licensing agreements with PARI and AstraZeneca, which we view as material to our business. For additional information regarding the

terms of these agreements, see *Business—License and Other Agreements* in Item 1 of Part I of this Annual Report on Form 10-K. These agreements impose a number of obligations on us and our business, including restrictions on our ability to freely develop or commercialize our product candidates and requirements to make milestone and royalty payments to our counterparties upon certain events. For example, under our license agreement with AstraZeneca, AstraZeneca retains a right of first negotiation pursuant to which it may exclusively negotiate with us before we can negotiate with a third party regarding any transaction to develop or commercialize brensocatib, subject to certain exceptions. While this right of first negotiation is not triggered by a change of control, it may impede or delay our ability to consummate certain other transactions involving brensocatib.

If we fail to comply with our obligations under these agreements, our counterparties may have the right to take action against us, up to and including termination of a relevant license. For instance, under our license agreement with AstraZeneca, AstraZeneca may terminate our license to brensocatib if we fail to use commercially reasonable efforts to develop and commercialize a product based on brensocatib, or we are subject to a bankruptcy or insolvency. Reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms and may materially harm our business.

Risks Related to Government Regulation

Government healthcare reform could materially increase our costs, which could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our industry is highly regulated and changes in or revisions to laws and regulations that make gaining regulatory approval, reimbursement and pricing more difficult or subject to different criteria and standards may adversely impact our business, operations or financial results.

There have been a number of legal challenges and certain changes to the ACA since it was enacted. On January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including, among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. It is unclear how the Supreme Court ruling, other such litigation and the healthcare reform measures of the Biden Administration will impact the ACA. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. The Biden Administration has also indicated that lowering prescription drug prices is a priority, and the IRA was signed into law on August 16, 2022. See Reimbursement of Pharmaceutical Products in Item 1 of Part I of this Annual Report on Form 10-K for more information. Changes to the ACA, to the Medicare or Medicaid programs, or to the ability of the federal government to negotiate or otherwise affect drug prices, or other federal legislation regarding healthcare access, financing or legislation in individual states, could affect our business, financial condition, results of operations and prospects and the value of our common stock. We may face similar challenges to gaining regulatory approval and sufficient reimbursement and pricing due to government healthcare reform in the EU, Japan and other jurisdictions where ARIKAYCE or any of our other product candidates are approved. It remains unclear how any new legislation or regulation might affect the prices we may obtain for ARIKAYCE or any of our product candidates for which regulatory approval is obtained.

If we are found in violation of federal or state "fraud and abuse" laws, we may be required to pay a penalty or may be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

In the US, we are subject to various federal and state healthcare "fraud and abuse" laws, including anti-kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state healthcare programs. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under these laws. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the US government, and our business, financial condition, results of operations and prospects and the value of our common stock may be adversely affected. Our reputation could also suffer. In addition, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act as well as under the false claims laws of several states.

Under the ACA and certain state laws, we are required to report information on payments or transfers of value to any US physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, or certified nurse-midwives (in each case who are not bona fide employees of the applicable manufacturer that is reporting the

payment) and teaching hospitals, which is posted in searchable form on a public website. Failure to submit required information may result in civil monetary penalties.

Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. In addition to the federal government, some states, as well as other countries, including France, require the disclosure of certain payments to healthcare professionals. The Health Insurance Portability and Accountability Act of 1996 (HIPAA), state, and foreign privacy laws may limit access to information identifying those individuals who may be prospective users or limit the ability to market to them. Some of these laws are new or ambiguous as to what is required to comply with their requirements, and we could be subject to penalties if it is determined that we have failed to comply with an applicable legal requirement.

We are subject to anti-corruption laws and trade control laws, as well as other laws governing our operations. If we fail to comply with these laws, we could be subject to negative publicity, civil or criminal penalties, other remedial measures, and legal expenses, which could adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our operations are subject to anti-corruption laws, including the US Foreign Corrupt Practices Act (FCPA), the UK Bribery Act and other anti-corruption laws that apply in countries where we do business. The FCPA, UK Bribery Act and these other laws generally prohibit us, our employees and our intermediaries from making prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We have conducted various studies at a broad range of trial sites around the world. Certain of these jurisdictions pose a risk of potential FCPA violations, and we have relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the US Department of Commerce's Bureau of Industry and Security, the US Department of Treasury's Office of Foreign Assets Control, and various non-US government entities, including applicable export control regulations, economic sanctions on countries and persons, customs requirements, currency exchange regulations and transfer pricing regulations (collectively, Trade Control laws).

We may not be effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and prospects and the value of our common stock. Likewise, even an investigation by US or foreign authorities of potential violations of the FCPA other anti-corruption laws or Trade Control laws could have an adverse impact on our reputation, business, financial condition, results of operations and prospects and the value of our common stock.

Our research, development and manufacturing activities used in the production of ARIKAYCE and our product candidates involve the use of hazardous materials, which could expose us to damages, fines, penalties and sanctions and materially adversely affect our results of operations and financial condition.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development program and manufacturing activities for ARIKAYCE and our product candidates involve the controlled use of hazardous materials and chemicals. We generally contract with third parties for the disposal of these materials and wastes.

Although we strive to comply with all pertinent regulations, the risk of environmental contamination, damage to facilities or injury to personnel from the accidental or improper use or control of these materials remains. In addition to any liability we could have for any misuse by us of hazardous materials and chemicals, we could also potentially be liable for activities of our CMOs or other third parties. Any such liability, or even allegations of such liability, could materially adversely affect our results of operations and financial condition. We also could incur significant costs as a result of civil or criminal fines and penalties.

In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

The ability of the FDA to review and approve new products, provide feedback on clinical trials and development programs, meet with sponsors and otherwise review regulatory submissions can be affected by a variety of factors, including government budget and funding levels; ability to hire and retain key personnel and accept the payment of user fees; and statutory, regulatory, and policy changes, among other factors. Average review times at the agency may fluctuate as a result. In addition, government funding of other government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies or to otherwise respond to regulatory submissions, which would adversely affect our business. For example, over the last several years, the US government has shut down multiple times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Our Financial Condition and Need for Additional Capital

We have a history of operating losses, expect to incur operating losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred losses each previous year of our operation, except in 2009, when we sold our manufacturing facility and certain other assets to Merck & Co, Inc. As of December 31, 2023, our accumulated deficit was $3.4 billion. For the years ended December 31, 2023, 2022 and 2021, our consolidated net loss was $749.6 million, $481.5 million and $434.7 million, respectively. Our ability to generate revenue depends on the success of commercial sales of ARIKAYCE; however, we do not anticipate our revenue from the sale of ARIKAYCE will be sufficient for us to become profitable without reductions in our operating expenses. Despite our commercialization of ARIKAYCE in the US, Europe and Japan, we expect to continue to incur substantial operating expenses, and resulting operating losses, for the foreseeable future as we:

- Initiate or continue clinical studies of our product candidates, including our Phase 3 ASPEN trial;
- Complete a post-marketing clinical trial of ARIKAYCE, consisting of the ARISE and ENCORE trials, as required by the FDA;
- Seek to discover or in-license additional product candidates;
- Support the sales and marketing efforts necessary for the continued commercialization of ARIKAYCE;
- Scale-up manufacturing capabilities for future ARIKAYCE production, including the increase of production capacity at Patheon and process improvements in order to manufacture at a larger commercial scale;
- Seek the approval and potential commercial launch of brensocatib in the US and other markets;
- Seek the approval and potential commercial launch of TPIP and other product candidates in various markets;
- File, prosecute, defend, and enforce patent claims related to ARIKAYCE, brensocatib, TPIP and our other product candidates; and
- Enhance operational, compliance, financial, quality and information management systems and hire more personnel, including personnel to support our commercialization efforts and development of our product candidates.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We may need to raise additional funds to continue our operations, but we face uncertainties with respect to our ability to access capital.

Our operations have consumed substantial amounts of cash since our inception. We expect to expend substantial financial resources to commercialize ARIKAYCE, fund the Phase 3 ASPEN trial and the confirmatory post-marketing ARISE and ENCORE trials, seek full regulatory approval for ARIKAYCE as well as continue research and development of brensocatib and TPIP, as well as our future product candidates, and fund pre-commercialization activities for brensocatib. We may need to raise additional capital to fund these activities, including due to changes in our product development plans or misjudgment of expected costs, to fund corporate development, to maintain our intellectual property portfolio or for other purposes, including to resolve litigation. Our operating expenses and long-term investments were significantly higher in 2023 than in 2022, reflecting our continued investment in the build-out of our commercial organization to support global expansion activities for ARIKAYCE and manufacture of commercial inventory, which includes capital and long-term investments, and continued investment in research and development as well as selling, general and administrative expenses. We do not know whether additional financing will be available when needed, or, if available, whether the terms will be favorable. If adequate funds are not available to us when needed, we may be forced to delay, restrict or eliminate all or a portion of our development programs or commercialization efforts.

We have outstanding indebtedness in the form of convertible senior notes, a term loan and a royalty financing arrangement and may incur additional indebtedness in the future, which could adversely affect our financial position, prevent us from implementing our strategy, and dilute the ownership interest of our existing shareholders.

In October 2022, we entered into a loan agreement (the Loan Agreement) with certain funds managed by Pharmakon and a revenue interest purchase agreement (the Royalty Financing Agreement) with OrbiMed.

The Loan Agreement provides for a $350 million senior secured term loan (the Term Loan) that matures on October 19, 2027. The Term Loan bears interest at a rate based upon the secured overnight financing rate (SOFR), subject to a SOFR floor of 2.5%, in addition to a margin of 7.75% per annum. Up to 50% of the interest payable during the first 24 months from the closing of the Term Loan may be paid-in-kind at our election. If elected, paid-in-kind interest will be capitalized and added to the principal amount of the Term Loan. The Term Loan will be repaid in eight equal quarterly payments starting in the 13th quarter following the closing of the Term Loan, except that the repayment start date may be extended at our option for an additional four quarters, so that repayments start in the 17th quarter following the closing of the Term Loan, subject to the achievement of specified ARIKAYCE data thresholds and certain other conditions.

Under the Royalty Financing Agreement, OrbiMed paid us $150 million in exchange for the right to receive, on a quarterly basis, royalties (the Royalty Financing) in an amount equal to 4% of ARIKAYCE global net sales prior to September 1, 2025 and 4.5% of ARIKAYCE global net sales on or after September 1, 2025, as well as 0.75% of brensocatib global net sales, if approved (the Revenue Interest Payments). In the event that OrbiMed has not received aggregate Revenue Interest Payments equal to or greater than $150 million on or prior to March 31, 2028, the royalty rate for ARIKAYCE will be increased for all subsequent fiscal quarters to a rate which, if applied retroactively, would have resulted in aggregate Revenue Interest Payments to OrbiMed for all fiscal quarters ended on or prior to March 31, 2028 equal to $150 million. In addition, we must make a one-time payment to OrbiMed in an amount that, when added to the aggregate amount of Revenue Interest Payments received by OrbiMed as of March 31, 2028, would equal $150 million. The total Revenue Interest Payments payable by us to OrbiMed are capped at 1.8x of the purchase price or up to a maximum of 1.9x of the purchase price under certain conditions.

In May 2021, we completed an underwritten offering of 0.75% convertible senior notes due 2028 (the 2028 Convertible Notes). The 2028 Convertible Notes may be convertible into common stock at an initial conversion rate of 30.7692 shares of common stock per $1,000 principal amount of 2028 Convertible Notes. We sold $575.0 million aggregate principal amount of the 2028 Convertible Notes, including the exercise in full of the underwriters' option to purchase additional 2028 Convertible Notes, resulting in net proceeds of approximately $559.3 million. Holders of the 2028 Convertible Notes may convert their 2028 Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding March 1, 2028 only under certain circumstances. On or after March 1, 2028 until the close of business on the second scheduled trading day immediately preceding the maturity date, holders may convert their 2028 Convertible Notes at any time. Upon conversion of the 2028 Convertible Notes, we may deliver cash, shares of our common stock or a combination of cash and shares of our common stock, at our election.

In January 2018, we completed an underwritten public offering of 1.75% convertible senior notes due 2025 (the 2025 Convertible Notes, and, together with the 2028 Convertible Notes, the Convertible Notes). The 2025 Convertible Notes may be convertible into common stock at an initial conversion rate of 25.5384 shares of common stock per $1,000 principal amount of 2025 Convertible Notes. We sold $450.0 million aggregate principal amount of the 2025 Convertible Notes, including the exercise in full of the underwriters' option to purchase additional 2025 Convertible Notes, resulting in net proceeds of approximately $435.8 million. A portion of the net proceeds from the 2028 Convertible Notes was used to repurchase $225.0 million of our outstanding 2025 Convertible Notes. Holders of the 2025 Convertible Notes may convert their 2025 Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding October 15, 2024 only under certain circumstances. On or after October 15, 2024 until the close of business on the second scheduled trading day immediately preceding the maturity date, holders may convert their 2025 Convertible Notes at any time. Upon conversion of the 2025 Convertible Notes, we may deliver cash, shares of our common stock or a combination of cash and shares of our common stock, at our election.

Our debt service obligations and the degree to which we are leveraged could have negative consequences on our business, such as the following:

- We may be more vulnerable to economic downturns, less able to withstand competitive pressures, and less flexible in responding to changing economic conditions;
- Our ability to obtain financing in the future may be limited;
- We may be required to sell debt or equity securities or to sell some of our core assets, possibly on unfavorable terms, to meet payment obligations;
- We may be placed at a possible competitive disadvantage with less leveraged competitors and competitors that may have better access to capital resources;

- A substantial portion of our cash flows from operations in the future may be required for the payment of our interest or principal payments under the Loan Agreement, Revenue Interest Payments under the Royalty Financing Agreement and the principal amounts of the Convertible Notes when they or any additional indebtedness become due, thereby reducing the amount of our cash flow available for other purposes, including funds for clinical development or to pursue future business opportunities; and
- We may elect to make cash payments upon conversion of the Convertible Notes, which would reduce our available cash.

Our ability to pay principal or interest on or, if desired, to refinance our indebtedness, including the Loan Agreement, the Royalty Financing Agreement and the Convertible Notes, depends on our future performance, which is subject to economic, financial, competitive and other factors, some of which are beyond our control. Our business may not generate cash flow from operations in the future sufficient to satisfy any obligations under the Loan Agreement, the Royalty Financing Agreement or the Convertible Notes or our obligations under any future indebtedness we may incur. If we are unable to generate such cash flow, we may be required to delay, restrict or eliminate all or a portion of our development programs or commercialization efforts or refinance or obtain additional equity capital on terms that may be onerous or highly dilutive. If we do not meet our debt obligations, it could materially adversely affect our results of operations, financial condition and the value of our common stock.

The Loan Agreement and the Royalty Financing Agreement each contain customary affirmative and negative covenants that restrict our operations, including, among other things, restrictions on our ability to incur liens, incur additional indebtedness, make investments, engage in certain mergers and acquisitions or asset sales, and declare dividends or redeem or repurchase capital stock. The Loan Agreement includes certain customary events of default. If a default occurs and is continuing, we may be required to repay all amounts outstanding under the Loan Agreement. The Royalty Financing Agreement gives OrbiMed the option (the Put Option) to terminate the Royalty Financing Agreement and to require us to repurchase future Revenue Interest Payments upon enumerated events such as a bankruptcy event, a payment default, an uncured material breach or a change of control. The triggering of the Put Option, including by our failure to comply with these covenants, could permit OrbiMed to declare certain amounts to be immediately due and payable. Further, if we are liquidated, Pharmakon's and OrbiMed's rights to repayment would be senior to the rights of the holders of our common stock. Any triggering of the Put Option or other event of default under the Loan Agreement or Royalty Financing Agreement could significantly harm our financial condition, business and prospects and could cause the price of our common stock to decline.

We may also incur additional indebtedness in the future which would result in increased fixed payment obligations and could also result in additional restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license assets or intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business.

The accounting method for the Convertible Notes may have an adverse effect on our reported financial results.

Holders may convert their 2028 Convertible Notes and 2025 Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding March 1, 2028 and October 15, 2024, respectively, only under certain circumstances. For example, during any calendar quarter commencing after the calendar quarter ending on March 31, 2018, holders may convert their 2025 Convertible Notes at their option during any quarter (and only during such quarter) if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding quarter is greater than or equal to 130% of the conversion price on each applicable trading day. If the 2028 Convertible Notes or 2025 Convertible Notes become convertible prior to March 1, 2028 or October 15, 2024, respectively, we may be required to reclassify the Convertible Notes and the related debt issuance costs as current liabilities and certain portions of our equity outside of equity to mezzanine equity, which would have an adverse impact on our reported financial results for such quarter, and could have an adverse impact on the market price of our common stock and the trading price of the Convertible Notes.

We may be unable to use certain of our net operating losses and other tax assets.

We have substantial tax loss carry forwards in the US (both federal and state), Ireland, the United Kingdom and Switzerland. In general, our net operating losses and tax credits have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. In particular, our ability to fully use certain US tax loss carry forwards and general business tax credit carry forwards recorded prior to December 2010 to offset future income or tax liability is limited under section 382 of the Internal Revenue Code of 1986, as amended. Changes in the ownership of our stock, including those resulting from the issuance of shares of our common stock offerings or upon exercise of outstanding options, may limit or eliminate our ability to use certain net operating losses and tax credit carry forwards in the future.

Changes in our effective income tax rates and future changes to US and non-US tax laws could adversely affect our results of operations.

We are subject to income taxes in the US and various ex-US jurisdictions in which we operate globally. Various factors may have favorable or unfavorable impacts on our effective tax rate, including changes in tax rates and laws,

interpretations of existing laws, changes in accounting standards, changes in the jurisdiction of our pre-tax earnings and examinations of our tax filings.

Goodwill impairment charges in the future could have a material adverse effect on our business, results of operations and financial condition.

We have recorded a significant amount of goodwill on our consolidated balance sheet as a result of acquisitions. We review the recoverability of goodwill annually and whenever events or circumstances indicate that the carrying value of a reporting unit may not be recoverable.

The impairment tests require us to make an estimate of the fair value of our reporting units. An impairment could be recorded as a result of changes in assumptions, estimates or circumstances, some of which are beyond our control. Since a number of factors may influence determinations of fair value of goodwill, we are unable to predict whether impairments of goodwill will occur in the future, and there can be no assurance that continued conditions will not result in future impairments of goodwill. The future occurrence of a potential indicator of impairment could include matters such as (i) a decrease in expected net earnings, (ii) adverse equity market conditions, (iii) a decline in current market multiples, (iv) a decline in our common stock price, (v) a significant adverse change in legal factors or the general business climate, and (vi) an adverse action or assessment by a regulator. Any such impairment would result in us recognizing a non-cash charge in our consolidated financial statements, which could adversely affect our business, results of operations and financial condition.

Risks Related to Ownership of Our Common Stock

Our shareholders may experience dilution of their ownership interests because of the future issuance of additional shares of our common stock for general corporate purposes and upon the conversion of the Convertible Notes.

In the future, we may issue additional equity securities for capital raising purposes, in connection with hiring or retaining employees, to fund acquisitions, or for other business purposes. We have previously funded, and expect to continue to fund, acquisitions using shares of our common stock as consideration. In addition, we may issue shares of our common stock upon the conversion of our Convertible Notes. The conversion of some or all of the Convertible Notes will dilute the ownership interests of our existing shareholders to the extent we deliver shares upon their conversion. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the Convertible Notes may encourage short selling by market participants because the conversion of the Convertible Notes could be used to satisfy short positions, or the anticipated conversion of the Convertible Notes into shares of our common stock could depress the price of our common stock. The future issuance of any additional shares of common stock will dilute our current shareholders and may create downward pressure on the value of our shares. The potential for the issuance of a significant amount of our common stock pursuant to the convertible notes could create a circumstance commonly referred to as an "overhang" and in anticipation of which the market price of our stock could fall. The existence of an overhang, whether or not sales have occurred or are occurring, could also hinder our ability to raise additional equity capital at a time and price that we deem reasonable or appropriate.

The market price of our stock has been and may continue to be highly volatile, which could lead to shareholder litigation against us.

Our common stock is listed on the Nasdaq Global Select Market under the ticker symbol "INSM". The market price of our stock has been and may continue to be highly volatile and could be subject to wide fluctuations in price in response to various factors, including those discussed herein, many of which are beyond our control. In addition, the stock market has from time to time experienced extreme price and volume fluctuations, which have particularly affected the market prices for emerging biotechnology and pharmaceutical companies like us, and which have often been unrelated to their operating performance.

Historically, when the market price of a stock has been volatile, shareholders are more likely to institute securities and derivative class action litigation against the issuer of such stock. We previously faced a shareholder suit following a decline in our stock price. If any of our shareholders bring a lawsuit against us in the future, it could have a material adverse effect on our business. We have insurance policies related to some of the risks associated with our business, including directors' and officers' liability insurance policies; however, our insurance coverage may not be sufficient and our insurance carriers may not cover all claims in a given litigation. If we are not successful in our defense of claims asserted in shareholder litigation, those claims are not covered by insurance or they exceed our insurance coverage, we may have to pay damage awards, indemnify our executive officers, directors and third parties from damage awards that may be entered against them and pay our and their costs and expenses incurred in defense of, or in any settlement of, such claims. In addition, such shareholder suits could divert the time and attention of management from our business.

Certain provisions of Virginia law, our articles of incorporation and amended and restated bylaws and arrangements between us and our employees could hamper a third party's acquisition of us or discourage a third party from attempting to acquire control of us.

Certain provisions of Virginia law, our articles of incorporation and amended and restated bylaws and arrangements with our employees could hamper a third party's acquisition of us or discourage a third party from attempting to acquire control of us, or limit the price that investors might be willing to pay for shares of our common stock. These provisions or arrangements include:

- The ability to issue preferred stock with rights senior to those of our common stock without any further vote or action by the holders of our common stock. The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of our common stock or could adversely affect the rights and powers, including voting rights, of the holders of our common stock. In certain circumstances, such issuance could have the effect of decreasing the market price of our common stock.
- The existence of a staggered board of directors in which there are three classes of directors serving staggered three-year terms, thus expanding the time required to change the composition of a majority of directors.
- The requirement that shareholders provide advance notice when nominating director candidates to serve on our board of directors.
- The inability of shareholders to convene a shareholders' meeting without the chairman of the board, the president or a majority of the board of directors first calling the meeting.
- The prohibition against entering into a business combination with the beneficial owner of 10% or more of our outstanding voting stock for a period of three years after the 10% or greater owner first reached that level of stock ownership, unless certain criteria are met.
- In addition to severance agreements with our officers and provisions in our incentive plans that permit acceleration of equity awards upon a change in control, a severance plan for eligible full-time employees that provides such employees with severance equal to six months of their then-current base salaries in connection with a termination of employment without cause upon, or within 18 months following, a change in control.

Under Virginia law, our board of directors may implement a shareholders' rights plan or "poison pill" without shareholder approval. Our board of directors regularly considers this matter, even in the absence of specific circumstances or takeover proposals, to facilitate its future ability to quickly and effectively protect shareholder value.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 1C. CYBERSECURITY

We incorporate assessment of our cybersecurity initiatives into our Enterprise Risk Management program. The Enterprise Risk Management program evaluates risk areas including, but not limited to, operational risk, intellectual property theft, fraud, harm to employees, patients, or third parties, and violation of privacy or security-related laws or regulations. As part of our efforts to mitigate cyber risk, we have implemented cybersecurity processes, technologies, and controls designed to identify and manage potential material cyber risks and have obtained cyber-specific insurance coverage.

We employ a range of tools and services, including regular network and endpoint monitoring, managed detection and response, system patching, managed security services, server and endpoint scheduled backups, awareness training and testing, periodic vulnerability assessment and penetration testing, to update our ongoing risk identification and mitigation efforts. We have a cybersecurity assessment process, which helps identify our cybersecurity risks by comparing our processes to standards set by the Center for Internet Security. Our processes also assess cybersecurity risks associated with our use of third-party service providers. We proactively engage with key vendors, industry participants, and law enforcement/cyber threat intelligence communities as part of our continuing efforts to evaluate and enhance the effectiveness of our information security policies and procedures.

