Risk Factors Comparison 2024-02-22 to 2023-02-23 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

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** ~~the degree of~~ 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. • ~~We~~ **Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time** may ~~not~~ **change as more patient data become available, may** be ~~able~~ **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 ~~approvals~~ **approval** ~~for~~ **or** ~~brensocatib, clearance of or our for our other~~ product ~~candidates~~ **devices , including Lamira, as a delivery system** ~~and we may not be able to receive approval~~ for ARIKAYCE **and the delivery system for TPIP, could** ~~in new markets. Any such failure to obtain regulatory approvals may~~ materially ~~adversely affect us~~ **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. • ~~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. •~~ 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 ~~our~~ **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. • ~~The COVID- 19 pandemic and efforts to reduce its spread have negatively impacted, and could continue to negatively impact, our business and 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. • ~~Our use of hazardous materials could expose us to damages, fines, penalties and sanctions and materially adversely affect our results of operations and financial condition. •~~ 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 ~~US~~ 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** ~~have commenced commercialization~~ --- **commercializing** ~~of~~ 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 ~~US~~ 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 ~~Limited Population Pathway for Antibacterial and Antifungal Drugs (~~ 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 ~~frontline~~ clinical trial program for ARIKAYCE in patients with MAC lung disease. The ~~frontline~~ **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. ~~We are running these global studies in parallel in approximately 200 sites for these clinical trials.~~ The ~~frontline~~ **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. ~~Pursuant to the~~ **The trial completion** timetable agreed upon with the FDA when the approval letter ~~of~~ **for** ARIKAYCE was received **has been delayed** ~~, confirmatory trial results are to be reported by 2024~~ . We ~~are~~ **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 ~~validated in~~ **approved as** the ~~ARISE trial~~ **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 ~~either~~ **the** trial, and we may not be able to enroll and conduct the ~~trials~~ **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. ~~Additionally, ARIKAYCE is subject to post- marketing commitments consisting of implementation of a healthcare provider communication plan, conducting a drug utilization assessment, and conducting further studies to identify an optimal quality control in vitro drug release method. We have fulfilled the post- marketing commitment for the identification of the in vitro drug release method.~~ 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 ~~anticipate~~ **experienced** a one- time, prospective price decrease for ARIKAYCE in Japan **of 9. 4 %** ~~in the high- single digit to low- double digit range~~ . 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, ~~inter alia~~ **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 ~~. For instance, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) expanded Medicare outpatient prescription drug coverage for the elderly through Part D prescription drug plans sponsored by private entities and authorized such plans to use formularies where they can limit the number of drugs that will be covered in any therapeutic class. The plans generally negotiate significant price concessions as a condition of formulary placement. The MMA also introduced a new reimbursement methodology based on average sales prices for physician- administered drugs, which is generally believed to have resulted in lower Medicare reimbursement for physician- administered drugs. These cost reduction initiatives and other provisions of this legislation provide additional pressure to contain and reduce drug prices and could decrease the coverage and price that we receive for any approved products and could seriously harm our business. Although the MMA applies only to drug benefits for Medicare~~

~~beneficiaries, private payors often follow Medicare coverage policy and payment limitations when setting their own reimbursement rates, and any reimbursement reduction resulting from the MMA may result in a similar reduction in payments from private payors. Additionally, the Patient Protection and Affordable Care Act (ACA) revised the definition of " average manufacturer price " for reporting purposes and increased the minimum percentage for Medicaid