Our information security program is managed by a senior director who reports to the Chief Information Officer (CIO), providing routine security program updates and briefings. The current senior director has more than 25 years of experience in cybersecurity, federal law enforcement, and cyber investigations, while possessing the required subject matter expertise, skills, experience, and industry certifications expected of an individual assigned to these duties. Our information security team, which includes the CIO and senior director, as well as additional professionals, is responsible for leading enterprise-wide cybersecurity strategy, policy, standards, and processes. Our CIO provides regular updates to our Chief Executive Officer and other members of management. The Audit Committee of the Board of Directors is responsible for oversight of the Company's cybersecurity risk exposure and the CIO provides reports to the Audit Committee, as well as the full Board of Directors, at least annually. The reports to management and our Board include updates on the Company's cyber risks and threats, the status of projects to strengthen our information security systems, assessments of the information security program, and the emerging threat landscape.

For the year ended December 31, 2023, we are not aware of any material cybersecurity incidents.

ITEM 2. PROPERTIES

We currently lease 117,022 square feet of office space for our corporate headquarters in Bridgewater, New Jersey. The initial lease, which commenced in the fourth quarter of 2019, provides us a one-time option to expand the leased premises by up to 50,000 square feet prior to the fifth anniversary of the initial lease commencement. The initial term of this lease will expire in 2030.

We lease laboratory space located in Bridgewater for which we exercised the renewal option to extend the lease term until December 2026. In July 2023, we expanded this lease to a total of 46,671 square feet and further extended the lease term until April 2027. We also lease facilities in California totaling 54,478 square feet and a facility in New Hampshire. In addition, we lease office space outside of the US in France, Ireland, the Netherlands, Switzerland and Japan.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we are a party to various lawsuits, claims and other legal proceedings that arise in the ordinary course of business. While the outcomes of these matters are uncertain, management does not expect that the ultimate costs to resolve these matters will have a material adverse effect on our consolidated financial position, results of operations or cash flows.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

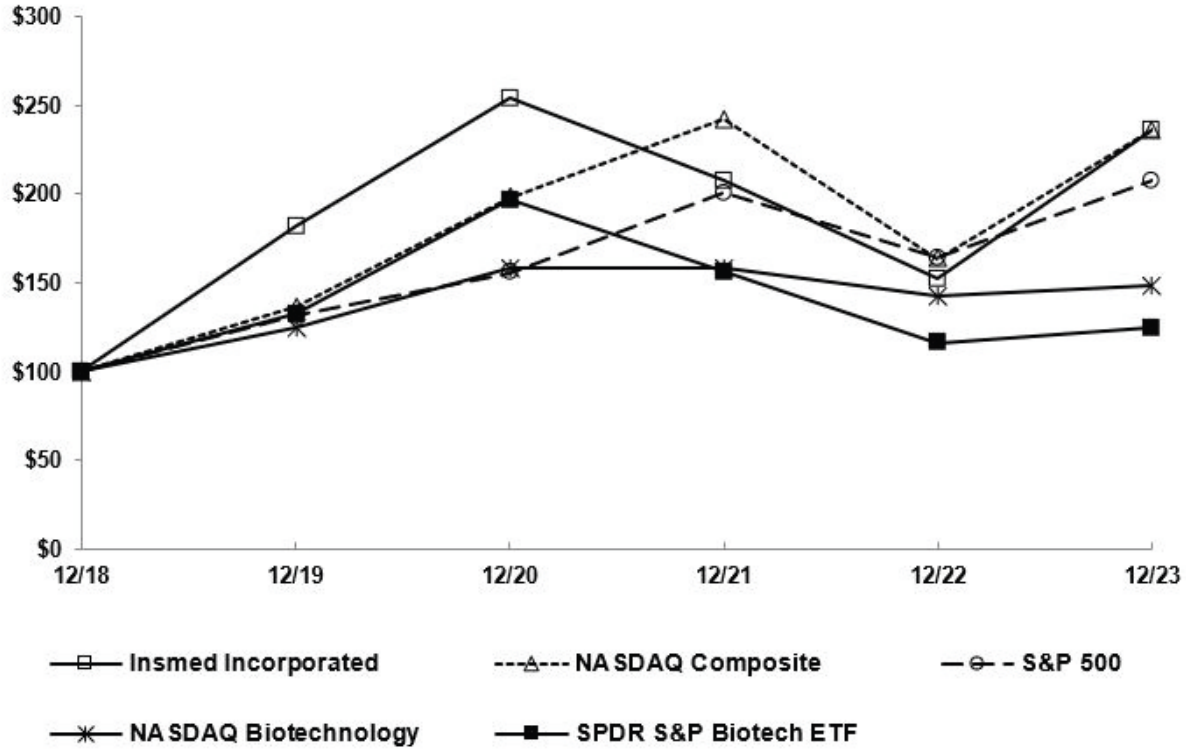
ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our trading symbol is "INSM." Our common stock currently trades on the Nasdaq Global Select Market. As of February 19, 2024, there were approximately 176 holders of record of our common stock.

We have never declared or paid cash dividends on our common stock. We anticipate that we will retain all earnings, if any, to support operations and to finance the growth and development of our business for the foreseeable future. Any future determination as to the payment of dividends will be dependent upon these and any contractual or other restrictions to which we may be subject and, to the extent permissible thereunder, will be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors our board of directors deems relevant at that time.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among Insmed Incorporated, the NASDAQ Composite Index,
the S&P 500 Index, the NASDAQ Biotechnology Index and the SPDR S&P Biotech ETF Index



* $100 invested on 12/31/18 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

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ITEM 6. [RESERVED]

Not applicable.

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

The following discussion also should be read in conjunction with our consolidated financial statements and the notes thereto contained elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth under the section entitled Risk Factors, Cautionary Note Regarding Forward-Looking Statements and elsewhere herein, our actual results may differ materially from those anticipated in these forward-looking statements.

EXECUTIVE OVERVIEW

We are a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. Our first commercial product, ARIKAYCE, was approved in the US in September 2018, in the EU in October 2020 and in Japan in March 2021. Our pipeline includes clinical-stage programs, brensocatib and TPIP, as well as other early-stage research programs. Brensocatib is a small molecule, oral, reversible inhibitor of DPP1, which we are developing for the treatment of patients with bronchiectasis and other neutrophil-mediated diseases, including CRSsNP. TPIP is an inhaled formulation of the treprostinil prodrug treprostinil palmitil which may offer a differentiated product profile for PH-ILD and PAH. Our early-stage research programs encompass a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA-end joining, and synthetic rescue. We have legal entities in the US, France, Germany, Ireland, Italy, the Netherlands, Switzerland, the UK and Japan.

Refer to Part I, Item 1. "Business" for a summary of our ongoing commercial and clinical programs for ARIKAYCE and our ongoing clinical activities for brensocatib, TPIP and early-stage research programs.

Prior to 2019, we had not generated significant revenue and through December 31, 2023, we had an accumulated deficit of $3.4 billion. We have financed our operations primarily through the public offerings of our equity securities, debt financings and revenue interest financings. Although it is difficult to predict our future funding requirements, based upon our current operating plan, we anticipate that our cash and cash equivalents and marketable securities as of December 31, 2023 will enable us to fund our operations for at least the next 12 months.

Our ability to reduce our operating loss and begin to generate positive cash flow from operations depends on the continued success in commercializing ARIKAYCE and achieving positive results from the ARIKAYCE confirmatory clinical trial program in order to obtain full approval of ARIKAYCE in the US and potentially reach more patients. Additionally, our continued success also depends on bringing additional clinical stage products to market, such as brensocatib, TPIP and our early-stage research programs. We expect to continue to incur substantial expenses related to our research and development activities as we continue the ARIKAYCE confirmatory clinical program, conduct the Phase 3 ASPEN trial for brensocatib, continue the trials for TPIP, and fund development of our early-stage research programs. We also expect to continue to incur significant costs related to the commercialization of ARIKAYCE and our pre-commercialization activities related to brensocatib. Our financial results may fluctuate from quarter to quarter and will depend on, among other factors, the net sales of ARIKAYCE; the scope and progress of our research and development efforts; and the timing of certain expenses. We cannot predict whether or when new products or new indications for marketed products will receive regulatory approval or, if any such approval is received, whether we will be able to successfully commercialize such products and whether or when they may become profitable.

KEY COMPONENTS OF OUR RESULTS OF OPERATIONS

Product Revenues, Net

Product revenues, net, consist of net sales of ARIKAYCE. In October 2018, we began shipping ARIKAYCE to our customers in the US, which include specialty pharmacies and specialty distributors. In December 2020, we began commercial sales of ARIKAYCE in Europe. In July 2021, we began recognizing product revenue from commercial sales of ARIKAYCE in Japan. We recognize revenue for product received by our customers net of allowances for customer credits, including prompt pay discounts, service fees, estimated rebates, including government rebates, such as Medicaid rebates and Medicare Part D coverage gap reimbursements in the US, and chargebacks.

Cost of Product Revenues (Excluding Amortization of Intangible Assets)

Cost of product revenues (excluding amortization of intangible assets) consist primarily of direct and indirect costs related to the manufacturing of ARIKAYCE sold, including third-party manufacturing costs, packaging services, freight, and allocation of overhead costs, in addition to royalty expenses and revenue-based milestones. We began capitalizing inventory upon FDA approval of ARIKAYCE in September 2018.

Research and Development (R&D) Expenses

R&D expenses consist of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our research and development functions, including medical affairs and program management. R&D expenses also includes other internal operating expenses, the cost of manufacturing product candidates, including the medical devices for drug delivery, for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. In addition, R&D expenses include payments to third parties for the license rights to products in development (prior to marketing approval), such as brensocatib, and may include the cost of asset acquisitions. Our R&D expenses related to manufacturing our product candidates and medical devices for clinical study are primarily related to activities at CMOs that manufacture brensocatib, TPIP and early-stage research activities. Our R&D expenses related to clinical trials are primarily related to activities at CROs that conduct and manage clinical trials on our behalf. These contracts with CROs set forth the scope of work to be completed at a fixed fee or amount per patient enrolled. Payments under these contracts with CROs primarily depend on performance criteria such as the successful enrollment of patients or the completion of clinical trial milestones as well as time-based fees. Expenses are accrued based on contracted amounts applied to the level of patient enrollment and to activity according to the clinical trial protocol. Deposits for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are then recognized as an expense as the related goods are delivered or the services are performed.

Selling, General and Administrative (SG&A) Expenses

SG&A expenses consist of salaries, benefits and other related costs, including stock-based compensation, for our non-employee directors and personnel serving in our executive, finance and accounting, legal and compliance, commercial and pre-commercial, corporate development, field sales, information technology and human resource functions. SG&A expenses also include professional fees for legal services, consulting services, including commercial activities, insurance, board of director fees, tax and accounting services and certain milestones related to ARIKAYCE.

Amortization of Intangible Assets

Upon commercialization of ARIKAYCE, our intangible assets began to be amortized over their estimated useful lives. The fair values assigned to our intangible assets are based on estimates and assumptions we believe are reasonable based on available facts and circumstances. Unanticipated events or circumstances may occur that require us to review the assets for impairment.

Change in Fair Value of Deferred and Contingent Consideration Liabilities

In connection with our acquisitions of Motus and AlgaeneX in August 2021 (the Business Acquisition), we recorded deferred and contingent consideration liabilities related to potential future milestone payments. Adjustments to the fair value are due to changes in: the probability of achieving milestones; our stock price; or certain other estimated assumptions. The change in fair value of deferred and contingent consideration liabilities is calculated quarterly with gains and losses recorded in the consolidated statements of comprehensive loss.

Investment Income and Interest Expense

Investment income consists of interest and dividend income earned on our cash and cash equivalents and marketable securities. Interest expense consists primarily of contractual interest costs, Royalty Financing Agreement non-cash interest expense and the amortization of debt issuance costs related to our debt. Debt issuance costs are amortized to interest expense using the effective interest rate method over the term of the debt. Our balance sheet reflects debt, net of the debt discount, debt issuance costs paid to the lender, and other third-party costs. Unamortized debt issuance costs associated with extinguished debt are expensed in the period of the extinguishment.

Change in Fair Value of Interest Rate Swap

We record derivative and hedge transactions in accordance with generally accepted accounting principles in the US (GAAP). In the fourth quarter of 2022, we entered into an interest rate swap contract (the Swap Contract) with a notional value of $350 million to economically hedge our variable rate-based term debt for three years, effectively changing the variable rate under the term debt to a fixed interest rate. Our interest rate swap has not been designated as a hedging instrument for accounting purposes. Consequently, all changes in the fair value of the Swap Contract are reported as a component of net loss in the consolidated statements of comprehensive loss.

RESULTS OF OPERATIONS

Comparison of the Years Ended December 31, 2023 and 2022

Overview - Operating Results

Our operating results for the year ended December 31, 2023, included the following:

- Product revenues, net, increased $59.9 million, or 24.4%, as compared to the prior year as a result of the growth in ARIKAYCE sales;
- Cost of product revenues (excluding amortization of intangibles) increased $10.4 million as compared to the prior year as a result of the increase in sales of ARIKAYCE;
- R&D expenses increased $173.5 million as compared to the prior year primarily resulting from the non-cash costs of the Adrestia and Vertuis acquisitions;
- SG&A expenses increased $78.7 million as compared to the prior year primarily resulting from increases in professional fees and other external expenses;
- Amortization of intangible assets was consistent with the prior year;
- Change in fair value of deferred and contingent consideration liabilities increased $49.5 million primarily as a result of the change in our share price; and
- Interest expense increased $55.2 million as compared to the prior year due to entering into the Term Loan and Royalty Financing Agreement in the fourth quarter of 2022.

Product Revenues, Net

Product revenues, net, consists of net sales of ARIKAYCE. The following table summarizes revenue by geography for the years ended December 31, 2023 and 2022 (in thousands):

	For the Year Ended December 31,		Increase (decrease)	
	2023	2022	$	%
US	$ 224,195	$ 185,994	$ 38,201	20.5%
Japan	65,733	56,506	9,227	16.3%
Europe and rest of world	15,280	2,858	12,422	NM
Total product revenues, net	$ 305,208	$ 245,358	$ 59,850	24.4%

Product revenues, net, for the year ended December 31, 2023 increased to $305.2 million as compared to $245.4 million in 2022 as a result of the growth in sales of ARIKAYCE in the US, Japan and Europe and the rest of the world. During the fourth quarter of 2022, we reached an agreement with the French authorities on the final reimbursement price related to the ATU program in France and we are required to refund the difference. This final pricing resulted in a change in estimate that reduced revenue by approximately $7.5 million in the fourth quarter of 2022, of which $5.8 million related to periods prior to 2022.

Cost of Product Revenues (Excluding Amortization of Intangibles)

Cost of product revenues (excluding amortization of intangibles) for the years ended December 31, 2023 and 2022 were comprised of the following (in thousands):

	For the Year Ended December 31,		Increase (decrease)	
	2023	2022	$	%
Cost of product revenues (excluding amortization of intangibles)	$ 65,573	$ 55,126	$ 10,447	19.0%
Cost of product revenues, as % of revenues	*21.5 %*	*22.5 %*		

Cost of product revenues (excluding amortization of intangibles) increased by $10.4 million, or 19.0%, to $65.6 million for the year ended December 31, 2023 as compared to $55.1 million in 2022. The increase in cost of product revenues (excluding amortization of intangibles) in the year ended December 31, 2023 was directly attributable to the increase in total revenues discussed above.

R&D Expenses

R&D expenses for the years ended December 31, 2023 and 2022 were comprised of the following (in thousands):

	For the Years Ended December 31,		Increase (decrease)	
	2023	2022	$	%
External Expenses				
Clinical development and research	$ 166,448	$ 144,846	$ 21,602	14.9%
Non-cash asset acquisitions	86,747	—	86,747	NA
Manufacturing	73,614	71,998	1,616	2.2%
Regulatory, quality assurance, and medical affairs	27,002	20,129	6,873	34.1%
Subtotal—external expenses	$ 353,811	$ 236,973	$ 116,838	49.3%
Internal Expenses				
Compensation and benefit-related expenses	$ 140,861	$ 104,094	$ 36,767	35.3%
Stock-based compensation	35,880	26,379	9,501	36.0%
Other internal operating expenses	40,459	30,072	10,387	34.5%
Subtotal—internal expenses	$ 217,200	$ 160,545	$ 56,655	35.3%
Total R&D expenses	$ 571,011	$ 397,518	$ 173,493	43.6%

R&D expenses increased to $571.0 million during the year ended December 31, 2023 from $397.5 million in 2022. The $173.5 million increase was primarily due to the $86.7 million one-time, non-cash asset acquisition costs of the Adrestia and Vertuis acquisitions, a $46.3 million increase in compensation and benefit-related expenses and stock-based compensation costs due to an increase in headcount, and a $21.6 million increase in clinical development and research expenses to support the Phase 3 ASPEN trial of brensocatib, the ARIKAYCE MAC lung disease clinical trial program, and the ongoing Phase 2 PAH and Phase 2 PH-ILD studies of TPIP.

External R&D expenses by product for the years ended December 31, 2023 and 2022 were comprised of the following (in thousands):

	For the Year Ended December 31,		Increase (decrease)	
	2023	2022	$	%
ARIKAYCE external R&D expenses	$ 62,418	$ 61,024	$ 1,394	2.3%
Brensocatib external R&D expenses	108,556	102,530	6,026	5.9%
TPIP external R&D expenses	50,185	39,220	10,965	28.0%
Non-cash asset acquisitions	86,747	—	86,747	NA
Other external R&D expenses	45,905	34,199	11,706	34.2%
Total external R&D expenses	$ 353,811	$ 236,973	$ 116,838	49.3%

We expect R&D expenses to increase in 2024 relative to 2023 primarily due to our clinical trial activities and related spend including our Phase 3 ASPEN trial of brensocatib, our confirmatory clinical trial of ARIKAYCE in a treatment setting for patients with MAC lung disease, our TPIP clinical trials and other research efforts for future product candidates.

SG&A Expenses

SG&A expenses for the years ended December 31, 2023 and 2022 were comprised of the following (in thousands):

	For the Years Ended December 31,		Increase (decrease)	
	2023	2022	$	%
Compensation and benefit-related expenses	$ 117,926	$ 92,709	$ 25,217	27.2%
Stock-based compensation	38,898	31,307	7,591	24.2%
Professional fees and other external expenses	138,151	105,352	32,799	31.1%
Facility related and other internal expenses	49,526	36,416	13,110	36.0%
Total SG&A expenses	$ 344,501	$ 265,784	$ 78,717	29.6%

SG&A expenses increased to $344.5 million during the year ended December 31, 2023 from $265.8 million in 2022. The $78.7 million increase was primarily due to commercial readiness activities for brensocatib, including a $32.8 million increase in professional fees and other external expenses and a $32.8 million increase in compensation and benefit-related expenses and stock-based compensation costs due to an increase in headcount. We expect SG&A expenses to continue to increase in 2024 relative to 2023 due, in part, to commercial readiness activities for brensocatib.

Amortization of Intangible Assets

Amortization of intangible assets for the years ended December 31, 2023 and 2022 was $5.1 million and $5.1 million, respectively. Amortization of intangible assets is comprised of amortization of acquired ARIKAYCE R&D and amortization of the milestones paid to PARI for the FDA and EMA approvals of ARIKAYCE.

Change in Fair Value of Deferred and Contingent Consideration Liabilities

The change in fair value of deferred and contingent consideration liabilities for the year ended December 31, 2023 was $28.7 million. The change is related to the fair value of the potential future consideration to be paid to former equityholders of the businesses we acquired. Adjustments to the fair value are due to changes in: the probability of achieving milestones; our stock price; or certain other estimated assumptions.

Investment Income

Investment income was $42.1 million for the year ended December 31, 2023 as compared to $11.1 million for 2022. The $31.1 million increase in investment income for the year ended December 31, 2023 as compared to the prior year period is primarily due to an increase in the marketable securities balance and interest rates in 2023 relative to 2022.

Interest Expense

Interest expense was $81.7 million for the year ended December 31, 2023 as compared to $26.4 million for 2022. The $55.2 million increase in interest expense for the year ended December 31, 2023 as compared to the prior year period is primarily due to entering into the Term Loan and Royalty Financing Agreement in the fourth quarter of 2022. See *Note 10 - Debt* and *Note 11 - Royalty Financing Agreement* for further details.

Change in Fair Value of Interest Rate Swap

The change in fair value of interest rate swap for the year ended December 31, 2023 was $0.3 million. Adjustments to the fair value are due to changes in interest rates as of December 31, 2023 relative to the interest rate of our Swap Contract as of December 31, 2022.

Provision for Income Taxes

The income tax provision was $2.6 million for the year ended December 31, 2023 as compared to $1.4 million for the year ended December 31, 2022. The income tax provision for the years ended December 31, 2023 and 2022 reflects the income tax expense recorded as a result of taxable income in certain of our subsidiaries in Europe and Japan as well as a liability for certain state income taxes.

Comparison of the Years Ended December 31, 2022 and 2021

Please refer to the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022 for a comparative discussion of our fiscal years ended December 31, 2022 and December 31, 2021.

LIQUIDITY AND CAPITAL RESOURCES

Overview

There is considerable time and cost associated with developing potential pharmaceutical products to the point of regulatory approval and commercialization. We commenced commercial shipments of ARIKAYCE in October 2018. We expect to continue to incur consolidated operating losses, including losses at our US and certain international entities, as we plan to fund R&D for ARIKAYCE, brensocatib, TPIP and our other pipeline programs, continue commercialization and regulatory activities for ARIKAYCE, fund pre-commercialization activities for brensocatib, and engage in other general and administrative activities.

In 2021, we entered into a sales agreement with SVB Leerink LLC (now known as Leerink Partners LLC) (Leerink Partners), to sell shares of our common stock, with aggregate gross sales proceeds of up to $250.0 million, from time to time, through an “at the market” equity offering program (the ATM program), under which Leerink Partners acts as sales agent. During the year ended December 31, 2023, we issued and sold an aggregate of 6,503,041 shares of common stock through the ATM program at a weighted-average public offering price of $24.12 per share and received net proceeds of $152.2 million. As of December 31, 2023, an aggregate of $58.7 million of shares of common stock remain available to be issued and sold under the ATM program.

In October 2022, we entered into a $350 million Term Loan with Pharmakon that matures on October 19, 2027. The Term Loan bears interest at a rate based upon the SOFR, subject to a SOFR floor of 2.5%, in addition to a margin of 7.75% per annum. Up to 50% of the interest payable during the first 24 months from the closing of the Term Loan may be paid-in-kind at our election. If elected, paid-in-kind interest will be capitalized and added to the principal amount of the Term Loan. The Term

Loan, including the paid-in-kind interest, will be repaid in eight equal quarterly payments starting in the 13th quarter following the closing of the Term Loan (i.e., the quarter ending March 31, 2026), except that the repayment start date may be extended at our option for an additional four quarters, so that repayments start in the 17th quarter following the closing of the Term Loan, subject to the achievement of specified ARIKAYCE data thresholds and certain other conditions. Net proceeds from the Term Loan, after deducting the lenders fees and deal expenses of $15.1 million, were $334.9 million.

In October 2022, we entered into the Royalty Financing Agreement with OrbiMed, whereby OrbiMed paid us $150 million in exchange for the right to receive, on a quarterly basis, royalties in an amount equal to 4% of ARIKAYCE global net sales prior to September 1, 2025 and 4.5% of ARIKAYCE global net sales on or after September 1, 2025, as well as 0.75% of brensocatib global net sales, if approved. In the event that OrbiMed has not received aggregate Revenue Interest Payments equal to or greater than $150 million on or prior to March 31, 2028, the royalty rate for ARIKAYCE will be increased for all subsequent fiscal quarters to a rate which, if applied retroactively, would have resulted in aggregate Revenue Interest Payments to OrbiMed for all fiscal quarters ended on or prior to March 31, 2028 equal to $150 million. In addition, we must make a one-time payment to OrbiMed in an amount that, when added to the aggregate amount of Revenue Interest Payments received by OrbiMed as of March 31, 2028, would equal $150 million. The total Revenue Interest Payments payable by us to OrbiMed are capped at 1.8x of the purchase price or up to a maximum of 1.9x of the purchase price under certain conditions. Net proceeds from the Royalty Financing Agreement, after deducting the lenders fees and deal expenses of $3.6 million, were $146.4 million.

In October 2022, we also completed an underwritten offering of 13,750,000 shares of our common stock at a public offering price of $20.00 per share. Our net proceeds from the sale of the shares, after deducting the underwriting discounts and offering expense of $16.2 million, were $258.8 million.

In May 2021, we completed an underwritten public offering of $575.0 million aggregate principal amount of the 2028 Convertible Notes, including the exercise in full of the underwriters' option to purchase additional notes. Our net proceeds from the offering, after deducting underwriting discounts and offering expenses of $15.7 million, were $559.3 million. A portion of the net proceeds from the 2028 Convertible Notes was used to repurchase $225.0 million of our outstanding 2025 Convertible Notes. We recorded a loss on early extinguishment of debt of $17.7 million, primarily related to the premium paid on extinguishment of a portion of the 2025 Convertible Notes.

In May 2021, we also completed an underwritten public offering of 11,500,000 shares of our common stock, including 1,500,000 shares issued pursuant to the exercise in full of the underwriters' option to purchase additional shares, at a public offering price of $25.00 per share. Our net proceeds from the sale of the shares, after deducting the underwriting discounts and offering expenses of $17.5 million, were $270.1 million.

We may need to raise additional capital to fund our operations, the continued commercialization of ARIKAYCE, launch readiness activities for the potential launch of brensocatib for the treatment of patients with bronchiectasis, if approved, clinical trials for brensocatib, TPIP, and our future product candidates, and to develop, acquire, in-license or co-promote other products or product candidates, including those that address orphan or rare diseases. While we believe we currently have sufficient funds to meet our financial needs for at least the next 12 months, we may opportunistically raise additional capital and may do so through equity or debt financing(s), strategic transactions or otherwise. Our cash requirements for the next 12 months will be impacted by a number of factors, the most significant of which we expect to be the ASPEN trial, expenses related to our commercialization efforts and our ARISE and ENCORE clinical trials for ARIKAYCE, and other development activities for brensocatib, and to a lesser extent, expenses related to the clinical development of TPIP and our early-research programs.

Cash Flows

As of December 31, 2023, we had cash and cash equivalents of $482.4 million, as compared with $1,074.0 million as of December 31, 2022. In addition, as of December 31, 2023, we had marketable securities of $298.1 million as compared with $74.2 million as of December 31, 2022. The $591.7 million decrease in cash and cash equivalents was primarily due to the cash used in operating activities and purchase of marketable securities. Our working capital was $703.4 million as of December 31, 2023 as compared with $1,083.1 million as of December 31, 2022.

Net cash used in operating activities was $536.2 million and $400.4 million for the years ended December 31, 2023 and 2022, respectively. The net cash used in operating activities during the years ended December 31, 2023 and 2022 was primarily for the commercial, clinical and manufacturing activities related to ARIKAYCE, as well as other SG&A expenses and clinical trial expenses related to brensocatib and TPIP. The increase in cash used in operating activities for the year ended December 31, 2023 compared to 2022 was primarily due to the increase in net loss, excluding the adjustments to reconcile net loss to net cash used in operating activities.

Net cash used in investing activities was $223.6 million and $34.6 million for the years ended December 31, 2023 and 2022, respectively. The increase in cash used for investing activities in 2023 is due to the purchases of marketable securities, partially offset by maturity of certain marketable securities.

Net cash provided by financing activities was $168.4 million and $793.3 million for the years ended December 31, 2023 and 2022, respectively. The decrease in 2023 is due to net cash proceeds from our Term Loan, Royalty Financing Agreement, and the issuance of our common stock in October 2022.

Contractual Obligations

In October 2022, we entered into financings resulting in aggregate gross proceeds of $500 million. We entered into the $350 million senior secured Term Loan with funds managed by Pharmakon, which matures on October 19, 2027. The Term Loan bears interest at a rate based upon SOFR, subject to a SOFR floor of 2.5%, in addition to a margin of 7.75% per annum. We also entered into a $150 million Royalty Financing Agreement with OrbiMed. Under the Royalty Financing Agreement, OrbiMed will be entitled to receive royalties of 4% on ARIKAYCE global net sales until September 1, 2025, and royalties of 4.5% on ARIKAYCE global net sales on or after September 1, 2025, as well as royalties of 0.75% on brensocatib global net sales, if approved. The total royalty payable to OrbiMed is capped at 1.8x of the $150 million purchase price or up to a maximum of 1.9x of the $150 million purchase price under certain conditions. For more information, see *Note 10 - Debt* and *Note 11 - Royalty Financing Agreement* in our notes to the consolidated financial statements.

In May 2021, we completed an underwritten public offering of $575.0 million aggregate principal amount of the 2028 Convertible Notes pursuant to an indenture between the Company and Wells Fargo Bank, National Association, as trustee (the Indenture). Net proceeds from the offering, after deducting underwriting discounts and offering expenses of $15.7 million, were $559.3 million. The 2028 Convertible Notes bear interest payable semiannually in arrears on June 1 and December 1 of each year, beginning on December 1, 2021. The 2028 Convertible Notes mature on June 1, 2028, unless earlier converted, redeemed, or repurchased. The 2028 Convertible Notes are convertible into common stock of the Company under certain circumstances described in the indenture. For more information, see *Note 10 - Debt* in our notes to the consolidated financial statements.

In January 2018, we completed an underwritten public offering of $450.0 million aggregate principal amount of the 2025 Convertible Notes pursuant to the Indenture. Net proceeds from the offering, after deducting underwriting discounts and commissions and other offering expenses of $14.2 million, were approximately $435.8 million. A portion of the net proceeds from the 2028 Convertible Notes was used to repurchase $225.0 million of the Company's outstanding 2025 Convertible Notes. The Company recorded a loss on early extinguishment of debt of $17.7 million, primarily related to the premium paid on extinguishment of a portion of the 2025 Convertible Notes. The 2025 Convertible Notes bear interest payable semiannually in arrears on January 15 and July 15 of each year, beginning on July 15, 2018. The 2025 Convertible Notes mature on January 15, 2025, unless earlier converted, redeemed, or repurchased. The 2025 Convertible Notes are convertible into common stock of the Company under certain circumstances described in the Indenture. For more information, see *Note 10 - Debt* in our notes to the consolidated financial statements.

In April 2020, we entered into a master services agreement with PPD pursuant to which we retained PPD to perform clinical development services in connection with certain of our clinical research programs. The master services agreement has an initial term of five years. Either party may terminate (i) any project addendum under the master services agreement for any reason and without cause upon 30 days' written notice, (ii) any project addendum in the event of the other party's breach of the master services agreement or such project addendum upon 30 days' written notice, provided that such breach is not cured within such 30-day period, (iii) the master services agreement or any project addendum immediately upon the occurrence of an insolvency event with respect to the other party or (iv) any project addendum upon 30 days' written notice if (a) the continuation of the services under such project addendum would post material ethical or safety risks to study participants, (b) any approval from a regulatory authority necessary to perform the applicable study is revoked, suspended or expires without renewal or (c) in the reasonable opinion of such party, continuation of the services provided under such project addendum would be in violation of applicable law. We have entered into project addenda with PPD to perform clinical development services over several years for, but not limited to, our ARISE, ENCORE, ASPEN studies and other brensocatib and TPIP studies. We currently expect to incur approximately $430.1 million of costs related to these project addenda.

In September 2018, we entered into an agreement (the Lease) with Exeter 700 Route 202/206, LLC to lease 117,022 square feet of office space located in Bridgewater, New Jersey for our corporate headquarters. Subject to certain conditions, we have the one-time option to expand the leased premises by up to 50,000 rentable square feet, exercisable prior to the fifth anniversary of the Commencement Date, which was October 1, 2019. The initial Lease term runs 130 months from the Commencement Date and we have the option to extend that term for up to three additional five-year periods. In addition, we are responsible for operating expenses and taxes pursuant to the Lease. Future minimum payments under the Lease during the initial Lease term are approximately $17.9 million. The Lease contains customary default provisions, including those relating to payment defaults, performance defaults and events of bankruptcy.

In October 2017, we entered into certain agreements with Patheon related to the increase of our long-term production capacity for ARIKAYCE. The agreements provide for Patheon to manufacture and supply ARIKAYCE for our anticipated commercial needs. Under these agreements, we are required to deliver to Patheon the required raw materials, including active pharmaceutical ingredients, and certain fixed assets needed to manufacture ARIKAYCE. Patheon's supply obligations will

commence once certain technology transfer and construction services are completed. Our manufacturing and supply agreement with Patheon will remain in effect for a fixed initial term, after which it will continue for successive renewal terms unless either we or Patheon have given written notice of termination. The technology transfer agreement will expire when the parties agree that the technology transfer services have been completed. The agreements may also be terminated under certain other circumstances, including by either party due to a material uncured breach of the other party or the other party's insolvency. These early termination clauses may reduce the amounts due to the relevant parties. The aggregate investment to increase our long-term production capacity, including under the Patheon agreements and related agreements or purchase orders with third parties for raw materials and fixed assets, is estimated to be approximately $104 million.

In October 2016, we entered into the AZ License Agreement, pursuant to which AstraZeneca granted us exclusive global rights for the purpose of developing and commercializing AZD7986 (which we renamed brensocatib). In consideration of the licenses and other rights granted by AstraZeneca, we made an upfront payment of $30.0 million, which was included as research and development expense in the fourth quarter of 2016. In December 2020, we incurred a $12.5 million milestone payment obligation upon first dosing in a Phase 3 clinical trial of brensocatib. Upon the earlier of our notification to AstraZeneca that we intend to file an NDA or releasing an official public statement that we intend to file an NDA, we will owe AstraZeneca an additional $12.5 million. Subsequent to this milestone, we are also obligated to make a series of additional contingent milestone payments totaling up to an additional $60.0 million upon the achievement of regulatory filing milestones. If we elect to develop brensocatib for a second indication, we will be obligated to make an additional series of contingent milestone payments totaling up to $42.5 million, the first of which occurs at the initiation of a Phase 3 trial in the additional indication. We are not obligated to make any additional milestone payments for any additional indications. In addition, we have agreed to pay AstraZeneca tiered royalties ranging from a high single-digit to mid-teens on net sales of any approved product based on brensocatib and one additional payment of $35.0 million upon the first achievement of $1 billion in annual net sales. The AZ License Agreement provides AstraZeneca with the option to negotiate a future agreement with us for commercialization of brensocatib in chronic obstructive pulmonary disease or asthma.

We have a licensing agreement with PARI for the use of optimized Lamira for delivery of ARIKAYCE in treating patients with NTM lung infections, CF and bronchiectasis. Under the licensing agreement, we have rights under several US and foreign issued patents, and patent applications involving improvements to optimized Lamira, to exploit the system with ARIKAYCE for the treatment of such indications, but we cannot manufacture the nebulizers except as permitted under our Commercialization Agreement with PARI, as described below. Lamira has been approved for use in the US (in combination with ARIKAYCE), the EU and Japan. Under the licensing agreement, we made an upfront license fee and milestone payments to PARI. Upon the FDA acceptance of our NDA and the subsequent FDA and EMA approvals of ARIKAYCE, we made additional milestone payments of €1.0 million, €1.5 million, and €0.5 million, respectively, to PARI. In October 2017, we exercised an option to buy-down the royalties payable to PARI, which was included within selling, general and administrative expenses in the fourth quarter of 2017. PARI is entitled to receive royalty payments in the mid-single digits on the annual global net sales of ARIKAYCE, pursuant to the licensing agreement, subject to certain specified annual minimum royalties.

In July 2014, we entered into a Commercialization Agreement with PARI for the manufacture and supply of Lamira as optimized for use with ARIKAYCE. Under the Commercialization Agreement, PARI manufactures Lamira except in the case of certain defined supply failures, when the Company will have the right to make Lamira and have it made by third parties (but not certain third parties deemed under the Commercialization Agreement to compete with PARI). The Commercialization Agreement has an initial term of 15 years that began in October 2018. The term of the Commercialization Agreement may be extended by us for an additional five years by providing written notice to PARI at least one year prior to the expiration of the Initial Term.

In February 2014, we entered into a contract manufacturing agreement with Therapure Biopharma Inc., which has been assumed by Resilience, for the manufacture of ARIKAYCE, on a non-exclusive basis, at a 200 kg scale. Pursuant to the agreement, we collaborated with Resilience to construct a production area for the manufacture of ARIKAYCE in Resilience's existing manufacturing facility in Canada. The agreement has an initial term of five years, which began in October 2018, and will renew automatically for successive periods of two years each, unless terminated by either party by providing the required two years' prior written notice to the other party. Under the agreement, we are obligated to pay certain minimum amounts for the batches of ARIKAYCE produced each calendar year.

In 2004 and 2009, we entered into research funding agreements with CFFT whereby we received $1.7 million and $2.2 million in research funding for the development of ARIKAYCE. As a result of the US approval of ARIKAYCE and in accordance with the agreements, as amended, we owe milestone payments to CFFT of $13.4 million in the aggregate payable through 2025, of which $7.4 million has been paid as of December 31, 2023. Furthermore, if certain global sales milestones were met within five years of the commercialization of ARIKAYCE, we would have owed up to an additional $3.9 million. Through December 31, 2023, we have met and paid $1.7 million of these additional global sales milestone payments.

Future Funding Requirements

We may need to raise additional capital to fund our operations, including the development and potential commercialization of brensocatib, continued commercialization of ARIKAYCE, current and future clinical trials related to ARIKAYCE, development of TPIP, and the potential development, acquisition, in-license or co-promotion of other products or product candidates, including those that address orphan or rare diseases. We expect that our future capital requirements may be substantial and will depend on many factors, including:

- The timing, outcome, and cost of our ongoing and anticipated clinical trials for our product candidates, including our Phase 3 ASPEN trial;
- The timing and cost of our current and future clinical trials of ARIKAYCE for the treatment of patients with NTM lung infections, including the ARISE and ENCORE trials;
- The cost of discovering or in-licensing additional product candidates;
- The costs of activities related to the regulatory approval process and the timing of approvals, if received;
- The cost of supporting the sales and marketing efforts necessary to support the continued commercial efforts of ARIKAYCE;
- The timing and costs of supporting the commercial launch activities of brensocatib;
- The cost of eventually supporting the commercial launches of TPIP and our other product candidates;
- The cost of filing, prosecuting, defending, and enforcing patent claims;
- The costs of our manufacturing-related activities;
- The cost of hiring more personnel to support our ongoing development and commercialization efforts; and
- The levels, timing and collection of revenue earned from sales of ARIKAYCE and other products approved in the future, if any.

We have raised $1.8 billion in net proceeds from securities offerings since 2021. We believe we currently have sufficient funds to meet our financial needs for at least the next 12 months. However, our business strategy may require us to raise additional capital at any time through equity or debt financing(s), strategic transactions or otherwise.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that have or are reasonably likely to have a current or future material effect on our financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources. We do not have any interest in special purpose entities, structured finance entities or other variable interest entities.

CRITICAL ACCOUNTING ESTIMATES

Preparation of financial statements in accordance with GAAP requires us to make estimates and assumptions affecting the reported amounts of assets, liabilities, revenues and expenses and the disclosures of contingent assets and liabilities. We use our historical experience and other relevant factors when developing our estimates and assumptions and we regularly evaluate these estimates and assumptions. The amounts of assets and liabilities reported in our consolidated balance sheets and the amounts reported in our consolidated statements of comprehensive loss are affected by estimates and assumptions, which are used for, but not limited to, the accounting for revenue recognition and indefinite-lived intangible assets. The accounting estimates discussed below involve a significant level of estimation uncertainty and have had or are reasonably likely to have a material impact on our financial condition or results of operations. Actual results could differ materially from our estimates. For additional accounting policies, see *Note 2 - Summary of Significant Accounting Policies* in our notes to the consolidated financial statements..

Revenue Recognition

In accordance with Accounting Standards Codification (ASC) 606, Revenue from Contracts with Customers, we recognize revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration we expect to receive in exchange for the goods or services provided. To determine revenue recognition for arrangements within the scope of ASC 606, we perform the following five steps: (1) identify the contracts with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when or as the entity satisfies a performance obligation. At contract inception, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied. For all contracts that fall into the scope of ASC 606, we have identified one performance obligation: the sale of ARIKAYCE to its customers. We have not incurred or capitalized any incremental costs associated with obtaining contracts with customers.

Product revenues, net, consist of net sales of ARIKAYCE. Our customers in the US include specialty pharmacies and specialty distributors. In December 2020, we began recognizing product revenue from commercial sales of ARIKAYCE in Europe. In July 2021, we began recognizing product revenue from commercial sales of ARIKAYCE in Japan. Globally, product revenues are recognized once we perform and satisfy all five steps of the revenue recognition criteria mentioned above.

Revenue is recorded at net selling price (transaction price), which includes estimates of variable consideration for which reserves are established for estimated government rebates, such as Medicaid and Medicare Part D reimbursements, and estimated managed care rebates. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as a current liability. Where appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the applicable contract. The amount of variable consideration 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 will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, we adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Rebates: We contract with certain government agencies and managed care organizations, or collectively, third-party payors, so that ARIKAYCE will be eligible for purchase by, or partial or full reimbursement from, such third-party payors. We estimate the rebates we will provide to third-party payors and deduct these estimated amounts from total gross product revenues at the time the revenues are recognized. These reserves are recorded in the same period in which the revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability. The current liability is included in accrued liabilities on the consolidated balance sheets. We estimate the rebates that will be provided to third-party payors based upon (i) our contracts with these third-party payors, (ii) the government mandated discounts applicable to government-funded programs, (iii) a range of possible outcomes that are probability-weighted for the estimated payor mix, and (iv) information obtained from our specialty pharmacies.

If any, or all, of our actual experience vary from the estimates above, we may need to adjust prior period accruals, affecting revenue in the period of adjustment.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As of December 31, 2023, our cash and cash equivalents were in cash accounts or were invested in money market funds. Our investments in money market funds are not insured by the federal government. As of December 31, 2023, our marketable securities were invested in US treasury notes with an original maturity of 90 days.

As of December 31, 2023, we had $225 million and $575 million of 2025 Convertible Notes and 2028 Convertible Notes outstanding, respectively. Our 2025 Convertible Notes and our 2028 Convertible Notes bear interest at a coupon rate of 1.75% and 0.75%, respectively. In addition, as of December 31, 2023, we had our $350 million term loan and a $150.0 million Royalty Financing Agreement outstanding. The Term Loan accrues interest quarterly at the SOFR plus a margin of 7.75% per annum. We entered into the Swap Contract as a hedge to the Term Loan variable interest rate. The Royalty Financing Agreement pays interest at 4% of ARIKAYCE global net sales prior to September 1, 2025 and 4.5% thereafter as well as 0.75% of brensocatib global net sales, if approved. If a 10% change in interest rates had occurred on December 31, 2023, it would not have had a material effect on the fair value of our debt as of that date, nor would it have a material effect on our future earnings or cash flows.

The majority of our business is conducted in US dollars. However, we do conduct certain transactions in other currencies, including Euros, British Pounds and Japanese Yen. Historically, fluctuations in foreign currency exchange rates have not materially affected our results of operations. During the years ended December 31, 2023, 2022 and 2021, our results of operations were not materially affected by fluctuations in foreign currency exchange rates.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by Item 8 is included in our Financial Statements and Supplementary Data set forth in Item 15 of Part IV of this Annual Report on Form 10-K.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2023. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file or submit with the SEC is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and to ensure 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 disclosure. Based on that evaluation our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2023 at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act, as a process designed by, or under the supervision of, our principal executive and principal financial and accounting officers and effected by our board of directors and management 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with US generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of our management and board of directors; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our 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. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2023, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework. Based on management's assessment, management concluded that the Company's internal control over financial reporting was effective as of December 31, 2023.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Attestation Report on Internal Control over Financial Reporting

Ernst & Young LLP, our independent registered public accounting firm, issued an attestation report on our internal control over financial reporting. The report of Ernst & Young LLP is contained in Item 15 of Part IV of this Annual Report on Form 10-K.

ITEM 9B. OTHER INFORMATION

Rule 10b5-1 Trading Plans

During the three months ended December 31, 2023, certain of our officers and directors adopted or terminated Rule 10b5-1 trading plans as follows:

Michael A. Smith, our Chief Legal Officer, entered into a prearranged stock trading arrangement (the Trading Plan) on December 14, 2023. Mr. Smith’s Trading Plan provides for the sale of an aggregate number of up to 44,722 shares of the Company's common stock between March 15, 2024 and September 16, 2024. The Trading Plan was entered into during an open insider trading window and is intended to satisfy the affirmative defense of Rule 10b5-1(c) under the Exchange Act and the Company’s policies regarding insider transactions.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by Item 10 of Form 10-K is incorporated by reference from the discussion responsive thereto under the captions *Election of Class II Directors, Corporate Governance and Delinquent Section 16(a) Reports* in our definitive proxy statement for our 2024 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 of Form 10-K is incorporated by reference from the discussion responsive thereto under the captions *Compensation Discussion and Analysis*, *Compensation Committee Report*, *Compensation Committee Interlocks and Insider Participation* and *Director Compensation* in our definitive proxy statement for our 2024 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by Item 12 of Form 10-K is incorporated by reference from the discussion responsive thereto under the captions *Compensation Discussion and Analysis*, *Security Ownership of Certain Beneficial Owners and Directors and Management* in our definitive proxy statement for our 2024 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

The information required by Item 13 of Form 10-K is incorporated by reference from the discussion responsive thereto under the captions *Corporate Governance* and *Certain Relationships and Related Transactions* in our definitive proxy statement for our 2024 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by Item 14 of Form 10-K is incorporated by reference from the discussion responsive thereto under the caption *Corporate Governance* and *Ratification of the Appointment of Independent Registered Public Accounting Firm* in our definitive proxy statement for our 2024 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) Documents filed as part of this report.

1. FINANCIAL STATEMENTS. The following consolidated financial statements of the Company are set forth herein, beginning on page 87:

(i) Reports of Independent Registered Public Accounting Firm (PCAOB ID: 42)

(ii) Consolidated Balance Sheets as of December 31, 2023 and 2022

(iii) Consolidated Statements of Comprehensive Loss for the Years Ended December 31, 2023, 2022 and 2021

(iv) Consolidated Statements of Shareholders' Equity for the Years Ended December 31, 2023, 2022 and 2021

(v) Consolidated Statements of Cash Flows for the Years Ended December 31, 2023, 2022 and 2021

(vi) Notes to Consolidated Financial Statements

2. FINANCIAL STATEMENT SCHEDULES.

None required.

3. EXHIBITS.

The exhibits that are required to be filed or incorporated by reference herein are listed in the Exhibit Index.

EXHIBIT INDEX

3.1	Articles of Incorporation of Insmed Incorporated, as amended through June 14, 2012 (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Annual Report on Form 10-K filed on March 18, 2013).
3.2	Amended and Restated Bylaws of Insmed Incorporated (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Current Report on Form 8-K filed on May 11, 2023).
4.1	Specimen stock certificate representing common stock, $0.01 par value per share, of the Registrant (incorporated by reference from Exhibit 4.2 to Insmed Incorporated's Registration Statement on Form S-4/A (Registration No. 333-30098) filed on March 24, 2000).
4.2	Indenture, dated as of January 26, 2018, by and between the Company and Wells Fargo Bank, National Association (incorporated by reference from Exhibit 4.1 to Insmed Incorporated’s Current Report on Form 8-K filed on January 26, 2018).
4.3	First Supplemental Indenture, dated as of January 26, 2018, by and between the Company and Wells Fargo Bank, National Association (incorporated by reference from Exhibit 4.2 to Insmed Incorporated’s Current Report on Form 8-K filed on January 26, 2018).
4.4	Second Supplemental Indenture, dated as of May 13, 2021, by and between the Company and Wells Fargo Bank, National Association (incorporated by reference from Exhibit 4.2 to Insmed Incorporated’s Current Report on Form 8-K filed on May 13, 2021).
4.5	Form of 1.75% Convertible Senior Note due 2025 (included in Exhibit 4.3).
4.6	Form of 0.75% Convertible Senior Note due 2028 (included in Exhibit 4.4).
4.7	Description of Securities Registered Under Section 12 of the Securities Exchange Act of 1934 (incorporated by reference from Exhibit 4.5 of Insmed Incorporated’s Annual Report on Form 10-K filed on February 25, 2021).
10.1**	Insmed Incorporated Amended and Restated 2000 Stock Incentive Plan (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on May 8, 2013).
10.2**	Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 99.1 to Insmed Incorporated's Registration Statement on Form S-8 filed on May 24, 2013).

10.2.1**	Form of Award Agreement for Incentive Stock Options pursuant to the Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 10.5 to Insmed Incorporated's Annual Report on Form 10-K filed on March 6, 2014).
10.2.2**	Form of Award Agreement for Non-Qualified Stock Options pursuant to the Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 10.6 to Insmed Incorporated's Annual Report on Form 10-K filed on March 6, 2014).
10.3**	Insmed Incorporated 2015 Incentive Plan (incorporated by reference from Exhibit 99.1 to Insmed Incorporated's Registration Statement on Form S-8 filed on May 28, 2015).
10.3.1**	Form of Award Agreement for Non-Qualified Stock Options pursuant to the Insmed Incorporated 2015 Incentive Plan (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Quarterly Report on Form 10-Q filed May 3, 2017).
10.4**	Insmed Incorporated 2017 Incentive Plan (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Quarterly Report on Form 10-Q filed August 3, 2017).
10.4.1**	Form of Award Agreements for Restricted Stock Units pursuant to the Insmed Incorporated 2017 Incentive Plan (incorporated by reference from Exhibit 10.4 to Insmed Incorporated's Quarterly Report on Form 10-Q filed August 3, 2017).
10.4.2**	Amendment to Form of Award Agreement for Restricted Stock Units pursuant to the Insmed Incorporated 2017 Incentive Plan (incorporated by reference from Exhibit 10.4.2 to Insmed Incorporated's Annual Report on Form 10-K filed on February 17, 2022).
10.4.3**	Form of Award Agreement for Non-Qualified Stock Options pursuant to the Insmed Incorporated 2017 Incentive Plan (incorporated by reference from Exhibit 10.5 to Insmed Incorporated's Quarterly Report on Form 10-Q filed August 3, 2017).
10.5**	Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Appendix A to Insmed Incorporated's Proxy Statement on Schedule 14A, filed on March 31, 2023).
10.5.1**	Form of Award Agreement for Restricted Stock Units pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.3 of Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).
10.5.2**	Form of Award Agreement for Restricted Stock Units to non-US employees pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.4 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).
10.5.3**	Form of Award Agreement for Non-Qualified Stock Options pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.1 of Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).
10.5.4**	Form of Award Agreement for Non-Qualified Stock Options issued to non-US employees pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.2 of Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).
10.5.5**	Form of Award Agreement for Restricted Stock Units issued to directors pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.5 of Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).
10.5.6**	Form of Award Agreement for Performance-Based Restricted Stock Units pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.6 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).
10.5.7**	Form of Award Agreement for Performance-Based Restricted Stock Units to non-US employees pursuant to the Insmed Incorporated Amended and Restated 2019 Incentive Plan (incorporated by reference from Exhibit 10.1.7 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 3, 2023).

10.6**	Omnibus Amendment to Insmed Incorporated Incentive Plans, dated December 10, 2020 (incorporated by reference from Exhibit 10.6 of Insmed Incorporated's Annual Report on Form 10-K filed on February 25, 2021).
10.7**	Insmed Incorporated Senior Executive Bonus Plan (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on November 5, 2013).
10.8**	Form of Non-Qualified Stock Option Inducement Award Agreement (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed May 4, 2023).
10.9**	Form of Non-Qualified Stock Option Inducement Award Agreement for non-U.S. employees (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Quarterly Report on Form 10-Q filed May 4, 2023).
10.10**	Form of Indemnification Agreement entered into with each of the Company's directors and officers (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on January 16, 2014).
10.11**	Employment Agreement, effective as of September 10, 2012, between Insmed Incorporated and William Lewis (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on September 11, 2012).
10.11.1**	Amendment to Employment Agreement, effective as of July 31, 2019, between Insmed Incorporated and William Lewis (incorporated by reference from Exhibit 10.5 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 1, 2019).
10.12**	Amended and Restated Employment Agreement, effective as of April 1, 2022, between Insmed Incorporated and S. Nicole Schaeffer (incorporated by reference from Exhibit 10.4 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on May 5, 2022).
10.13**	Amended and Restated Employment Agreement, effective as of April 1, 2022, between Insmed Incorporated and Roger Adsett (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed May 5, 2022).
10.13.1**	Side Letter to Amended and Restated Employment Agreement, effective as of August 8, 2022, between Insmed Incorporated and Roger Adsett (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Quarterly Report on Form 10-Q filed October 27, 2022).
10.14**	Amended and Restated Employment Agreement, effective as of April 1, 2022, between Insmed Incorporated and Sara Bonstein (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Annual Report on Form 10-Q filed May 5, 2022).
10.15**	Amended and Restated Employment Agreement, effective as of April 1, 2022, by and between Insmed Incorporated and Martina Flammer, M.D. (incorporated by reference from Exhibit 10.3 of Insmed Incorporated's Quarterly Report on Form 10-Q filed May 5, 2022).
10.16**	Amended and Restated Employment Agreement, effective as of April 1, 2022, by and between Insmed Incorporated and Michael Smith (incorporated by reference from Exhibit 10.5 of Insmed Incorporated's Quarterly Report on Form 10-Q filed May 5, 2022).
10.17**	Employment Agreement, effective as of May 23, 2022, by and between Insmed Incorporated and J. Drayton Wise (incorporated by reference from Exhibit 10.1 of Insmed Incorporated's Quarterly Report on Form 10-Q filed August 4, 2022).
10.18*	License Agreement, dated April 25, 2008, between Transave, Inc. and PARI Pharma GmbH, and Amendments No. 1-4 thereto (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on October 29, 2020).
10.18.1*	Amendment No. 5 to License Agreement between Insmed Incorporated and PARI Pharma GmbH, effective as of October 5, 2015 (incorporated by reference from Exhibit 10.14.1 to Insmed Incorporated's Annual Report on Form 10-K filed on February 25, 2016).
10.18.2*	Amendment No. 6 to License Agreement between Insmed Incorporated and PARI Pharma GmbH, effective as of October 9, 2015 (incorporated by reference from Exhibit 10.14.2 to Insmed Incorporated's Annual Report on Form 10-K filed on February 25, 2016).

10.18.3*	Amendment No. 7 to License Agreement between Insmed Incorporated and PARI Pharma GmbH, effective as of July 21, 2017 (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on November 2, 2017).
10.18.4*	Amendment No. 8 to License Agreement between Insmed Incorporated and PARI Pharma GmbH, effective as of December 19, 2018 (incorporated by reference from Exhibit 10.15.4 to Insmed Incorporated's Annual Report on Form 10-K filed on February 22, 2019).
10.19*	Contract Manufacturing Agreement, dated February 7, 2014, between Insmed Incorporated and Resilience Biotechnologies Inc. (successor to Therapure Biopharma Inc.) (incorporated by reference from Exhibit 10.2.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on October 29, 2020).
10.19.1*	Amending Agreement, dated March 13, 2014, between Insmed Incorporated and Resilience Biotechnologies Inc. (successor to Therapure Biopharma Inc.) (incorporated by reference from Exhibit 10.2.2 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on October 29, 2020).
10.20*	Commercialization Agreement dated July 8, 2014 between Insmed Incorporated and PARI Pharma GmbH (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on November 6, 2014).
10.20.1*	Amendment No. 1 to Commercialization Agreement between Insmed Incorporated and PARI Pharma GmbH, effective as of July 21, 2017 (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on November 2, 2017).
10.21*	Manufacturing and Supply Agreement between Insmed Incorporated and Patheon UK Limited, dated as of October 20, 2017 (incorporated by reference from Exhibit 10.39 to Insmed Incorporated's Annual Report on Form 10-K filed February 23, 2018).
10.22*	Technology Transfer Agreement between Insmed Incorporated and Patheon UK Limited, dated as of October 20, 2017 (incorporated by reference from Exhibit 10.40 to Insmed Incorporated's Annual Report on Form 10-K filed February 23, 2018).
10.22.1*	Amendment to the Technology Transfer Agreement and to the Manufacturing and Supply Agreement, by and between Insmed Incorporated and Patheon UK Limited, dated as of March 11, 2021 (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Quarterly Report on Form 10-Q filed May 6, 2021).
10.23*	License Agreement, dated October 4, 2016, between Insmed Incorporated and AstraZeneca AB (incorporated by reference from Exhibit 10.29 to Insmed Incorporated's Annual Report on Form 10-K filed February 23, 2017).
10.24	Lease Agreement, dated September 11, 2018, by and between Insmed Incorporated and Exeter 700 Route 202/206, LLC (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on September 17, 2018).
10.25	Sales Agreement, dated as of February 25, 2021, by and between Insmed Incorporated and SVB Leerink LLC (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on February 25, 2021).
10.26*	Revenue Interest Purchase Agreement, dated October 19, 2022, between Insmed Incorporated and OrbiMed Royalty & Credit Opportunities III, LP (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on October 27, 2022).
10.27*	Loan Agreement, dated October 19, 2022, between Insmed Incorporated, BioPharma Credit PLC, BPCR Limited Partnership and BioPharma Credit Investments V (Master) LP (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on October 27, 2022).
21.1	Subsidiaries of Insmed Incorporated (filed herewith).
23.1	Consent of Ernst & Young LLP (filed herewith).
31.1	Certification of William H. Lewis, Chair and Chief Executive Officer (Principal Executive Officer) of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes Oxley Act of 2003 (filed herewith).

31.2	Certification of Sara Bonstein, Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer) of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes Oxley Act of 2003 (filed herewith).
32.1	Certification of William H. Lewis, Chair and Chief Executive Officer (Principal Executive Officer) of Insmed Incorporated, pursuant to 18 USC Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2003 (filed herewith).
32.2	Certification of Sara Bonstein, Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer) of Insmed Incorporated, pursuant to 18 USC Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2003 (filed herewith).
97	Compensation Recovery Policy (filed herewith).
101	The following materials from Insmed Incorporated's Annual Report on Form 10-K for the year ended December 31, 2023 formatted in iXBRL (Inline eXtensible Business Reporting Language): (i) Consolidated Balance Sheets as of December 31, 2023 and 2022, (ii) Consolidated Statements of Comprehensive Loss for the years ended December 31, 2023, 2022 and 2021, (iii) Consolidated Statements of Shareholders' Equity for the years ended December 31, 2023, 2022 and 2021, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2023, 2022, and 2021, and (v) Notes to the Consolidated Financial Statements, and (vi) Cover Page.
104	The cover page from the Annual Report on Form 10-K for the year ended December 31, 2023, formatted in iXBRL and contained in Exhibit 101.
*	Certain portions of this exhibit have been redacted.
**	Management contract or compensatory plan or arrangement.

ITEM 16. FORM 10-K SUMMARY

Not applicable.

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 22, 2024.

INSMED INCORPORATED
a Virginia corporation
(Registrant)

By: /s/ WILLIAM H. LEWIS

William H. Lewis
Chair and Chief Executive Officer
(Principal Executive Officer)

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 indicated on February 22, 2024.

Signature	Title
/s/ WILLIAM H. LEWIS William H. Lewis	Chair and Chief Executive Officer (Principal Executive Officer)
/s/ SARA BONSTEIN Sara Bonstein	Chief Financial Officer (Principal Financial and Accounting Officer)
/s/ DAVID R. BRENNAN David R. Brennan	Lead Independent Director
/s/ ALFRED F. ALTOMARI Alfred F. Altomari	Director
/s/ ELIZABETH MCKEE ANDERSON Elizabeth McKee Anderson	Director
/s/ CLARISSA DESJARDINS, PH.D. Clarissa Desjardins, Ph.D.	Director
/s/ LEO LEE Leo Lee	Director
/s/ DAVID W.J. MCGIRR David W.J. McGirr	Director
/s/ CAROL A. SCHAFER Carol A. Schafer	Director
/s/ MELVIN SHAROKY, M.D. Melvin Sharoky, M.D.	Director

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Insmed Incorporated

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Insmed Incorporated (the Company) as of December 31, 2023 and 2022, the related consolidated statements of comprehensive loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 22, 2024 expressed an unqualified opinion thereon.

Adoption of ASU No. 2020-06

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for convertible notes in 2022 due to the adoption of Accounting Standards Update (ASU) No. 2020-06, Debt— (Subtopic 470-20 & 815-40), and the related amendments.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the account or disclosure to which it relates.

Variable consideration in contracts with customers

Description of the Matter	As discussed in Note 4 of the consolidated financial statements, the transaction price for product sales is typically adjusted for variable consideration, which includes rebates paid to government agencies, specifically Medicaid. The Company estimates these reserves based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. Auditing the Company's estimate of variable consideration for amounts to be paid to government agencies was complex and judgmental due to uncertainty about the ultimate third-party payor at the time of shipment to the specialty pharmacies and the amounts of rebates to be paid to those government agencies. The transaction price is sensitive to assumptions used in the rebate calculations.
How We Addressed the Matter in Our Audit	We identified, evaluated and tested controls over management's review of the calculated reductions to gross product prices related to government agencies including management's review of the significant assumptions and the data utilized in its calculations. To test the revenue adjustments related to government agencies our audit procedures included, among others, using internal specialists to assist with recalculating government rebates. We also tested the underlying data and inputs used by the Company in its determination of the estimated payor mix. We compared the inputs used by management to historical trends, evaluated the change in the estimated rebates amounts recorded throughout the year and assessed the historical accuracy of management's estimates against actual results.

/s/ Ernst & Young LLP

We have served as the Company's auditor since at least 1999, but we are unable to determine the specific year.

Iselin, New Jersey
February 22, 2024

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Insmed Incorporated

Opinion on Internal Control Over Financial Reporting

We have audited Insmed Incorporated's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Insmed Incorporated (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2023 and 2022, the related consolidated statements of comprehensive loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2023, and the related notes and our report dated February 22, 2024 expressed an unqualified opinion.

Basis for Opinion

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

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

Iselin, New Jersey
February 22, 2024

INSMED INCORPORATED
Consolidated Balance Sheets
(in thousands, except par value and share data)

	As of December 31,	
	2023	**2022**
Assets		
Current assets:		
Cash and cash equivalents	$ 482,374	$ 1,074,036
Marketable securities	298,073	74,244
Accounts receivable	41,189	29,713
Inventory	83,248	69,922
Prepaid expenses and other current assets	24,179	25,468
Total current assets	929,063	1,273,383
Fixed assets, net	65,384	56,491
Finance lease right-of-use assets	20,985	23,697
Operating lease right-of-use assets	18,017	21,894
Intangibles, net	63,704	68,756
Goodwill	136,110	136,110
Other assets	96,574	76,104
Total assets	$ 1,329,837	$ 1,656,435
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable and accrued liabilities	$ 214,987	$ 182,117
Finance lease liabilities	2,610	1,217
Operating lease liabilities	8,032	6,909
Total current liabilities	225,629	190,243
Debt, long-term	1,155,313	1,125,250
Royalty financing agreement	155,034	148,015
Contingent consideration	84,600	51,100
Finance lease liabilities, long-term	27,026	29,636
Operating lease liabilities, long-term	11,013	14,853
Other long-term liabilities	3,145	9,387
Total liabilities	1,661,760	1,568,484
Shareholders' equity:		
Common stock, $0.01 par value; 500,000,000 authorized shares, 147,977,960 and 135,653,731 issued and outstanding shares at December 31, 2023 and December 31, 2022, respectively	1,480	1,357
Additional paid-in capital	3,113,487	2,782,416
Accumulated deficit	(3,446,145)	(2,696,578)
Accumulated other comprehensive (loss) income	(745)	756
Total shareholders' (deficit) equity	(331,923)	87,951
Total liabilities and shareholders' equity	$ 1,329,837	$ 1,656,435

See accompanying notes to consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Comprehensive Loss
(in thousands, except per share data)

	Years Ended December 31,		
	2023	**2022**	**2021**
Product revenues, net	$ 305,208	$ 245,358	$ 188,461
Operating expenses:			
Cost of product revenues (excluding amortization of intangible assets)	65,573	55,126	44,152
Research and development	571,011	397,518	272,744
Selling, general and administrative	344,501	265,784	234,273
Amortization of intangible assets	5,052	5,053	5,052
Change in fair value of deferred and contingent consideration liabilities	28,697	(20,802)	7,334
Total operating expenses	1,014,834	702,679	563,555
Operating loss	(709,626)	(457,321)	(375,094)
Investment income	42,132	11,081	174
Interest expense	(81,694)	(26,446)	(40,473)
Change in fair value of interest rate swap	320	(1,526)	—
Loss on extinguishment of debt	—	—	(17,689)
Other income (expense), net	1,856	(5,939)	(3,330)
Loss before income taxes	(747,012)	(480,151)	(436,412)
Provision (benefit) for income taxes	2,555	1,383	(1,758)
Net loss	$ (749,567)	$ (481,534)	$ (434,654)
Basic and diluted net loss per share	$ (5.34)	$ (3.91)	$ (3.88)
Weighted average basic and diluted common shares outstanding	140,433	123,035	112,111
Net loss	$ (749,567)	$ (481,534)	$ (434,654)
Other comprehensive income (loss):			
Foreign currency translation and other (losses) gains	(2,214)	303	775
Unrealized gain (loss) on marketable securities	713	(515)	—
Total comprehensive loss	$ (751,068)	$ (481,746)	$ (433,879)

See accompanying notes to audited consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Shareholders' Equity
(in thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
	Shares	Amount				
Balance at December 31, 2020	102,763	$ 1,028	$ 2,105,252	$ (1,830,589)	$ 193	$ 275,884
Comprehensive loss:						
Net loss				(434,654)		(434,654)
Other comprehensive income					775	775
Exercise of stock options and ESPP shares issuance	1,359	13	22,022			22,035
Net proceeds from issuance of common stock	11,500	115	269,771			269,886
Equity component of convertible debt issuance			196,358			196,358
Equity component of convertible debt redemption			(37,846)			(37,846)
Issuance of common stock for vesting of RSUs	217	2				2
Issuance of common stock for Business Acquisition	2,899	29	71,978			72,007
Stock-based compensation expense			46,021			46,021
Balance at December 31, 2021	118,738	$ 1,187	$ 2,673,556	$ (2,265,243)	$ 968	$ 410,468
Cumulative impact of ASU 2020-06 adoption			(264,609)	50,199		(214,410)
Comprehensive loss:						
Net loss				(481,534)		(481,534)
Other comprehensive loss					(212)	(212)
Exercise of stock options and ESPP shares issuance	1,328	14	19,486			19,500
Net proceeds from issuance of common stock	15,040	150	292,003			292,153
Issuance of common stock for vesting of RSUs	377	4				4
Deferred payment for Business Acquisition	171	2	4,294			4,296
Stock-based compensation expense			57,686			57,686
Balance at December 31, 2022	135,654	$ 1,357	$ 2,782,416	$ (2,696,578)	$ 756	$ 87,951
Comprehensive loss:						
Net loss				(749,567)		(749,567)
Other comprehensive loss					(1,501)	(1,501)
Exercise of stock options and ESPP shares issuance	1,142	12	18,387			18,399
Net proceeds from issuance of common stock	6,531	65	152,410			152,475
Issuance of common stock for vesting of RSUs	543	5				5
Deferred payment for Business Acquisition	177	2	3,895			3,897
Issuance of common stock for asset acquisitions	3,931	39	81,601			81,640
Stock-based compensation expense			74,778			74,778
Balance at December 31, 2023	147,978	$ 1,480	$ 3,113,487	$ (3,446,145)	$ (745)	$ (331,923)

See accompanying notes to audited consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2023	**2022**	**2021**
Operating activities			
Net loss	$(749,567)	$(481,534)	$(434,654)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	5,527	5,278	9,130
Amortization of intangible assets	5,052	5,053	5,052
Stock-based compensation expense	74,778	57,686	46,021
Loss on extinguishment of debt	—	—	17,689
Amortization of debt issuance costs	7,320	3,991	1,890
Accretion of debt discount	—	—	29,149
Paid-in-kind interest capitalized	23,372	4,165	—
Royalty Financing non-cash interest expense	18,846	3,687	—
Accretion of discount on marketable securities, net	(9,383)	—	—
Finance lease amortization expense	2,712	1,960	1,078
Non-cash operating lease expense	9,206	11,976	12,589
Change in fair value of deferred and contingent consideration liabilities	28,697	(20,802)	7,334
Change in fair value of interest rate swap	(320)	1,526	—
Vertuis acquisition	10,250	—	—
Adrestia acquisition	76,481	—	—
Changes in operating assets and liabilities:			
Accounts receivable	(11,963)	(6,423)	(8,118)
Inventory	(13,613)	(1,714)	(17,456)
Prepaid expenses and other current assets	2,265	2,528	(5,549)
Other assets	(20,074)	(25,243)	(24,435)
Accounts payable and accrued liabilities	15,155	50,011	(7,575)
Other liabilities	(10,988)	(12,584)	4,553
Net cash used in operating activities	(536,247)	(400,439)	(363,302)
Investing activities			
Purchase of fixed assets	(13,288)	(9,878)	(7,289)
Purchase of marketable securities	(588,733)	(99,706)	(50,292)
Cash acquired in asset acquisition	3,417	—	—
Maturities of marketable securities	375,000	75,000	—
Cash paid for Business Acquisition, net	—	—	(6,704)
Net cash used in investing activities	(223,604)	(34,584)	(64,285)
Financing activities			
Proceeds from exercise of stock options and ESPP	18,399	19,504	22,037
Proceeds from issuance of common stock, net	152,475	292,153	269,886
Payment on extinguishment of 1.75% convertible senior notes due 2025	—	—	(12,578)
Payment of principal of 1.75% convertible senior notes due 2025	—	—	(225,000)
Proceeds from issuance of 0.75% convertible senior notes due 2028	—	—	575,000
Proceeds from issuance of Term Loan	—	350,000	—
Proceeds from issuance Royalty Financing Agreement	—	150,000	—

INSMED INCORPORATED
Consolidated Statements of Cash Flows
(in thousands)

Payment of debt issuance costs	(1,218)	(17,783)	(15,718)
Payments of finance lease principal	(1,217)	(601)	(1,081)
Net cash provided by financing activities	168,439	793,273	612,546
Effect of exchange rates on cash and cash equivalents	(250)	(996)	(933)
Net (decrease) increase in cash and cash equivalents	(591,662)	357,254	184,026
Cash and cash equivalents at beginning of period	1,074,036	716,782	532,756
Cash and cash equivalents at end of period	$ 482,374	$1,074,036	$ 716,782
Supplemental disclosures of cash flow information:			
Cash paid for interest	$ 35,787	$ 10,157	$ 10,890
Cash paid for income taxes	$ 1,955	$ 1,717	$ 1,558

See accompanying notes to audited consolidated financial statements

1. The Company and Basis of Presentation

Insmed is a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. The Company's first commercial product, ARIKAYCE, is approved in the US as ARIKAYCE® (amikacin liposome inhalation suspension), in Europe as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion and in Japan as ARIKAYCE inhalation 590mg (amikacin sulfate inhalation drug product). ARIKAYCE received accelerated approval in the US in September 2018 for the treatment of MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options in a refractory setting. In October 2020, the EC approved ARIKAYCE for the treatment of NTM lung infections caused by MAC in adults with limited treatment options who do not have CF. In March 2021, Japan's MHLW approved ARIKAYCE for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen. NTM lung disease caused by MAC (which the Company refers to as MAC lung disease) is a rare and often chronic infection that can cause irreversible lung damage and can be fatal. The Company's pipeline includes brensocatib, TPIP and early-stage research programs. Brensocatib is a small molecule, oral, reversible inhibitor of DPP1, which the Company is developing for the treatment of patients with bronchiectasis and other neutrophil-mediated diseases, including CRSsNP. TPIP is an inhaled formulation of the treprostinil prodrug treprostinil palmitil which may offer a differentiated product profile for PH-ILD and PAH. The Company is also advancing its early-stage research programs encompassing a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA-end joining, and synthetic rescue.

The Company was incorporated in the Commonwealth of Virginia on November 29, 1999 and its principal executive offices are located in Bridgewater, New Jersey. The Company has legal entities in the US, France, Germany, Ireland, Italy, the Netherlands, Switzerland, the UK, and Japan.

The Company had $482.4 million in cash and cash equivalents and $298.1 million of marketable securities as of December 31, 2023 and reported a net loss of $749.6 million for the year ended December 31, 2023. The Company has funded its operations through public offerings of equity securities, debt financings and revenue interest financings. The Company expects to continue to incur consolidated operating losses, including losses in its US and certain international entities, while funding R&D activities for ARIKAYCE, brensocatib, TPIP and its other pipeline programs, continuing commercialization and regulatory activities for ARIKAYCE and pre-commercial, regulatory and, if approved, commercialization activities for brensocatib, and funding other general and administrative activities.

The Company expects its future cash requirements to be substantial. While the Company currently has sufficient funds to meet its financial needs for at least the next 12 months, the Company may raise additional capital in the future to fund its operations, its ongoing commercialization and clinical trial activities, and its future product candidates, and to develop, acquire, in-license or co-promote other products or product candidates, including those that address orphan or rare diseases. The source, timing and availability of any future financing or other transaction will depend principally upon continued progress in the Company’s commercial, regulatory and development activities. Any future financing will also be contingent upon market conditions. If the Company is unable to obtain sufficient additional funds when required, the Company may be forced to delay, restrict or eliminate all or a portion of its development programs or commercialization efforts.

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Celtrix Pharmaceuticals, Inc., Insmed Holdings Limited, Insmed Gene Therapy LLC, Insmed Ireland Limited, Insmed France SAS, Insmed Germany GmbH, Insmed Limited, Insmed Netherlands Holdings B.V., Insmed Netherlands B.V., Insmed Godo Kaisha, Insmed Switzerland GmbH, Insmed Italy S.R.L., Insmed Innovation UK Limited, and Adrestia Therapeutics Inc. All intercompany transactions and balances have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates—The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions. The amounts of assets and liabilities reported in the Company's balance sheets and the amounts of revenues and expenses reported for each period presented are affected by estimates and assumptions, which are used for, but not limited to, the accounting for revenue allowances, stock-based compensation, income taxes, loss contingencies, acquisition related intangibles including in process research and development (IPR&D) and goodwill, fair value of contingent consideration, and accounting for research and development costs. Actual results could differ from those estimates.

2. Summary of Significant Accounting Policies (Continued)

Cash and Cash Equivalents—The Company considers cash equivalents to be highly liquid investments with maturities of three months or less from the date of purchase.

Accounts Receivable—Accounts receivable are recorded net of customer allowances for prompt pay discounts, chargebacks, and any estimated expected credit losses. The Company's measurement of expected credit losses is based on relevant information about past events, including historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount. To date, credit losses have not been material.

Marketable Securities—Marketable securities consists of available-for-sale investments in US Treasury Notes with an original maturity of greater than 90 days. Marketable securities under this classification are recorded at fair value and unrealized gains and losses are recorded within accumulated other comprehensive (loss) income. The estimated fair value of available-for-sale marketable securities is determined based on quoted market prices. Marketable securities maturing in one year or less are classified as current assets and marketable securities maturing in more than one year are classified as non-current assets. The Company did not have available-for-sale securities with a maturity of more than one year as of December 31, 2023. As of December 31, 2022, management did not expect the Company's available-for-sale securities with a maturity of more than one year to be sold or redeemed within the next year and therefore has classified the marketable securities as long-term assets in the consolidated balance sheet.

Fixed Assets, Net—Fixed assets are recorded at cost and are depreciated on a straight-line basis over the estimated useful lives of the assets. Estimated useful lives of three years to five years are used for computer equipment. Estimated useful lives of seven years are used for laboratory equipment, office equipment, manufacturing equipment and furniture and fixtures. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

Finite-lived Intangible Assets—Finite-lived intangible assets are measured at their respective fair values on the date they were recorded. The fair values assigned to the Company's intangible assets are based on reasonable estimates and assumptions given available facts and circumstances. See *Note 6 - Intangibles, Net and Goodwill* for further details.

Impairment Assessment—The Company reviews the recoverability of its finite-lived intangible assets and long-lived assets for indicators of impairments. Events or circumstances that may require an impairment assessment include negative clinical trial results, a significant decrease in the market price of the asset, or a significant adverse change in legal factors or the manner in which the asset is used. If such indicators are present, the Company assesses the recoverability of affected assets by determining if the carrying value of such assets is less than the sum of the undiscounted future cash flows of the assets. If such assets are found to not be recoverable, the Company measures the amount of the impairment by comparing the carrying value of the assets to the fair value of the assets. The Company determined that no indicators of impairment of finite-lived intangible assets or long-lived assets existed at December 31, 2023.

Business Combinations and Asset Acquisitions—The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen to determine if substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If the screen is met, the transaction is accounted for as an asset acquisition. If the screen is not met, further determination is required as to whether or not the Company has acquired inputs and processes that have the ability to create outputs, which would meet the requirements of a business. If determined to be a business combination, the Company accounts for the transaction under the acquisition method of accounting as indicated in Accounting Standards Update (ASU) 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business, which requires the acquiring entity in a business combination to recognize the fair value of all assets acquired, liabilities assumed, and any non-controlling interest in the acquiree and establishes the acquisition date as the fair value measurement point. Accordingly, the Company recognizes assets acquired and liabilities assumed in business combinations, including contingent assets and liabilities, and non-controlling interest in the acquiree based on the fair value estimates as of the date of acquisition. In accordance with ASC 805, Business Combinations, the Company recognizes and measures goodwill as of the acquisition date, as the excess of the fair value of the consideration paid over the fair value of the identified net assets acquired.

The consideration for the Company’s business acquisitions may include future payments that are contingent upon the occurrence of a particular event or events. The obligations for such contingent consideration payments are recorded at fair value on the acquisition date. The contingent consideration obligations are then evaluated each reporting period. Changes in the fair value of contingent consideration, other than changes due to payments, are recognized as a gain or loss and recorded within change in the fair value of deferred and contingent consideration liabilities in the consolidated statements of comprehensive loss.

2. Summary of Significant Accounting Policies (Continued)

If determined to be an asset acquisition, the Company accounts for the transaction under ASC 805-50, which requires the acquiring entity in an asset acquisition to recognize assets acquired and liabilities assumed based on the cost to the acquiring entity on a relative fair value basis, which includes transaction costs in addition to consideration given. No gain or loss is recognized as of the date of acquisition unless the fair value of non-cash assets given as consideration differs from the assets' carrying amounts on the acquiring entity's books. Consideration transferred that is non-cash will be measured based on either the cost (which shall be measured based on the fair value of the consideration given) or the fair value of the assets acquired and liabilities assumed, whichever is more reliably measurable. Goodwill is not recognized in an asset acquisition and any excess consideration transferred over the fair value of the net assets acquired is allocated to the identifiable assets based on relative fair values. If the in-licensed agreement for IPR&D does not meet the definition of a business and the assets have not reached technological feasibility and therefore have no alternative future use, the Company expenses payments made under such license agreements as acquired IPR&D expense in its consolidated statements of comprehensive loss.

Contingent consideration payments in asset acquisitions are recognized when the contingency is resolved and the consideration is paid or becomes payable, unless the contingent consideration meets the definition of a derivative, in which case the amount becomes part of the basis in the asset acquired. None of the Company's contingent consideration met the definition of a derivative. Upon recognition of the contingent consideration payment, the amount is included in the cost of the acquired asset or group of assets.

Indefinite-lived Intangible Assets—Indefinite-lived intangible assets consist of IPR&D. IPR&D acquired directly in a transaction other than a business combination is capitalized if the projects will be further developed or have an alternative future use; otherwise, they are expensed. The fair values of IPR&D project assets acquired in business combinations are capitalized. The Company generally utilizes the Multi-Period Excess Earning Method to determine the estimated fair value of the IPR&D assets acquired in a business combination. The projections used in this valuation approach are based on many factors, such as relevant market size, patent protection, and expected pricing and industry trends. The estimated future net cash flows are then discounted to the present value using an appropriate discount rate. These assets are treated as indefinite-lived intangible assets until completion or abandonment of the projects, at which time the assets are amortized over the remaining useful life or written off, as appropriate. Intangible assets with indefinite lives, including IPR&D, are tested for impairment if impairment indicators arise and, at a minimum, annually. However, an entity is permitted to first assess qualitative factors to determine if a quantitative impairment test is necessary. Further testing is only required if the entity determines, based on the qualitative assessment, that it is more likely than not that an indefinite-lived intangible asset's fair value is less than its carrying amount. The indefinite-lived intangible asset impairment test consists of a one-step analysis that compares the fair value of the intangible asset with its carrying amount. If the carrying amount of an intangible asset exceeds its fair value, an impairment loss is recognized in an amount equal to that excess. The Company considers many factors in evaluating whether the value of its intangible assets with indefinite lives may not be recoverable, including, but not limited to, expected growth rates, the cost of equity and debt capital, general economic conditions, the Company's outlook and market performance of the Company's industry and recent and forecasted financial performance. The Company performs a qualitative test for its indefinite-lived intangible assets annually as of October 1. During the year ended December 31, 2023, the Company concluded that no impairment exists.

Goodwill—Goodwill represents the amount of consideration paid in excess of the fair value of net assets acquired as a result of the Company's business acquisitions accounted for using the acquisition method of accounting. Goodwill is not amortized and is subject to impairment testing at a reporting unit level on an annual basis or when a triggering event occurs that may indicate the carrying value of the goodwill is impaired. An entity is permitted to first assess qualitative factors to determine if a quantitative impairment test is necessary. Further testing is only required if the entity determines, based on the qualitative assessment, that it is more likely than not that the fair value of the reporting unit is less than its carrying amount. The Company reassesses its reporting units as part of its annual segment review. As of December 31, 2023, the Company concluded that it continues to operate as one reporting unit. As of October 1, 2023, the Company's single reporting unit for purposes of its goodwill impairment test had a negative carrying value and the Company performed a qualitative impairment test for goodwill. During the year ended December 31, 2023, the Company concluded that no impairment exists.

Leases—A lease is a contract, or part of a contract, that conveys the right to control the use of explicitly or implicitly identified property, plant or equipment in exchange for consideration. Control of an asset is conveyed to the Company if the Company obtains the right to obtain substantially all of the economic benefits of the asset or the right to direct the use of the asset. The Company recognizes right-of-use (ROU) assets and lease liabilities at the lease commencement date based on the present value of future, fixed lease payments over the term of the arrangement. ROU assets are amortized on a straight-line basis over the term of the lease or are amortized based on consumption, if this approach is more representative of the pattern in which benefit is expected to be derived from the underlying asset. Lease liabilities accrete to yield and are reduced at the time

2. Summary of Significant Accounting Policies (Continued)

when the lease payment is payable to the vendor. Variable lease payments are recognized at the time when the event giving rise to the payment occurs and are recognized in the consolidated statements of comprehensive loss in the same line item as expenses arising from fixed lease payments.

Leases are measured at present value using the rate implicit in the lease or, if the implicit rate is not determinable, the lessee's implicit borrowing rate. As the implicit rate is not typically available, the Company uses its implicit borrowing rate based on the information available at the lease commencement date to determine the present value of future lease payments. The implicit borrowing rate approximates the rate the Company would pay to borrow on a collateralized basis over a similar term an amount equal to the lease payments. See *Note 9 - Leases* for further details.

Debt Issuance Costs—Debt issuance costs are amortized to interest expense using the effective interest rate method over the term of the debt. Unamortized debt issuance costs paid to the lender and third parties are reflected as a discount to the debt in the consolidated balance sheets. Unamortized debt issuance costs associated with extinguished debt are expensed in the period of the extinguishment.

Foreign Currency—The Company has operations in the US, France, Germany, Ireland, Italy, the Netherlands, Switzerland, the UK, and Japan. The results of the Company's non-US dollar based functional currency operations are translated to US dollars at the average exchange rates during the period. Assets and liabilities are translated at the exchange rate prevailing at the balance sheet date. Equity is translated at the prevailing exchange rate at the date of the equity transaction. Translation adjustments are included in shareholders' (deficit) equity, as a component of accumulated other comprehensive (loss) income.

The Company realizes foreign currency transaction gains and losses in the normal course of business based on movements in the applicable exchange rates. These gains and losses are included as a component of other (expense) income, net.

Derivatives—In the normal course of business, the Company is exposed to the effects of interest rate changes. The Company may enter into derivative instruments, including interest rate swaps and caps, to manage or hedge interest rate risk. Derivative instruments are recorded at fair value on the balance sheet date. The Company has not elected hedge accounting treatment for the changes in the fair value of derivatives. Changes in the fair value of derivatives are recorded each period and are included in change in fair value of interest rate swap in the consolidated statements of comprehensive loss and consolidated statements of cash flows.

Concentration of Credit Risk—Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company places its cash equivalents with high credit-quality financial institutions and may invest its short-term investments in US treasury securities, mutual funds and government agency bonds. The Company has established guidelines relative to credit ratings and maturities that seek to maintain safety and liquidity.

The Company is exposed to risks associated with extending credit to customers related to the sale of products. The Company does not require collateral to secure amounts due from its customers. The Company uses an expected loss methodology to calculate allowances for trade receivables. The Company's measurement of expected credit losses is based on relevant information about past events, including historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount. The Company does not currently have a material allowance for uncollectible trade receivables. The following table presents the percentage of gross product revenue represented by the Company's three largest customers as of the year ended December 31, 2023 and their respective percentages for the year ended December 31, 2022.

	December 31,	
	2023	2022
Customer A	35%	34%
Customer B	34%	36%
Customer C	19%	20%

The Company relies on third-party manufacturers and suppliers for manufacturing and supply of its products. The inability of the suppliers or manufacturers to fulfill supply requirements of the Company could materially impact future operating results. A change in the relationship with the suppliers or manufacturers, or an adverse change in their business, could materially impact future operating results.

2. Summary of Significant Accounting Policies (Continued)

Inventory and Cost of Product Revenues (excluding amortization of intangible assets)—Inventory is stated at the lower of cost and net realizable value. Inventory is sold on a first-in, first-out (FIFO) basis. The Company periodically reviews inventory for expiry and obsolescence and, if necessary, writes down accordingly. If quality specifications are not met during the manufacturing process, such inventory is written off to cost of product revenues (excluding amortization of intangible assets) in the period identified.

Cost of product revenues (excluding amortization of intangible assets) consist primarily of direct and indirect costs related to the manufacturing of ARIKAYCE sold, including third-party manufacturing costs, packaging services, freight, and allocation of overhead costs, in addition to royalty expenses and revenue-based milestone payments. Cost is determined using a standard cost method, which approximates actual cost, and assumes a FIFO flow of goods.

Prior to FDA approval of ARIKAYCE, the Company expensed all inventory-related costs in the period incurred. Inventory used for clinical development purposes is expensed to R&D expense when consumed.

Research and Development—R&D expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in the Company's research and development functions, including medical affairs. R&D expense also includes other internal operating expenses, the cost of manufacturing a product candidate, including the medical devices for drug delivery, for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. In addition, R&D expenses include payments to third parties for the license rights to products in development (prior to marketing approval), such as brensocatib, and may include the cost of asset acquisitions (as described further above). The Company's expenses related to manufacturing its product candidates and medical devices for clinical study are primarily related to activities at CMOs that manufacture its clinical product supply of ARIKAYCE, brensocatib, TPIP and early-stage research. The Company's expenses related to clinical trials are primarily related to activities at CROs that conduct and manage clinical trials on the Company's behalf. These contracts set forth the scope of work to be completed at a fixed fee or amount per patient enrolled. Payments under these contracts primarily depend on performance criteria such as the successful enrollment of patients or the completion of clinical trial milestones as well as time-based fees. Expenses are accrued based on contracted amounts applied to the level of patient enrollment and to activity according to the clinical trial protocol. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are then recognized as an expense as the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided.

Stock-based Compensation—The Company recognizes stock-based compensation expense for awards of equity instruments to employees and directors based on the grant-date fair value of those awards. The grant-date fair value of the award is recognized as compensation expense ratably over the requisite service period, which generally equals the vesting period of the award. The Company may also grant performance-based stock options and performance stock units (PSUs) to employees from time to time. The grant-date fair value of performance-based stock options is recognized as compensation expense over the implicit service period using the accelerated attribution method once it is probable that the performance condition will be achieved. The grant-date fair value of performance stock units is recognized as compensation expense on the date the performance conditions become probable, with an initial recording of the cumulative expense that would have been recognized if the PSU expense had been recognized on a straight-line basis since the date of grant. The remaining unamortized fair value of the awards will then be expensed prospectively on a straight-line basis over the remaining service period. Stock-based compensation expense is included in both R&D and SG&A expenses in the consolidated statements of comprehensive loss.

Investment Income and Interest Expense—Investment income consists of interest income earned on the Company's cash and cash equivalents and marketable securities. Interest expense consists primarily of contractual interest costs related to the Company's debt, non-cash interest expense related to the Company's Royalty Financing Agreement (see Note 11) and amortization of debt issuance costs related to the Company's debt.

Income Taxes—The Company accounts for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss carry forwards. 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 income in the period that includes the enactment date.

A valuation allowance is recorded to reduce the deferred tax assets to the amount that is expected to be realized. In evaluating the need for a valuation allowance, the Company takes into account various factors, including the expected level of

2. Summary of Significant Accounting Policies (Continued)

future taxable income and available tax planning strategies. If actual results differ from the assumptions made in the evaluation of a valuation allowance, the Company records a change in valuation allowance through income tax expense in the period such determination is made.

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 taxing authorities, based solely on the technical merits of the position. The tax benefits recognized in the financial statements from such a position should be measured based on the largest benefit that is more likely than not to be sustained upon ultimate settlement. As any adjustment to the Company's uncertain tax positions would not result in a cash tax liability, it has not recorded any accrued interest or penalties related to its uncertain tax positions.

The Company's policy for interest and penalties related to income tax exposures is to recognize interest and penalties as a component of the income tax provision in the consolidated statements of comprehensive loss.

Net Loss Per Share—Basic net loss per share is computed by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed by dividing net loss by the weighted average number of common shares and other dilutive securities outstanding during the period. Potentially dilutive securities from stock options, restricted stock (RS), restricted stock units (RSUs), PSUs and convertible debt securities would be anti-dilutive as the Company incurred a net loss. Potentially dilutive common shares resulting from the assumed exercise of outstanding stock options and from the assumed conversion of the Company's convertible notes are determined based on the treasury stock method.

The following table sets forth the reconciliation of the weighted average number of shares used to compute basic and diluted net loss per share for the years ended December 31, 2023, 2022 and 2021.

	Years Ended December 31,		
	2023	2022	2021
	(in thousands, except per share amounts)		
Numerator:			
Net loss	$ (749,567)	$ (481,534)	$ (434,654)
Denominator:			
Weighted average common shares used in calculation of basic net loss per share:	140,433	123,035	112,111
Effect of dilutive securities:			
Common stock options	—	—	—
RS and RSUs	—	—	—
PSUs	—	—	—
Convertible debt securities	—	—	—
Weighted average common shares outstanding used in calculation of diluted net loss per share	140,433	123,035	112,111
Net loss per share:			
Basic and diluted	$ (5.34)	$ (3.91)	$ (3.88)

The following potentially dilutive securities have been excluded from the computations of diluted weighted average common shares outstanding as of December 31, 2023, 2022 and 2021 as their effect would have been anti-dilutive (in thousands).

	As of December 31,		
	2023	2022	2021
Common stock options	22,513	17,525	14,089
Unvested RS and RSUs	2,750	1,520	1,020
PSUs	666	671	—
Convertible debt securities	23,438	23,438	23,438

2. Summary of Significant Accounting Policies (Continued)

Segment Information—The Company currently operates in one business segment, which is the development and commercialization of therapies for patients with rare diseases. The Company has a single management team that reports to the Chief Executive Officer, the chief operating decision maker, who comprehensively manages the entire business. The Company does not operate separate lines of business with respect to its products or product candidates. Accordingly, the Company has one reportable segment.

Recently Adopted Accounting Pronouncements—In August 2020, the Financial Accounting Standards Board (FASB) issued ASU 2020-06, Debt — Accounting for Convertible Instruments, to reduce the complexity associated with applying GAAP to certain financial instruments with characteristics of liabilities and equity. For convertible instruments, the number of accounting models for convertible debt instruments is reduced, which results in fewer embedded conversion features being separately recognized from the host contract as compared with current GAAP. Only convertible instruments that meet the definition of a derivative or are issued with substantial premiums will continue to be subject to the separation models. ASU 2020-06 is effective for fiscal years beginning after December 15, 2021. A modified retrospective and a fully retrospective transition method are both permitted. The Company transitioned using the modified retrospective method. The impact of adopting ASU 2020-06 on January 1, 2022 resulted in an opening balance sheet adjustment increasing debt by approximately $221.9 million and issuance costs classified to debt by approximately $6.1 million, decreasing the deferred tax liability by $1.4 million, as well as an increase to retained earnings of approximately $50.2 million, with an offsetting reduction to additional paid-in-capital of $264.6 million, net of tax.

Recent Accounting Pronouncements (Not Yet Adopted)—In December 2023, the FASB issued ASU 2023-09 Income Taxes—Improvements to Income Tax Disclosures, in order to enhance the transparency and decision usefulness of income tax disclosures. ASU 2023-09 requires greater disaggregation of income tax disclosures related to the income tax rate reconciliation and income taxes paid. ASU 2023-09 will be effective for fiscal years beginning after December 15, 2024. The Company is currently evaluating the impact of adoption of ASU 2023-09 on its consolidated financial statements.

3. Fair Value Measurements

The Company categorizes its financial assets and liabilities measured and reported at fair value in the financial statements on a recurring basis based upon the level of judgment associated with the inputs used to measure their fair value. Hierarchical levels, which are directly related to the amount of subjectivity associated with the inputs used to determine the fair value of financial assets and liabilities, are as follows:

- Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.
- Level 2—Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the assets or liability through correlation with market data at the measurement date and for the duration of the instrument’s anticipated life.
- Level 3—Inputs reflect management’s best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

Each major category of financial assets and liabilities measured at fair value on a recurring basis is categorized based upon the lowest level of significant input to the valuations. The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. Financial instruments in Level 1 generally include US treasuries and mutual funds listed in active markets. The Company's cash and cash equivalents permit daily redemption and the fair values of these investments are based upon the quoted prices in active markets provided by the holding financial institutions.

3. Fair Value Measurements (Continued)

The following table shows assets and liabilities that are measured at fair value on a recurring basis and their carrying value (in millions):

	As of December 31, 2023			
		Fair Value		
	Carrying Value	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents	$ 482.4	$ 482.4	$ —	$ —
Marketable securities	$ 298.1	$ 298.1	$ —	$ —
Collateral for interest rate swap	$ 6.0	$ 6.0	$ —	$ —
Liabilities				
Interest rate swap	$ 1.2	$ —	$ 1.2	$ —
Deferred consideration	$ 5.7	$ —	$ 5.7	$ —
Contingent consideration	$ 84.6	$ —	$ —	$ 84.6

	As of December 31, 2022			
		Fair Value		
	Carrying Value	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents	$ 1,074.0	$ 1,074.0	$ —	$ —
Marketable securities	$ 74.2	$ 74.2	$ —	$ —
Collateral for interest rate swap	$ 5.0	$ 5.0	$ —	$ —
Liabilities				
Interest rate swap	$ 1.5	$ —	$ 1.5	$ —
Deferred consideration	$ 7.4	$ —	$ 7.4	$ —
Contingent consideration	$ 58.1	$ —	$ —	$ 58.1

During the year ended December 31, 2023, the Company purchased $588.7 million of marketable securities consisting of US Treasury Notes.

As of December 31, 2023, the Company held $298.1 million of available-for-sale securities, including an unrealized gain of $0.7 million recorded in accumulated other comprehensive (loss) income. As of December 31, 2022, the Company held $74.2 million of available-for-sale securities, net of an unrealized loss of $0.5 million that were in an unrealized gain or loss position.

During the year ended December 31, 2022, the Company entered into an interest rate swap in connection with the Company's Term Loan. The Company entered into the interest rate swap to hedge its variable interest rate in an exchange for a fixed interest rate. The collateral for interest rate swap and the interest rate swap are recorded in other assets and accounts payable and accrued liabilities, respectively, in the consolidated balance sheet as of December 31, 2023 and 2022. The collateral for interest rate swap is cash, a Level 1 asset. The interest rate swap is a Level 2 liability as it uses observable inputs other than quoted market prices in an active market.

There were no transfers in or out of Level 1, Level 2 or Level 3 during the years ended December 31, 2023 and 2022.

The Company reviews the status of each security quarterly to determine whether an other-than-temporary impairment has occurred. In making its determination, the Company considers a number of factors, including: (1) the significance of the decline; (2) whether the security was rated below investment grade; (3) failure of the issuer to make scheduled interest or principal payments; and (4) the Company's ability and intent to retain the investment for a sufficient period of time for it to recover. The Company has determined that there were no other-than-temporary impairments during the year ended December 31, 2023.

3. Fair Value Measurements (Continued)

Deferred Consideration

The deferred consideration arose from the Business Acquisition in August 2021 (see Note 18). The Company is obligated to issue to Motus equityholders an aggregate of 184,433 shares of the Company's common stock on each of the first, second and third anniversaries of the closing date, subject to certain reductions. During August 2022 and August 2023, the Company fulfilled the payments due on the first and second anniversary of the closing date by issuing 171,427 and 177,203 shares of the Company's common stock, respectively, after certain reductions. A valuation of the deferred consideration is performed quarterly, based on the Company's current stock price, with gains and losses included within change in fair value of deferred and contingent consideration liabilities in the consolidated statements of comprehensive loss. As the deferred consideration is settled in shares, there is no discount rate applied in the fair value calculation.

The deferred consideration has been classified as a Level 2 recurring liability as its valuation utilizes an input, the Insmed share price, which is a directly observable input at the measurement date and for the duration of the liabilities' anticipated lives. Deferred consideration expected to be settled within twelve months or less is classified as a current liability and are included in accrued liabilities. As of December 31, 2023, the fair value of deferred consideration included in accrued liabilities was $5.7 million. Deferred consideration expected to be settled in more than twelve months are classified as a non-current liability and are included in other long-term liabilities.

The following observable input was used in the valuation of the deferred consideration as of December 31, 2023 and 2022:

	Fair Value as of December 31, 2023 (in millions)	Observable Input	Input Value
Deferred consideration	$5.7	Insmed share price on December 31, 2023	$30.99

	Fair Value as of December 31, 2022 (in millions)	Observable Input	Input Value
Deferred consideration	$7.4	Insmed share price on December 31, 2022	$19.98

Contingent Consideration Liabilities

The contingent consideration liabilities arose from the Business Acquisition in August 2021 (see Note 18). The contingent consideration liabilities consist of developmental and regulatory milestones, a priority review voucher milestone and net sales milestones. Upon the achievement of certain development and regulatory milestone events, the Company is obligated to issue to Motus equityholders up to 5,348,572 shares in the aggregate and AlgaeneX equityholders up to 368,867 shares in the aggregate. The fair value of the development and regulatory milestones are estimated utilizing a probability-adjusted approach. At December 31, 2023, the weighted average probability of success was 42%. The development and regulatory milestones will be settled in shares of the Company's common stock. As such, there is no discount rate applied in the fair value calculation.

If the Company were to receive a priority review voucher, the Company is obligated to pay to the Motus equityholders a portion of the value of the priority review voucher, subject to certain reductions. The potential payout will be either 50% of the after-tax net proceeds received by the Company from a sale of the priority review voucher or 50% of the average of the sales prices for the last three publicly disclosed priority review voucher sales, less certain adjustments. The fair value of the priority review voucher milestone is estimated utilizing a probability-adjusted discounted cash flow approach. This obligation will be settled in cash.

The contingent consideration liabilities for net sales milestones were valued using an option pricing model with Monte Carlo simulation. As of December 31, 2023, the fair value of these net sales milestones were deemed immaterial to the overall fair value of the contingent consideration.

The contingent consideration liabilities have been classified as a Level 3 recurring liability as its valuation requires substantial judgment and estimation of factors that are not currently observable in the market. If different assumptions were used for the inputs to the valuation approach, the estimated fair value could be significantly different than the fair value the Company determined. Contingent consideration liabilities expected to be settled within twelve months are classified as a current

3. Fair Value Measurements (Continued)

liability withing accounts payable and accrued liabilities in the consolidated balance sheet. Contingent consideration liabilities expected to be settled in more than twelve months are classified as a non-current liability in the consolidated balance sheet. A valuation of the contingent consideration liabilities is performed quarterly with gains and losses included within change in fair value of contingent consideration liabilities in the consolidated statements of comprehensive loss.

The following significant unobservable inputs were used in the valuation of the contingent consideration liabilities as of December 31, 2023 and 2022 (in millions):

Contingent Consideration Liabilities	Fair Value as of December 31, 2023	Valuation Technique	Unobservable Inputs	Values
Development and regulatory milestones	$74.8	Probability-adjusted	Probabilities of success	14% - 97%
Priority review voucher milestone	$6.0	Probability-adjusted discounted cash flow	Probability of success	16.4%
			Discount rate	10.0%

Contingent Consideration Liabilities	Fair Value as of December 31, 2022	Valuation Technique	Unobservable Inputs	Values
Development and regulatory milestones	$48.1	Probability-adjusted	Probabilities of success	14% - 95%
Priority review voucher milestone	$6.8	Probability-adjusted discounted cash flow	Probability of success	16.4%
			Discount rate	8.5%

A rollforward of the Company's valuations deferred and contingent consideration liabilities for the years ended December 31, 2023 and 2022 follows (in thousands):

	Deferred Consideration (level 2 liabilities)	Contingent Consideration (level 3 liabilities)
Balance as of December 31, 2021	$ 14,931	$ 75,668
Additions	—	—
Change in Fair Value	(3,234)	(17,568)
Payments	(4,297)	—
Balance as of December 31, 2022	7,400	58,100
Additions	—	—
Change in Fair Value	2,197	26,500
Payments	(3,897)	—
Balance as of December 31, 2023	$ 5,700	$ 84,600

The change in fair value of deferred and contingent consideration liabilities are due to changes in factors such as the probability of achieving milestones, our stock price, or certain other estimated assumptions.

Convertible Notes

The estimated fair value of the liability component of the Company's 0.75% convertible senior notes due 2028 (the 2028 Convertible Notes) (categorized as a Level 2 liability for fair value measurement purposes) as of December 31, 2023 was $665.5 million, determined using current market factors and the ability of the Company to obtain debt on comparable terms to the 2028 Convertible Notes. The $565.0 million carrying value of the 2028 Convertible Notes as of December 31, 2023 excludes the $10.0 million of unamortized issuance costs.

The estimated fair value of the liability component of the Company's 1.75% convertible senior notes due 2025 (the 2025 Convertible Notes) (categorized as a Level 2 liability for fair value measurement purposes) as of December 31, 2023 was $240.2 million, determined using current market factors and the ability of the Company to obtain debt on comparable terms to

3. Fair Value Measurements (Continued)

the 2025 Convertible Notes. The $223.9 million carrying value of the 2025 Convertible Notes as of December 31, 2023 excludes the $1.1 million of unamortized issuance costs.

Synthetic Royalty Financing Agreement

In October 2022, the Company entered into the Royalty Financing Agreement with OrbiMed. Under the Royalty Financing Agreement, OrbiMed paid the Company $150 million in exchange for the right to receive, on a quarterly basis, royalties in an amount equal to 4% of ARIKAYCE global net sales prior to September 1, 2025 and 4.5% of ARIKAYCE global net sales on or after September 1, 2025, as well as 0.75% of brensocatib global net sales, if approved. In the event that OrbiMed has not received aggregate Revenue Interest Payments of at least $150 million on or prior to March 31, 2028, the Company must make a one-time payment to OrbiMed for the difference between the $150 million and the aggregated Revenue Interest Payments that have been paid. In addition, the royalty rate for ARIKAYCE will be increased beginning March 31, 2028 to the rate which would have resulted in aggregate Revenue Interest Payments as of March 31, 2028 equaling $150 million. The total Revenue Interest Payments payable by us to OrbiMed are capped at 1.8x of the purchase price or up to a maximum of 1.9x of the purchase price under certain conditions. Net proceeds from the Royalty Financing Agreement, after deducting the lenders fees and deal expenses of $3.6 million, were $146.4 million.

The fair value of the Royalty Financing Agreement at the time of the transaction was based on the Company's estimates of future royalties expected to be paid to OrbiMed over the life of the arrangement, which was determined using forecasts from market data sources, which are considered Level 3 inputs. This liability is being amortized using the effective interest method over the life of the arrangement, in accordance ASC 470, Debt and ASC 835, Interest. The Company will utilize the prospective method to account for subsequent changes in the estimated future payments to be made to OrbiMed and will update the effective interest rate on a quarterly basis. For more information, see *Note - 11 Royalty Financing Agreement.*

4. Product Revenues, Net

In accordance with ASC 606, Revenue from Contracts with Customers, the Company recognizes revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration the Company expects to receive in exchange for the goods or services provided. To determine revenue recognition for arrangements within the scope of ASC 606, the Company performs the following five steps: (1) identify the contracts with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when or as the entity satisfies a performance obligation. At contract inception, the Company assesses the goods or services promised within each contract to determine which are performance obligations and to assess whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied. For all contracts that fall into the scope of ASC 606, the Company has identified one performance obligation: the sale of ARIKAYCE to its customers. The Company has not incurred or capitalized any incremental costs associated with obtaining contracts with customers.

Product revenues, net consist of net sales of ARIKAYCE. The Company's customers in the US include specialty pharmacies and specialty distributors. In December 2020, the Company began recognizing product revenue from commercial sales of ARIKAYCE in Europe. In July 2021, the Company began recognizing product revenue from commercial sales of ARIKAYCE in Japan. Globally, product revenues are recognized once the Company performs and satisfies all five steps of the revenue recognition criteria mentioned above.

The following table presents a geographic summary of the Company's product revenues, net for the years ended December 31, 2023 and 2022 (in thousands).

	For the Year Ended December 31,	
	2023	2022
US	$ 224,195	$ 185,994
Japan	65,733	56,506
Europe and rest of world	15,280	2,858
Total product revenues, net	$ 305,208	$ 245,358

During the fourth quarter of 2022, the Company agreed with French authorities on the final reimbursement price related to the temporary authorization for use (Autorisation Temporaire d'Utilisation or ATU) program in France. This final pricing resulted in a change in estimate that reduced revenue by approximately $5.8 million in the fourth quarter of 2022, which

4. Product Revenues, Net (Continued)

related to periods prior to 2022. The accrued France ATU reimbursement payable is recorded within accounts payable and accrued liabilities in the consolidated balance sheets (see Note 8).

Revenue is recorded at net selling price (transaction price), which includes estimates of variable consideration for which reserves are established for (a) customer credits, such as invoice discounts for prompt pay, (b) estimated government rebates, such as Medicaid and Medicare Part D reimbursements, and estimated managed care rebates, (c) estimated chargebacks, and (d) estimated costs of co-payment assistance. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (prompt pay discounts and chargebacks), prepaid expenses (co-payment assistance), or as a current liability (rebates). Where appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted for relevant factors such as the Company's historical experience, current contractual and statutory requirements, 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 applicable contract. The amount of variable consideration 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 will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

Customer credits: Certain of the Company's customers are offered various forms of consideration, including prompt payment discounts. The payment terms for sales to specialty pharmacies and specialty distributors for prompt payment discounts are based on contractual rates agreed with the respective specialty pharmacies and distributors. The Company anticipates that its customers will earn these discounts and, therefore, deducts the full amount of these discounts from total gross product revenues at the time such revenues are recognized.

Rebates: The Company contracts with certain government agencies and managed care organizations, or collectively, third-party payors, so that ARIKAYCE will be eligible for purchase by, or partial or full reimbursement from, such third-party payors. The Company estimates the rebates it will provide to third-party payors and deducts these estimated amounts from total gross product revenues at the time the revenues are recognized. These reserves are recorded in the same period in which the revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability. The current liability is included in accounts payable and accrued liabilities on the consolidated balance sheets. The Company estimates the rebates that it will provide to third-party payors based upon (i) the Company's contracts with these third-party payors, (ii) the government mandated discounts applicable to government-funded programs, (iii) a range of possible outcomes that are probability-weighted for the estimated payor mix, and (iv) information obtained from the Company's specialty pharmacies.

Chargebacks: Chargebacks are discounts that occur when certain contracted customers, currently public health service institutions and federal government entities purchasing via the Federal Supply Schedule, purchase directly from the Company's specialty distributor. Contracted customers generally purchase the product at a discounted price and the specialty distributor, in turn, charges back to the Company the difference between the price the specialty distributor initially paid and the discounted price paid by the contracted customers. The Company estimates chargebacks provided to the specialty distributor and deducts these estimated amounts from gross product revenues, and from accounts receivable, at the time revenues are recognized.

Co-payment assistance: Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. Based upon the terms of the program and information regarding programs provided for similar specialty pharmaceutical products, the Company estimates the average co-pay mitigation amounts and the percentage of patients that it expects to participate in the program in order to establish accruals for co-payment assistance. These reserves are recorded in the same period in which the related revenue is recognized, resulting in a reduction of product revenue. The Company adjusts its accruals for co-pay assistance based on actual redemption activity and estimates of future redemptions related to sales in the current period.

The following table provides a summary rollforward of the Company's sales allowances and related accruals for the years ended December 31, 2023 and 2022, which have been deducted in arriving at product revenues, net (in thousands).

4. Product Revenues, Net (Continued)

	Customer Credits, Fees and Discounts	Rebates, Chargebacks and Co-pay Assistance	Total
Balance as of December 31, 2022	$ 14,232	$ 5,564	$ 19,796
Allowances for current period sales	12,494	33,834	46,328
Allowances for prior period sales	—	(118)	(118)
Payments and credits	(11,244)	(29,103)	(40,347)
Balance as of December 31, 2023	$ 15,482	$ 10,177	$ 25,659
Balance as of December 31, 2021	$ 3,122	$ 5,276	$ 8,398
Allowances for current period sales	13,125	23,737	36,862
Allowances for prior period sales	5,787	(471)	5,316
Payments and credits	(7,802)	(22,978)	(30,780)
Balance as of December 31, 2022	$ 14,232	$ 5,564	$ 19,796

The Company also recognizes revenue related to various EAPs in Europe. EAPs are intended to make products available on a named patient basis before they are commercially available in accordance with local regulations. The allowance for prior period sales of customer credits, fees and discounts in the year ended December 31, 2022 is related to the change in estimate for the final France ATU pricing.

5. Inventory

The Company's inventory balance consists of the following (in thousands):

	As of December 31,	
	2023	2022
Raw materials	$ 24,562	$ 27,245
Work-in-process	33,480	22,460
Finished goods	25,206	20,217
	$ 83,248	$ 69,922

Inventory is stated at the lower of cost and net realizable value and consists of raw materials, work-in-process and finished goods. The Company has not recorded any significant inventory write-downs. The Company currently uses a limited number of third-party CMOs to produce its inventory.

6. Intangibles, Net and Goodwill

Intangibles, Net

Finite-lived Intangible Assets

As of December 31, 2023, the Company's finite-lived intangible assets consisted of acquired ARIKAYCE R&D and the milestones paid to PARI for the license to use Lamira for the delivery of ARIKAYCE to patients as a result of the FDA and EC approvals of ARIKAYCE in September 2018 and October 2020, respectively. The Company began amortizing its acquired ARIKAYCE R&D and PARI milestones intangible assets in October 2018, over ARIKAYCE's initial regulatory exclusivity period of 12 years. Amortization of these assets during each of the next five years is estimated to be approximately $5.1 million per year.

Indefinite-lived Intangible Assets

As of December 31, 2023, the Company's indefinite-lived intangible assets consisted of acquired IPR&D from the Business Acquisition (see Note 18). Indefinite-lived intangible assets are not amortized.

6. Intangibles, Net and Goodwill (Continued)

A rollforward of the Company's intangible assets for the years ended December 31, 2023 and 2022 follows (in thousands):

	2023			
Intangible Asset	January 1,	Additions	Amortization	December 31,
Acquired ARIKAYCE R&D	$ 37,588	$ —	$ (4,850)	$ 32,738
Acquired IPR&D	29,600	—	—	29,600
PARI milestones	1,568	—	(202)	1,366
	$ 68,756	$ —	$ (5,052)	$ 63,704

	2022			
Intangible Asset	January 1,	Additions	Amortization	December 31,
Acquired ARIKAYCE R&D	$ 42,439	$ —	$ (4,851)	$ 37,588
Acquired IPR&D	29,600	—	—	29,600
PARI milestones	1,770	—	(202)	1,568
	$ 73,809	$ —	$ (5,053)	$ 68,756

Goodwill

The Company's goodwill balance of $136.1 million as of December 31, 2023 and 2022 resulted from the August 2021 Business Acquisition (see Note 18).

7. Fixed Assets, Net

Fixed assets are stated at cost and depreciated using the straight-line method, based on useful lives as follows (in thousands):

	Estimated	As of December 31,	
Asset Description	Useful Life (years)	2023	2022
Lab equipment	7	$ 22,660	$ 16,403
Furniture and fixtures	7	6,428	6,428
Computer hardware and software	3 - 5	6,001	5,227
Office equipment	7	89	89
Manufacturing equipment	7	1,336	1,203
Leasehold improvements	2 - 10	38,049	37,057
Construction in progress	—	35,449	29,529
		110,012	95,936
Less accumulated depreciation		(44,628)	(39,445)
		$ 65,384	$ 56,491

Depreciation expense was $5.5 million, $5.3 million and $9.1 million for the years ended December 31, 2023, 2022 and 2021, respectively.

8. Accounts Payable and Accrued Liabilities

Accounts payable and accrued liabilities consist of the following (in thousands):

	As of December 31,	
	2023	2022
Accounts payable and other accrued operating expenses	$ 65,393	$ 50,461
Accrued clinical trial expenses	23,711	36,456
Accrued professional fees	13,885	14,403
Accrued technical operation expenses	9,187	3,345
Accrued compensation and employee related costs	48,933	32,040
Accrued royalty and milestones payable	5,674	4,710
Accrued interest payable	2,175	6,340
Revenue Interest Payments payable	3,347	2,149
Accrued sales allowances and related costs	10,937	6,974
Accrued France ATU reimbursement payable	14,685	12,943
Deferred and contingent consideration	6,700	10,700
Other accrued liabilities	10,360	1,596
	$ 214,987	$ 182,117

9. Leases

The Company's lease portfolio consists primarily of office and laboratory space, manufacturing facilities, research equipment and fleet vehicles. All of the Company's leases are classified as operating leases, except for the Company's leases of its corporate headquarters and a research facility in San Diego, which are classified as finance leases. The terms of the Company's lease agreements that have commenced range from less than one year to ten years, ten months. In its assessment of the term of each such lease, the Company has not included any options to extend or terminate the lease due to the absence of economic incentives in its lease agreements. Leases that qualify for treatment as a short-term lease are expensed as incurred. These short-term leases are not material to the Company's financial position. Furthermore, the Company does not separate lease and non-lease components for all classes of underlying assets. The Company's leases do not contain residual value guarantees and it does not sublease any of its leased assets.

The Company outsources its manufacturing operations to CMOs. Upon review of the agreements with its CMOs, the Company determined that these contracts contain embedded leases for dedicated manufacturing facilities. The Company obtains substantially all of the economic benefits from the use of the manufacturing facilities, the Company has the right to direct how and for what purpose the facility is used throughout the period of use, and the supplier does not have the right to change the operating instructions of the facility. The operating lease right-of-use assets and corresponding lease liabilities associated with the manufacturing facilities is the sum of the minimum guarantees over the life of the production contracts.

9. Leases (Continued)

The table below summarizes the Company's total lease costs included in its consolidated financial statements, as well as other required quantitative disclosures (in thousands).

	As of December 31, 2023		As of December 31, 2022	
Finance lease cost:				
Amortization of right-of-use assets	$ 2,712		$ 1,960	
Interest on lease liabilities	2,417		1,808	
Total finance lease cost		$ 5,129		$ 3,768
Operating lease cost		10,385		12,920
Variable lease cost		14,148		11,254
Total lease cost		$ 29,662		$ 27,942
Other information:				
Cash paid for amounts included in the measurement of lease liabilities				
Operating cash flows for finance leases		$ 2,417		$ 1,907
Operating cash flows for operating leases		$ 9,098		$ 11,450
Financing cash flows for finance leases		$ 1,217		$ 601
Right-of-use assets obtained in exchange for new finance lease liabilities		$ —		$ 16,741
Right-of-use assets obtained in exchange for new operating lease liabilities		$ 5,329		$ 565
Weighted average remaining lease term - finance leases		7.6 years		8.6 years
Weighted average remaining lease term - operating leases		2.5 years		3.2 years
Weighted average discount rate - finance leases		7.9 %		7.9 %
Weighted average discount rate - operating leases		7.6 %		7.0 %

The Company records variable consideration for variable lease payments in excess of fixed fees or minimum guarantees. Variable costs related to CMO manufacturing agreements are direct costs related to the manufacturing of ARIKAYCE and are capitalized within inventory in the Company's consolidated balance sheet, while the variable costs related to other leasing arrangements, not related to the manufacturing of ARIKAYCE, have been classified within operating expenses in the Company's consolidated statements of comprehensive loss.

9. Leases (Continued)

The table below presents the maturity of lease liabilities on an annual basis for the remaining years of the Company's commenced lease agreements (in thousands).

Year Ending December 31,	Finance Leases	Operating Leases
2024	$ 4,840	$ 8,701
2025	4,967	8,219
2026	5,097	2,106
2027	5,228	654
2028	5,361	408
Thereafter	14,157	70
Total	39,650	20,158
Less: present value discount	10,014	1,113
Present value of lease liabilities	$ 29,636	$ 19,045
Balance Sheet Classification at December 31, 2023:		
Current lease liabilities	$ 2,610	$ 8,032
Long-term lease liabilities	27,026	11,013
Total lease liabilities	$ 29,636	$ 19,045

In addition to the Company's lease agreements that have previously commenced and are reflected in the consolidated financial statements, the Company has entered into additional lease agreements that have not yet commenced. The Company entered into certain agreements with Patheon related to increasing its long-term production capacity for ARIKAYCE commercial inventory. The Company has determined that these agreements with Patheon contain an embedded lease for the manufacturing facility and the specialized equipment contained therein. Costs of $49.1 million incurred by the Company under these additional agreements have been classified within other assets in the Company's consolidated balance sheet. Upon the commencement date, prepaid costs and minimum guarantees specified in the agreement will be combined to establish an operating lease ROU asset and operating lease liability.

10. Debt

Debt, long-term consists of the following commitments as of December 31, 2023 and 2022 (in thousands):

	As of December 31,	
	2023	2022
Convertible notes	$ 788,909	$ 785,621
Term Loan	366,404	339,629
Debt, long-term	$ 1,155,313	$ 1,125,250

Secured Senior Term Loan

In October 2022, the Company entered into a $350 million Term Loan with Pharmakon that matures on October 19, 2027. The Term Loan bears interest at a rate based upon the SOFR, subject to a SOFR floor of 2.5%, in addition to a margin of 7.75% per annum. Up to 50% of the interest payable during the first 24 months from the closing of the Term Loan may be paid-in-kind at the Company's election. If elected, paid-in-kind interest will be capitalized and added to the principal amount of the Term Loan. The Term Loan, including the paid-in-kind interest, will be repaid in eight equal quarterly payments starting in the 13th quarter following the closing of the Term Loan (i.e., the quarter ending March 31, 2026), except that the repayment start date may be extended at the Company's option for an additional four quarters, so that repayments start in the 17th quarter following the closing of the Term Loan, subject to the achievement of specified ARIKAYCE data thresholds and certain other conditions. Net proceeds from the Term Loan, after deducting the lenders fees and deal expenses of $15.1 million, were $334.9 million.

The following table presents the carrying value of the Company’s Term Loan balance as of December 31, 2023 and 2022 (in thousands):

10. Debt (Continued)

	As of December 31,	
	2023	**2022**
Original Term Loan balance	$ 350,000	$ 350,000
Paid-in-kind interest capitalized	27,537	4,165
Term Loan issuance costs, unamortized	(11,133)	(14,536)
Term Loan	$ 366,404	$ 339,629

Convertible Notes

In May 2021, the Company completed an underwritten public offering of the 2028 Convertible Notes, in which the Company sold $575.0 million aggregate principal amount of the 2028 Convertible Notes, including the exercise in full of the underwriters' option to purchase an additional $75.0 million in aggregate principal amount of 2028 Convertible Notes. The Company's net proceeds from the offering, after deducting underwriting discounts and commissions and other offering expenses of $15.7 million, were approximately $559.3 million. The 2028 Convertible Notes bear interest payable semiannually in arrears on June 1 and December 1 of each year, beginning on December 1, 2021. The 2028 Convertible Notes mature on June 1, 2028, unless earlier converted, redeemed, or repurchased.

In January 2018, the Company completed an underwritten public offering of the Convertible Notes, in which the Company sold $450.0 million aggregate principal amount of the 2025 Convertible Notes, including the exercise in full of the underwriters' option to purchase an additional $50.0 million in aggregate principal amount of 2025 Convertible Notes. The Company's net proceeds from the offering, after deducting underwriting discounts and commissions and other offering expenses of $14.2 million, were approximately $435.8 million. The 2025 Convertible Notes bear interest payable semiannually in arrears on January 15 and July 15 of each year, beginning on July 15, 2018. The 2025 Convertible Notes mature on January 15, 2025, unless earlier converted, redeemed, or repurchased.

A portion of the net proceeds from the 2028 Convertible Notes was used to repurchase $225.0 million of the Company's outstanding 2025 Convertible Notes. The Company recorded a loss on early extinguishment of debt of $17.7 million, primarily related to the premium paid on extinguishment of a portion the 2025 Convertible Notes.

On or after October 15, 2024, until the close of business on the second scheduled trading day immediately preceding January 15, 2025, holders may convert their 2025 Convertible Notes at any time. The initial conversion rate for the 2025 Convertible Notes is 25.5384 shares of common stock per $1,000 principal amount of 2025 Convertible Notes (equivalent to an initial conversion price of approximately $39.16 per share of common stock). On or after March 1, 2028, until the close of business on the second scheduled trading day immediately preceding June 1, 2028, holders may convert their 2028 Convertible Notes at any time. The initial conversion rate for the 2028 Convertible Notes is 30.7692 shares of common stock per $1,000 principal amount of 2028 Convertible Notes (equivalent to an initial conversion price of approximately $32.50 per share of common stock). Upon conversion of either the 2025 Convertible Notes or the 2028 Convertible Notes, holders may receive cash, shares of the Company's common stock or a combination of cash and shares of the Company's common stock, at the Company's option. The conversion rates will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest.

Holders may convert their 2025 Convertible Notes prior to October 15, 2024 or their 2028 Convertible Notes prior to March 1, 2028, only under the following circumstances, subject to the conditions set forth in the applicable indenture: (i) during the five business day period immediately after any five consecutive trading day period (the measurement period) in which the trading price per $1,000 principal amount of the applicable series of convertible notes, as determined following a request by a holder of such convertible notes, for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the common stock and the conversion rate on such trading day, (ii) the Company elects to distribute to all or substantially all holders of the common stock (a) any rights, options or warrants (other than in connection with a stockholder rights plan for so long as the rights issued under such plan have not detached from the associated shares of common stock) entitling them, for a period of not more than 45 days from the declaration date for such distribution, to subscribe for or purchase shares of common stock at a price per share that is less than the average of the last reported sale prices of the common stock for the 10 consecutive trading day period ending on, and including, the trading day immediately preceding the declaration date for such distribution, or (b) the Company's assets, debt securities or rights to purchase securities of the Company, which distribution has a per share value, as reasonably determined by the board of directors, exceeding 10% of the last reported sale price of the common stock on the trading day immediately preceding the declaration date for such distribution, (iii) if a

10. Debt (Continued)

transaction or event that constitutes a fundamental change or a make-whole fundamental change occurs, or if the Company is a party to (a) a consolidation, merger, combination, statutory or binding share exchange or similar transaction, pursuant to which the common stock would be converted into, or exchanged for, cash, securities or other property or assets, or (b) any sale, conveyance, lease or other transfer or similar transaction in one transaction or a series of transactions of all or substantially all of the consolidated assets of the Company and its subsidiaries, taken as a whole, all or any portion of the applicable series of convertible notes may be surrendered by a holder for conversion at any time from or after the date that is 30 scheduled trading days prior to the anticipated effective date of the transaction, (iv) if during any calendar quarter commencing after the calendar quarter ending on March 31, 2018 or June 30, 2021 for the 2025 Convertible Notes and the 2028 Convertible Notes, respectively (and only during such calendar quarter), the last reported sale price of the common stock for at least 20 trading days (whether or not consecutive) during the period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day, or (v) if the Company sends a notice of redemption, a holder may surrender all or any portion of its convertible notes to which the notice of redemption relates for conversion at any time on or after the date the applicable notice of redemption was sent until the close of business on (a) the second business day immediately preceding the related redemption date or (b) if the Company fails to pay the redemption price on the redemption date as specified in such notice of redemption, such later date on which the redemption price is paid. To date, there have not been any holder-initiated redemption requests of either series of convertible notes.

Each series of convertible notes can be settled in cash, common stock, or a combination of cash and common stock at the Company's option, and thus, the Company determined the embedded conversion options in both series of convertible notes are not required to be separately accounted for as a derivative. However, since the convertible notes are within the scope of the accounting guidance for cash convertible instruments, the Company is required to separate each series of convertible notes into liability and equity components. The carrying amount of the liability component of each series of convertible notes as of the date of issuance was calculated by measuring the fair value of a similar liability that did not have an associated equity component. The fair value was based on data from readily available pricing sources which utilize market observable inputs and other characteristics for similar types of instruments. The carrying amount of the equity component representing the embedded conversion option for each series of convertible notes was determined by deducting the fair value of the liability component from the gross proceeds of the applicable convertible notes. The excess of the principal amount of the liability component over its carrying amount is amortized to interest expense over the expected life of a similar liability that does not have an associated equity component using the effective interest method. The equity component is not remeasured as long as it continues to meet the conditions for equity classification in the accounting guidance for contracts in an entity’s own equity. The fair value of the liability component of the 2025 Convertible Notes on the date of issuance was estimated at $309.1 million using an effective interest rate of 7.6% and, accordingly, the residual equity component on the date of issuance was $140.9 million. The fair value of the liability component of the 2028 Convertible Notes on the date of issuance was estimated at $371.6 million using an effective interest rate of 7.1% and, accordingly, the residual equity component on the date of issuance was $203.4 million. The respective discounts were amortized to interest expense over the term of the applicable series of convertible notes through December 31, 2021, prior to the adoption of ASU 2020-06. The 2025 Convertible Notes and the 2028 Convertible Notes have remaining periods of approximately 1.04 years and 4.42 years, respectively. The following table presents the carrying value of the Company’s debt balance as of December 31, 2023 and 2022 (in thousands):

	As of December 31,	
	2023	2022
Face value of outstanding convertible notes	$ 800,000	$ 800,000
Debt issuance costs, unamortized	(11,091)	(14,379)
Convertible notes	$ 788,909	$ 785,621

10. Debt (Continued)

As of December 31, 2023, future principal repayments of debt for each of the fiscal years through maturity were as follows (in thousands):

Year Ending December 31:	
2024	$ —
2025	225,000
2026	188,769
2027	188,768
2028	575,000
2029 and thereafter	—
	$ 1,177,537

The estimated fair value of the debt (categorized as a Level 2 liability for fair value measurement purposes) is determined using current market factors and the ability of the Company to obtain debt at comparable terms to those that are currently in place.

Interest expense for the years ended December 31, 2023, 2022, and 2021, is as follows (in thousands):

	Years Ended December 31,		
	2023	**2022**	**2021**
Convertible debt contractual interest expense	$ 8,250	$ 8,250	$ 8,134
Term Loan contractual interest expense	46,743	8,330	—
Royalty Financing Agreement non-cash interest expense	18,846	3,687	—
Amortization of debt issuance costs	7,320	3,991	1,890
Amortization of debt discount	—	—	29,149
Swap interest (income) expense	(1,882)	380	—
Total debt interest expense	$ 79,277	$ 24,638	$ 39,173
Finance lease interest expense	2,417	1,808	1,300
Total interest expense	$ 81,694	$ 26,446	$ 40,473

In accordance with the Company's transition using the modified retrospective method upon adopting ASU 2020-06 on January 1, 2022, the Company ceased accreting debt discount.

11. Royalty Financing Agreement

In October 2022, the Company entered into the Royalty Financing Agreement with OrbiMed. Under the Royalty Financing Agreement, OrbiMed paid the Company $150 million in exchange for the right to receive, on a quarterly basis, royalties in an amount equal to 4% of ARIKAYCE global net sales prior to September 1, 2025 and 4.5% of ARIKAYCE global net sales on or after September 1, 2025, as well as 0.75% of brensocatib global net sales, if approved. In the event that OrbiMed has not received aggregate Revenue Interest Payments of at least $150 million on or prior to March 31, 2028, the Company must make a one-time payment to OrbiMed for the difference between the $150 million and the aggregated Revenue Interest Payments that have been paid. In addition, the royalty rate for ARIKAYCE will be increased beginning March 31, 2028 to the rate which would have resulted in aggregate Revenue Interest Payments as of March 31, 2028 equaling $150 million. The total Revenue Interest Payments payable by us to OrbiMed are capped at 1.8x of the purchase price or up to a maximum of 1.9x of the purchase price under certain conditions. Net proceeds from the Royalty Financing Agreement, after deducting the lenders fees and deal expenses of $3.6 million were, $146.4 million.

The fair value of the Royalty Financing Agreement at the time of the transaction was based on the Company’s estimates of future royalties expected to be paid to OrbiMed over the life of the arrangement, which was determined using forecasts from market data sources, which are considered Level 3 inputs. This liability is being amortized using the effective

11. Royalty Financing Agreement (Continued)

interest method over the life of the arrangement, in accordance ASC 470, Debt and ASC 835, Interest. The initial annual effective interest rate was determined to be 12.4%. The Company will utilize the prospective method to account for subsequent changes in the estimated future payments to be made to OrbiMed and will update the effective interest rate on a quarterly basis.

The following table presents the carrying value of the Company's Royalty Financing Agreement balance as of December 31, 2023 and 2022 (in thousands):

	December 31,	
	2023	2022
Royalty financing agreement liability - beginning balance	$ 151,538	$ 150,000
Revenue Interest Payments paid and payable	(12,222)	(2,149)
Interest expense recognized	18,846	3,687
Royalty financing agreement liability - ending balance	$ 158,162	$ 151,538
Royalty financing issuance costs, unamortized - beginning balance	$ (3,523)	$ (3,624)
Amortization of issuance costs	521	101
Other	(126)	—
Deferred issuance costs, unamortized - ending balance	$ (3,128)	$ (3,523)
Royalty Financing Agreement	$ 155,034	$ 148,015

The Revenue Interest Payments payable in connection with the royalty financing agreement were $3.3 million and $2.1 million as of December 31, 2023 and 2022, respectively, which were recorded within accounts payable and accrued expenses on the consolidated balance sheet. Non-cash interest expense is recorded within interest expense in the consolidated statements of comprehensive loss.

12. Shareholders' Equity

Common Stock—As of December 31, 2023, the Company had 500,000,000 shares of common stock authorized with a par value of $0.01 per share and 147,977,960 shares of common stock issued and outstanding. In addition, as of December 31, 2023, the Company had reserved 22,512,569 shares of common stock for issuance upon the exercise of outstanding common stock options, 2,750,294 shares of common stock for issuance upon the vesting of RSUs and 666,382 shares for issuance upon the vesting of PSUs. The Company has also reserved 23,438,430 shares of common stock in the aggregate for issuance upon conversion of the 2025 Convertible Notes and 2028 Convertible Notes, subject to adjustment in accordance with the applicable indentures. In connection with the Business Acquisition, the Company reserved 9,406,112 shares of the Company's common stock, subject to certain closing-related reductions. The shares of the Company's common stock reserved in connection with the Motus acquisition were partly issued as acquisition consideration at closing and on the first and second anniversaries of the closing date of the acquisition, and will also be issued upon the third anniversary of the closing date of the acquisition and upon the achievement of certain development and regulatory milestone events, subject to certain reductions. The shares of the Company's common stock reserved in connection with the AlgaeneX acquisition will be issued upon the achievement of a development milestone event, subject to certain reductions.

Of the 9,406,112 shares reserved, subject to certain closing-related reductions, the Company issued 2,889,367 shares of the Company's common stock in connection with the Business Acquisition (Note 18) in the third quarter of 2021, after certain closing-related deductions. In the third quarter of 2022, the Company issued 171,427 shares of the Company's common stock to fulfill the payment required to Motus equityholders on the first anniversary of the Business Acquisition. In the third quarter of 2023, the Company issued 177,203 shares of the Company's common stock to fulfill the payment required to Motus equityholders on the second anniversary of the Business Acquisition.

In the second quarter of 2023, in connection with the Company's acquisition of Adrestia, the Company issued 3,430,867 shares of the Company's common stock as consideration at closing. See *Note 18 - Acquisitions* for further details.

In connection with the Company's acquisition of Vertuis, the Company reserved 550,000 shares of the Company's common stock, subject to future adjustment. An aggregate of 500,000 of the reserved shares were issued as acquisition consideration at closing. An additional $1 million of shares of common stock will be issued to Vertuis' former stockholders on July 1, 2024, based on the share price on June 28, 2024. See *Note 18 - Acquisitions* for further details.

12. Shareholders' Equity (Continued)

In the fourth quarter of 2022, the Company completed an underwritten offering of 13,750,000 shares of the Company's common stock, at an offering price of $20.00 per share. The Company's net proceeds from the sale of the shares, after deducting the underwriting discounts and offering expenses of approximately $16.2 million, were approximately $258.8 million.

In the second quarter of 2021, the Company completed an underwritten public offering of 11,500,000 shares of the Company's common stock, including 1,500,000 shares issued pursuant to the exercise in full of the underwriters' option to purchase additional shares from the Company, at a public offering price of $25.00 per share. The Company's net proceeds from the sale of the shares, after deducting the underwriting discounts and offering expenses of $17.5 million, were $270.1 million.

In the first quarter of 2021, the Company entered into a sales agreement with Leerink Partners, to sell shares of the Company's common stock, with aggregate gross sales proceeds of up to $250.0 million, from time to time, through the ATM program, under which Leerink Partners acts as sales agent. For the year ended December 31, 2023, the Company issued and sold an aggregate of 6,503,041 shares of common stock through the ATM program at a weighted-average public offering price of $24.12 per share and received net proceeds of $152.2 million. As of December 31, 2023, an aggregate of $58.7 million of shares of common stock remain available to be issued and sold under the ATM program.

Preferred Stock—As of December 31, 2023 and 2022, the Company had 200,000,000 shares of preferred stock authorized with a par value of $0.01 and no shares of preferred stock were issued and outstanding.

13. Stock-Based Compensation

The Company's current equity compensation plan, the Insmed Incorporated Amended and Restated 2019 Incentive Plan (the 2019 Incentive Plan), was approved by shareholders at the Company's Annual Meeting of Shareholders on May 11, 2023. The 2019 Incentive Plan replaced the Insmed Incorporated 2019 Incentive Plan, as amended (the Old 2019 Incentive Plan). The 2019 Incentive Plan is administered by the Compensation Committee of the Board of Directors of the Company. Under the terms of the 2019 Incentive Plan, the Company is authorized to grant a variety of incentive awards based on its common stock, including stock options (both incentive stock options and non-qualified stock options), RSUs, performance options/shares and other stock awards to eligible employees and non-employee directors. On May 16, 2019, upon the approval of the Old 2019 Incentive Plan by shareholders, 3,500,000 shares were authorized for issuance thereunder, plus any shares subject to then-outstanding awards under the Company's 2017 Incentive Plan, the 2015 Incentive Plan and the 2013 Incentive Plan that subsequently were canceled, terminated unearned, expired, were forfeited, lapsed for any reason or were settled in cash without the delivery of shares. On May 12, 2020, at the Company's 2020 Annual Meeting of Shareholders, the Company's shareholders approved an amendment of the Old 2019 Incentive Plan providing for the issuance of an additional 4,500,000 shares under the plan. On May 12, 2021, at the Company's 2021 Annual Meeting of Shareholders, the Company's shareholders approved the second amendment to the Old 2019 Incentive Plan providing for the issuance of an additional 2,750,000 shares under the plan. On May 11, 2022, at the Company's 2022 Annual Meeting of Shareholders, the Company's shareholders approved the third amendment to the Old 2019 Incentive Plan, providing for the issuance of an additional 3,000,000 shares under the plan. At the May 2023 Annual Meeting of Shareholders, in connection with approval of the 2019 Incentive Plan, the Company's shareholders approved the issuance of an additional 10,500,000 shares under the 2019 Incentive Plan. As of December 31, 2023, 7,180,171 shares remained for future issuance under the 2019 Incentive Plan. The 2019 Incentive Plan will terminate on May 16, 2029 unless it is extended or terminated earlier pursuant to its terms. In addition, from time to time, the Company makes inducement grants of stock options to new hires, which awards are made pursuant to the Nasdaq's inducement grant exception to the shareholder approval requirement for grants of equity compensation. During the twelve months ended December 31, 2023 and 2022, the Company granted inducement stock options covering 2,674,290 and 1,068,310 shares, respectively, of the Company's common stock to new employees.

Stock Options—The Company calculates the fair value of stock options granted using the Black-Scholes valuation model. The following table summarizes the grant date fair value and assumptions used in determining the fair value of all stock options granted, including grants of inducement options, during the years ended December 31, 2023, 2022 and 2021.

	2023	2022	2021
Volatility	62% - 70%	69% - 70%	70% - 71%
Risk-free interest rate	3.36% - 4.72%	1.37% - 4.27%	0.36% - 1.20%
Dividend yield	0.0%	0.0%	0.0%
Expected option term (in years)	6.05	5.93	5.84
Weighted average fair value of stock options granted	$13.12	$13.19	$18.50

For the years ended December 31, 2023, 2022 and 2021, the volatility factor was based on the Company’s historical volatility during the expected option term. The company accounts for forfeitures as they occur.

13. Stock-Based Compensation (Continued)

From time to time, the Company has granted performance-conditioned options to certain of its employees. Vesting of these options is subject to the Company achieving certain performance criteria established at the date of grant and the grantees fulfilling a service condition (continued employment). As of December 31, 2023 and December 31, 2022, the Company had performance-conditioned options covering 114,780 shares outstanding. As of December 31, 2023 and December 31, 2022, the performance conditions are not probable and therefore, no stock-based compensation was recorded in the consolidated statements of comprehensive loss.

The following table summarizes stock option activity for stock options granted for the years ended December 31, 2023, 2022 and 2021 as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in '000)
Options outstanding at December 31, 2020	12,263,402	$ 18.84		
Granted	4,039,360	$ 30.18		
Exercised	(1,235,186)	$ 15.50		
Forfeited and expired	(978,616)	$ 24.35		
Options outstanding at December 31, 2021	14,088,960	$ 22.00		
Exercisable at December 31, 2021	7,292,851	$ 17.97		
Granted	5,614,220	$ 20.89		
Exercised	(1,151,341)	$ 14.41		
Forfeited and expired	(1,026,543)	$ 25.70		
Options outstanding at December 31, 2022	17,525,296	$ 21.93		
Exercisable at December 31, 2022	8,587,820	$ 20.35		
Granted	6,650,880	$ 20.20		
Exercised	(871,933)	$ 16.03		
Forfeited and expired	(791,674)	$ 24.01		
Options outstanding at December 31, 2023	22,512,569	$ 21.58	7.08	$ 216,537
Exercisable at December 31, 2023	11,125,232	$ 21.41	5.42	$ 109,109

The total intrinsic value of stock options exercised during the years ended December 31, 2023, 2022 and 2021 was $6.0 million, $11.1 million and $22.1 million, respectively.

As of December 31, 2023, there was $130.3 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 2.7 years.

Restricted Stock and Restricted Stock Units—The Company may grant RS and RSUs to employees and non-employee directors. Each share of RS vests upon and each RSU represents a right to receive one share of the Company's common stock upon the completion of a specific period of continued service.

RS and RSU awards granted are valued at the market price of the Company's common stock on the date of grant. The Company recognizes non-cash compensation expense for the fair values of these RS and RSUs on a straight-line basis over the requisite service period of these awards.

13. Stock-Based Compensation (Continued)

The following table summarizes RSU awards granted during the years ended December 31, 2023, 2022 and 2021:

	Number of RSUs	Weighted Average Grant Price
Outstanding at December 31, 2020	844,391	$ 25.43
Granted	607,578	$ 29.40
Released	(291,823)	$ 25.93
Forfeited	(140,432)	$ 27.73
Outstanding at December 31, 2021	1,019,714	$ 27.33
Granted	1,021,219	$ 20.34
Released	(417,894)	$ 26.79
Forfeited	(103,139)	$ 24.04
Outstanding at December 31, 2022	1,519,900	$ 23.00
Granted	1,934,822	$ 19.26
Released	(574,219)	$ 22.89
Forfeited	(130,209)	$ 20.87
Outstanding at December 31, 2023	2,750,294	$ 20.50

As of December 31, 2023, there was $40.7 million of unrecognized compensation expense related to unvested awards, which is expected to be recognized over a weighted average period of 2.7 years.

Performance Stock Units — In January 2022, the Company issued 271,612 PSUs. For these PSUs, there are two performance conditions, a service condition, and a market condition. The performance conditions are the issuance of a press release announcing certain top-line results from a clinical trial and the acceptance of an NDA by the FDA for brensocatib. The service condition is continuous employment with the Company through the later of the third anniversary of the grant date of the PSU award and the date an NDA for brensocatib is accepted by the FDA. The potential payout of the awards ranges from 0% to 250% of the target, dependent on a market condition that is based on the Company's total shareholder return compared to a defined peer group. Due to the multiple vesting conditions, uncertain timing and variable payout of these PSUs, a Monte Carlo simulation was performed to determine the fair value of the awards. Compensation cost will be recognized on the date the performance conditions become probable, with an initial recording of the cumulative expense that would have been recognized if the PSU expense had been recognized on a straight-line basis since the date of grant. The remaining unamortized fair value of the awards will then be expensed prospectively on a straight-line basis over the remaining service period. Since the market condition is reflected in the grant-date fair value and is not a condition for the award to vest, it does not impact the requisite service period. The volatility, risk-free interest rate and weighted-average grant date fair value of the PSUs granted are 65.4%, 1.03% and $39.12, respectively. Any forfeitures that occur after compensation cost recognition commences will result in the cumulative reversal of expense in the period in which the forfeiture occurs. As of December 31, 2023, there were 266,550 PSUs outstanding with an unrecognized compensation expense of $10.4 million, which assumes a payout of 100% of the target.

13. Stock-Based Compensation (Continued)

The following table summarizes the aggregate stock-based compensation expense recorded in the consolidated statements of comprehensive loss related to stock options, RSUs and ESPP during the years ended December 31, 2023, 2022 and 2021 (in millions):

	Years Ended December 31,		
	2023	2022	2021
Research and development expenses	$ 35.9	$ 26.4	$ 17.8
Selling, general and administrative expenses	38.9	31.3	28.2
Total stock-based compensation expense	$ 74.8	$ 57.7	$ 46.0

There was no stock-based compensation expense recorded in the consolidated statements of comprehensive loss related to PSUs during the year ended December 31, 2023, as the performance conditions associated with the PSU awards were not probable as of December 31, 2023.

Employee Stock Purchase Plan - On May 15, 2018, the Company's shareholders approved the Company's 2018 Employee Stock Purchase Plan (ESPP). As part of the ESPP, eligible employees may acquire an ownership interest in the Company by purchasing common stock, at a discount, through payroll deductions. The ESPP is compensatory under GAAP and the Company recorded stock-based compensation expense of $1.9 million, $1.3 million and $1.3 million for the years ended December 31, 2023, 2022 and 2021, respectively.

14. Income Taxes

The Company recorded a provision (benefit) for income taxes of $2.6 million, $1.4 million and $(1.8) million and the effective rates were approximately 0% for the years ended December 31, 2023, 2022 and 2021. The income tax provision for the years ended December 31, 2023 and December 31, 2022 reflected current income tax expense recorded as a result of the taxable income in certain of the Company's non-US subsidiaries and certain state income taxes. The income tax (benefit) for the year ended December 31, 2021 is primarily due to the partial reversal of a valuation allowance as a result of the Business Acquisition (see Note 18), partially offset by current income tax expense. While the Business Acquisition resulted in a deferred tax liability recorded under ASC 805, an adjustment to the valuation allowance is required as this deferred tax liability provides a future reversal of a taxable temporary difference.

The Company's loss before income taxes in the US and globally was as follows (in thousands):

	Years Ended December 31,		
	2023	2022	2021
US	$ (666,181)	$ (406,262)	$ (348,845)
Foreign	(80,831)	(73,889)	(87,567)
Total	$ (747,012)	$ (480,151)	$ (436,412)

The Company's income tax provision (benefit) consisted of the following (in thousands):

	Years Ended December 31,		
	2023	**2022**	**2021**
Current:			
Federal	$ —	$ —	$ —
State	378	269	104
Foreign	2,231	1,345	1,585
	2,609	1,614	1,689
Deferred:			
Federal	(13)	13	(2,835)
State	(41)	(244)	(612)
Foreign	—	—	—
	(54)	(231)	(3,447)
Total	$ 2,555	$ 1,383	$ (1,758)

The reconciliation between the federal statutory tax rates and the Company's effective tax rate is as follows:

	Years Ended December 31,		
	2023	**2022**	**2021**
Statutory federal tax rate	21 %	21 %	21 %
Permanent items	(1)%	— %	(1)%
State income taxes, net of federal benefit	3 %	1 %	4 %
R&D and other tax credits	3 %	3 %	4 %
Foreign income taxes	(1)%	— %	(1)%
Change in valuation allowance	(21)%	(22)%	(27)%
Asset acquisitions (see Note 18)	(3)%	— %	— %
Stock-based compensation	(1)%	(2)%	— %
Other	— %	(1)%	— %
Effective tax rate	— %	— %	— %

14. Income Taxes (Continued)

Deferred tax assets and liabilities are determined based on the difference between financial statement and tax bases using enacted tax rates in effect for the year in which the differences are expected to reverse. The components of the deferred tax assets and liabilities consist of the following:

	As of December 31,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	$ 563,869	$ 499,029
General business credits	182,006	157,181
Product license	3,867	4,317
Inventory	2,341	1,470
Lease liabilities	12,000	12,965
Stock-based compensation	27,916	23,724
Capitalized R&D	115,299	56,275
Other	19,286	15,001
Deferred tax assets	926,584	769,962
Valuation allowance	(904,078)	(745,135)
Deferred tax assets, net of valuation allowance	$ 22,506	$ 24,827
Deferred tax liabilities:		
Intangibles	$ (13,006)	$ (13,739)
Right-of-use assets	(9,585)	(11,227)
Deferred tax liabilities	$ (22,591)	$ (24,966)
Net deferred tax liabilities	$ (85)	$ (139)

The deferred tax assets, net of valuation allowance of $22.5 million and $24.8 million at December 31, 2023 and 2022, respectively, primarily consist of net operating loss and tax credit carryforwards for income tax purposes. As required by the 2017 Tax Cuts and Jobs Act, effective January 1, 2022, our research and development expenditures were capitalized resulting in a deferred tax asset. Due to the Company's history of operating losses, the Company recorded a valuation allowance on its net deferred tax assets by increasing the valuation allowance by $158.9 million and $157.7 million in 2023 and 2022, respectively, as it was more likely than not that such tax benefits will not be realized. A portion of the valuation allowance increase in 2022 is charged to tax expense and the remainder was charged to equity resulting from the adoption of ASU 2020-06, under which the net deferred tax liability associated with the convertible debt is removed through equity.

At December 31, 2023, the Company had federal net operating loss (NOL) carryforwards for income tax purposes of approximately $1.8 billion and federal tax credit carryforwards of $190.2 million. Due to the limitation on NOLs as more fully discussed below, $1.6 billion of the NOLs are available to offset future taxable income, if any. The NOL carryovers and general business tax credits expire in various years beginning in 2024. For state tax purposes, the Company has approximately $1.1 billion of NOLs in various states available to offset against future taxable income and state tax credit carryforwards of $4.7 million, expiring in various years beginning in 2024. The Company has $361.0 million of non-trading loss carryforwards in Ireland and loss carryforwards in the United Kingdom and Switzerland of $21.2 million and $75.8 million, respectively. The loss carryforwards in Ireland and the United Kingdom carry forward indefinitely while the loss carryforward in Switzerland begins to expire in 2030. The Company has disallowed interest expense carryover of $28.3 million which carries forward indefinitely.

The Company completed an Internal Revenue Code Section 382 (Section 382) analysis in order to determine the amount of losses that are currently available for potential offset against future taxable income, if any. It was determined that the utilization of the Company's NOL and general business tax credit carryforwards generated in tax periods up to and including December 2010 were subject to substantial limitations under Section 382 due to ownership changes that occurred at various points from the Company's original organization through December 2010. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of shareholders that own, directly or indirectly, 5% or more of a corporation's stock, in the stock of a corporation by more than 50 percentage points over a testing period (usually 3 years). Since the Company's formation in 1999, it has raised capital through the issuance of common stock on several occasions

14. Income Taxes (Continued)

which, combined with the purchasing shareholders' subsequent disposition of those shares, have resulted in multiple changes in ownership, as defined by Section 382. These ownership changes resulted in substantial limitations on the use of the Company's NOLs and general business tax credit carryforwards up to and including December 2010. The Company continues to track all of its NOLs and tax credit carryforwards but has provided a full valuation allowance to offset those amounts.

Law Changes

On August 16, 2022, the IRA was enacted into law containing corporate income tax provisions such as the corporate alternative minimum tax and an excise tax on the repurchase of corporate stock. These provisions are not expected to have a material impact on the Company’s income taxes in the near term.

The financial statement recognition of the benefit for a tax position is dependent upon the benefit being more likely than not to be sustainable upon audit by the applicable taxing authority. If this threshold is met, the tax benefit is then measured and recognized at the largest amount that is greater than 50% likely of being realized upon ultimate settlement. If such unrecognized tax benefits were realized and not subject to valuation allowances, the Company would recognize a tax benefit of $14.8 million. The following table summarizes the gross amounts of unrecognized tax benefits (in thousands):

	2023	2022
Balance as of January 1,	$ 11,539	$ 7,382
Additions related to prior period tax positions	230	1,564
Reductions related to prior period tax positions	—	—
Additions related to current period tax positions	2,984	2,593
Balance as of December 31,	$ 14,753	$ 11,539

The Company is subject to US federal and state income taxes and the statute of limitations for tax audit is open for the federal tax returns for the years ended 2020 and later, and is generally open for certain states for the years 2019 and later. The Company has incurred net operating losses since inception, except for the year ended December 31, 2009. Such loss carryforwards would be subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin.

The Company's policy is to recognize interest accrued related to unrecognized tax benefits and penalties in income tax expense. The Company has recorded no such expense. As of December 31, 2023 and 2022, the Company has recorded reserves for unrecognized income tax benefits of $14.8 million and $11.5 million, respectively. As any adjustment to the Company’s uncertain tax positions would not result in a cash tax liability, it has not recorded any accrued interest or penalties related to its uncertain tax positions. If any of these unrecognized tax benefits were released, there would be no impact to the Company's effective tax rate. The Company does not anticipate any material changes in the amount of unrecognized tax positions over the next 12 months.

15. License and Other Agreements

In-License Agreements

PARI Pharma GmbH—In April 2008, the Company entered into a licensing agreement with PARI for use of the optimized Lamira Nebulizer System for delivery of ARIKAYCE in treating patients with NTM lung infections, CF and bronchiectasis. Under the licensing agreement, the Company has rights under several US and foreign issued patents and patent applications involving improvements to the optimized Lamira Nebulizer System, to exploit the system with ARIKAYCE for the treatment of such indications, but the Company cannot manufacture the nebulizers except as permitted under the commercialization agreement with PARI, which is described in further detail below. The Lamira Nebulizer System has been approved for use in the US (in combination with ARIKAYCE), the EU and Japan. Under the licensing agreement, the Company paid PARI an upfront license fee and certain milestone payments. Upon FDA acceptance of the Company's NDA and the subsequent FDA and EMA approval of ARIKAYCE, the Company paid PARI additional milestone payments of €1.0 million, €1.5 million and €0.5 million, respectively. In October 2017, the Company exercised an option to buy-down the royalties that will be paid to PARI on ARIKAYCE net sales. As a result, PARI is entitled to receive royalty payments in the mid-single digits on the annual global net sales of ARIKAYCE, pursuant to the licensing agreement, subject to certain specified annual minimum royalties. See below for information related to the commercialization agreement with PARI.

Other Agreements

PPD Development, L.P.—In April 2020, the Company entered into a master services agreement with PPD pursuant to which it retained PPD to perform clinical development services in connection with certain of its clinical research programs. The master services agreement has an initial term of five years. Either party may terminate (i) any project addendum under the master services agreement for any reason and without cause upon 30 days' written notice, (ii) any project addendum in the event of the other party's breach of the master services agreement or such project addendum upon 30 days' written notice, provided that such breach is not cured within such 30-day period, (iii) the master services agreement or any project addendum immediately upon the occurrence of an insolvency event with respect to the other party or (iv) any project addendum upon 30 days' written notice if (a) the continuation of the services under such project addendum would post material ethical or safety risks to study participants, (b) any approval from a regulatory authority necessary to perform the applicable study is revoked, suspended or expires without renewal or (c) in the reasonable opinion of such party, continuation of the services provided under such project addendum would be in violation of applicable law. The Company entered into project addenda with PPD to perform clinical development services over several years for, but not limited to, its ARISE, ENCORE and ASPEN studies and other brensocatib and TPIP studies.

Patheon UK Limited—In October 2017, the Company entered into certain agreements with Patheon related to the increase of its long-term production capacity for ARIKAYCE commercial inventory. The agreements provide for Patheon to manufacture and supply ARIKAYCE for its anticipated commercial needs. Under these agreements, the Company is required to deliver to Patheon the required raw materials, including active pharmaceutical ingredients, and certain fixed assets needed to manufacture ARIKAYCE. Patheon's supply obligations will commence once certain technology transfer and construction services are completed. The Company's manufacturing and supply agreement with Patheon will remain in effect for a fixed initial term, after which it will continue for successive renewal terms unless either party has given written notice of termination. The technology transfer agreement will expire when the parties agree that the technology transfer services have been completed. The agreements may also be terminated under certain other circumstances, including by either party due to a material uncured breach of the other party or the other party's insolvency. These early termination clauses may reduce the amounts due to the relevant parties.

AstraZeneca AB—In October 2016, the Company entered into a license agreement (AZ License Agreement) with AstraZeneca, a Swedish corporation. Pursuant to the terms of the AZ License Agreement, AstraZeneca granted the Company exclusive global rights for the purpose of developing and commercializing AZD7986 (renamed brensocatib). In consideration of the licenses and other rights granted by AstraZeneca, the Company made an upfront payment of $30.0 million, which was included as research and development expense in the fourth quarter of 2016. In December 2020, the Company incurred a $12.5 million milestone payment obligation upon the first dosing in a Phase 3 clinical trial of brensocatib. Upon the earlier of Insmed's notification to AstraZeneca that Insmed intends to file NDA or Insmed releasing an official public statement that it intends to file an NDA, the Company will owe AstraZeneca an additional $12.5 million. Subsequent to this milestone, the Company is also obligated to make a series of additional contingent milestone payments totaling up to an additional $60.0 million upon the achievement of regulatory filing milestones. If the Company elects to develop brensocatib for a second indication, the Company will be obligated to make an additional series of contingent milestone payments to AstraZeneca totaling up to $42.5 million, the first of which occurs at the initiation of a Phase 3 trial in the additional indication. The

15. License and Other Agreements (Continued)

Company is not obligated to make any additional milestone payments for additional indications. In addition, the Company will pay AstraZeneca tiered royalties ranging from a high single-digit to mid-teens on net sales of any approved product based on brensocatib and one additional payment of $35.0 million upon the first achievement of $1.0 billion in annual net sales. The AZ License Agreement provides AstraZeneca with the option to negotiate a future agreement with the Company for commercialization of brensocatib in chronic obstructive pulmonary disease or asthma.

PARI Pharma GmbH—In July 2014, the Company entered into the Commercialization Agreement for the manufacture and supply of the Device as optimized for use with ARIKAYCE. Under the Commercialization Agreement, PARI manufactures the Device except in the case of certain defined supply failures, when the Company will have the right to make the Device and have it made by third parties (but not certain third parties deemed under the Commercialization Agreement to compete with PARI). The Commercialization Agreement has an initial term of fifteen years from the first commercial sale of ARIKAYCE in October 2018. The term of the agreement may be extended by the Company for an additional five years by providing written notice to PARI at least one year prior to the expiration of the Initial Term. Notwithstanding the foregoing, the parties have certain rights and obligations under the agreement prior to the commencement of the Initial Term.

Resilience Biotechnologies Inc. (successor to Therapure Biopharma Inc.)—In February 2014, the Company entered into a contract manufacturing agreement with Therapure Biopharma Inc., which was assumed by Resilience for the manufacture of ARIKAYCE, on a non-exclusive basis, at a 200 kg scale. Pursuant to the agreement, the Company and Resilience collaborated to construct a production area for the manufacture of ARIKAYCE in Resilience's existing manufacturing facility in Canada. The agreement has an initial term of five years, which began in October 2018, and will renew automatically for successive periods of two years each, unless terminated by either party by providing the required two years prior written notice to the other party. Notwithstanding the foregoing, the parties have rights and obligations under the agreement prior to the commencement of the initial term. Under the agreement, the Company is obligated to pay a minimum of $6.0 million for commercial ARIKAYCE batches produced and certain manufacturing activities each calendar year.

Cystic Fibrosis Foundation Therapeutics, Inc.—In 2004 and 2009, the Company entered into research funding agreements with CFFT whereby it received $1.7 million and $2.2 million in research funding for the development of ARIKAYCE. As a result of the US approval of ARIKAYCE and in accordance with the agreements, as amended, the Company owes milestone payments to CFFT of $13.4 million in the aggregate payable through 2025, of which $7.4 million has been paid through December 31, 2023. Furthermore, if certain global sales milestones were met within five years of the commercialization of ARIKAYCE, the Company would have owed up to an additional $3.9 million. The Company met and paid $1.7 million of these additional global sales milestone payments.

16. Commitments and Contingencies

Commitments

In September 2018, the Company entered into a lease for its new corporate headquarters in Bridgewater, New Jersey. The initial lease term commenced in October 2019 and expires in September 2030. In July 2016, the Company signed an operating lease for laboratory space, also located in Bridgewater, for which the initial lease term was extended through December 2026. In July 2023, the Company signed an amendment to expand the laboratory space in Bridgewater until 2027. In January 2022, the Company entered into a lease for research activities in San Diego, California. The lease term commenced in February 2022 and expires in June 2032. In February 2023, the Company signed an agreement to lease warehouse space in San Diego through March 2029. Future minimum rental payments under the Bridgewater leases and San Diego leases are $23.1 million and $23.9 million, respectively.

Rent expense charged to operations was $9.2 million, $8.0 million, and $4.9 million for the years ended December 31, 2023, 2022 and 2021, respectively. Rent expense is recorded on a straight-line basis over the term of the applicable leases.

In addition to rent, the Company has several firm purchase commitments, primarily related to the manufacturing of ARIKAYCE and annual minimum royalties on global net sales of ARIKAYCE. Future firm purchase commitments under these agreements, the last of which ends in 2034, total $92.7 million. These amounts do not represent the Company's entire anticipated purchases in the future, but instead represent only purchases that are the subject of contractually obligated minimum purchases. The minimum commitments disclosed are determined based on non-cancelable minimum spend amounts or termination amounts. Additionally, the Company purchases products and services as needed with no firm commitment.

Legal Proceedings

16. Commitments and Contingencies (continued)

From time to time, the Company is a party to various lawsuits, claims and other legal proceedings that arise in the ordinary course of business. While the outcomes of these matters are uncertain, management does not expect that the ultimate costs to resolve these matters will have a material adverse effect on the Company's consolidated financial position, results of operations or cash flows.

17. Retirement Plan

The Company has a 401(k) defined contribution plan for the benefit for all US employees and permits voluntary contributions by employees subject to IRS-imposed limitations. The Company matches 100% of eligible employee contributions on the first 4% of employee compensation (up to the IRS maximum). Employer contributions for the year ended December 31, 2023, 2022 and 2021 were $5.5 million, $4.6 million and $3.0 million, respectively.

18. Acquisitions

Asset Acquisitions

Adrestia Therapeutics Ltd.

In June 2023, the Company acquired all of the issued and outstanding share capital of Adrestia, a privately held, preclinical stage company. At the closing of the transaction, the Company issued an aggregate of 3,430,867 shares of the Company's common stock to Adrestia's former shareholders (collectively, the Adrestia shareholders). The closing share price on the date of the transaction was $21.10, resulting in a purchase price of $72.4 million. The Adrestia shareholders may also become entitled to receive contingent payments up to an aggregate of $326.5 million in cash upon the achievement of certain development, regulatory and commercial milestone events, as well as royalty payments based upon a low single-digit percentage of net sales of certain products, both subject to the terms and conditions of the agreement.

The shares of the Company's common stock issued to the Adrestia shareholders were issued pursuant to Section 4(a)(2) of the Securities Act of 1933 (and, with respect to certain Adrestia shareholders, in reliance on Regulation S promulgated under the Securities Act of 1933). The Company did not receive any net proceeds from the issuance of common stock to the Adrestia shareholders.

The Company evaluated the acquisition under ASC 805 and ASU 2017-01 and concluded that substantially all of the fair value of the gross assets acquired are concentrated in a single identifiable asset or a group of similar identifiable assets and accounted for the transaction as an asset acquisition. The Company determined that the IPR&D acquired did not have any future alternative use and, in accordance with ASC 730, Research and Development, expensed the assets within research and development in the consolidated statement of comprehensive loss as of the date of the acquisition. The Company recognized $76.5 million as IPR&D expense for the year ending December 31, 2023, after adjusting for working capital assumed in connection with the asset acquisition.

Vertuis Bio, Inc.

In January 2023, the Company acquired Vertuis, a privately held, preclinical stage company. At the closing of the transaction, the Company issued an aggregate of 500,000 shares of the Company's common stock to Vertuis' former stockholders and an individual who are entitled to receive a portion of the acquisition consideration (collectively, the Vertuis equityholders). The closing share price on the date of the transaction was $18.50. The Company is obligated to issue to Vertuis equityholders shares of the Company's common stock on July 1, 2024 with an aggregate value of $1.0 million, based on the share price on June 28, 2024, and pay to the Vertuis equityholders up to an aggregate of $23.0 million in cash upon the achievement of certain development and regulatory milestone events, and up to an aggregate of $63.8 million in cash upon the achievement of certain net sales-based milestone events, in each case, subject to certain reductions.

The shares of the Company's common stock issued to the Vertuis equityholders were issued, and the shares issuable in the future will be issued, pursuant to Section 4(a)(2) of the Securities Act of 1933.

The following table summarizes the purchase price (in millions).

Shares of Insmed common stock issued on closing	$	9.25
Shares of Insmed common stock issuable on July 1, 2024		1.00
Total purchase price	$	10.25

18. Acquisitions (Continued)

The Company evaluated the acquisition under ASC 805 and ASU 2017-01 and concluded that substantially all of the fair value of the gross assets acquired are concentrated in a single identifiable asset or a group of similar identifiable assets and accounted for the transaction as an asset acquisition. The Company determined that the assets acquired did not have any future alternative use and, in accordance with ASC 730, Research and Development, expensed the assets within research and development in the consolidated statement of comprehensive loss as of the date of the acquisition. The Company recognized $10.3 million as IPR&D expense for the year ending December 31, 2023.

Business Combination

On August 4, 2021, the Company acquired all of the equity interests of Motus and AlgaeneX, each a privately held, preclinical stage company. In connection with the closing of the Company's acquisition of Motus, the Company issued an aggregate of 2,889,367 shares of the Company's common stock, following certain closing-related reductions, to Motus's former stockholders and option holders and certain individuals who are entitled to receive a portion of the acquisition consideration (collectively, Motus equityholders), subject to certain adjustments. The Company is obligated to issue to Motus equityholders an aggregate of 184,433 shares of the Company's common stock on each of the first, second and third anniversaries of the closing date and up to 5,348,572 shares in the aggregate upon the achievement of certain development and regulatory milestone events, and to pay to the Motus equityholders an aggregate of $35 million upon the achievement of certain net sales-based milestones and a portion of the value of a priority review voucher (to the extent issued to the Company), in each case, subject to certain reductions. During August 2022 and August 2023, the Company fulfilled the payments due on the first and second anniversaries of the closing date by issuing 171,427 shares and 177,203 shares of the Company's common stock, after certain reductions.

At the closing of the Company's acquisition of AlgaeneX, the Company paid $1.5 million in cash to AlgaeneX's former stockholders and certain individuals who are entitled to receive a portion of the acquisition consideration (collectively, the AlgaeneX equityholders). The Company is obligated to issue to AlgaeneX's equityholders an aggregate of 368,867 shares of the Company's common stock upon the achievement of a development milestone event and pay to AlgaeneX equityholders a mid-single digits licensing fee on certain future payments received by the Company in licensing transactions for AlgaeneX's manufacturing technology, in each case, subject to certain reductions.

The shares of the Company's common stock issued to the Motus equityholders and the AlgaeneX equityholders were issued, and the shares issuable in the future will be issued, pursuant to Section 4(a)(2) of the Securities Act of 1933, and the numbers of such issued and issuable shares was calculated based on a per share value of $27.11, which was the weighted average price per share of the Company's common stock preceding the closing of the Business Acquisition for the 45 consecutive trading day period beginning on May 24, 2021. The Company will not receive any proceeds from the issuance of common stock to the Motus equityholders or the AlgaeneX equityholders.

The Company evaluated the Business Acquisition under ASC 805 and ASU 2017-01. The Company concluded that substantially all of the fair value of the gross assets acquired is not concentrated in a single identifiable asset or a group of similar identifiable assets. The transaction does not pass the screen test and thus management performed a full assessment to determine if the acquired entities met the definition of a business. For the full assessment, management considered whether it has acquired (a) inputs, (b) substantive processes, and (c) outputs. Under ASC 805, to be considered a business, a set of activities and assets is required to have only the first two of the three elements, which together are or will be used in the future to create outputs. Management determined that the acquired entities met the definition of a business since the Company acquired inputs and substantive processes capable of producing outputs.

Therefore, the transaction has been accounted for under the acquisition method of accounting. Under the acquisition method, the total purchase price of the acquisition is allocated to the net tangible and identifiable intangible assets acquired and liabilities assumed based on the fair values as of the date of the acquisition.

The fair value of the consideration totaled approximately $165.5 million, summarized as follows (in thousands):

18. Acquisitions (Continued)

	Fair Value of Consideration
Cash consideration	$ 10,500
Fair value of Insmed common stock issued	71,570
Estimated fair value of contingent consideration liabilities	69,706
Estimated fair value of deferred consideration	13,700
	$ 165,476

The Company recorded the assets acquired and liabilities assumed as of the date of the acquisition based on the information available at that date. As of December 31, 2021, the Company finalized the fair values of the assets acquired and liabilities assumed. No purchase price adjustments were recorded during the measurement period, which is the period from the acquisition date through the period ended December 31, 2021. The following table presents the allocation of the purchase price to the estimated fair values of the assets acquired and liabilities assumed as of the acquisition date (in thousands).

	Purchase Price Allocation
Cash and cash equivalents	$ 3,580
Intangible assets - IPR&D	29,600
Fixed assets	228
Other assets	17
Liabilities assumed	(558)
Deferred tax liability	(3,501)
Fair value of net assets acquired	29,366
Goodwill	136,110
	$ 165,476

The Company incurred approximately $0.6 million in acquisition-related expenses, which were included in selling, general and administrative expenses in the consolidated statements of comprehensive loss for the period ended December 31, 2021. The results of Motus's and AlgaeneX's operations have been included in the consolidated statements of comprehensive loss beginning on the acquisition date.

The fair value of IPR&D was capitalized as of the acquisition date and accounted for as indefinite-lived intangible assets until completion or disposition of the assets or abandonment of the associated research and development efforts. Upon successful completion of the development efforts, the useful lives of the IPR&D assets will be determined based on the anticipated period of regulatory exclusivity and will be amortized within operating expenses. Until that time, the IPR&D assets will be subject to impairment testing and will not be amortized. The goodwill recorded related to the acquisition is the excess of the fair value of the consideration transferred by the acquirer over the fair value of the net identifiable assets acquired and liabilities assumed at the date of acquisition. The goodwill recorded is not deductible for tax purposes.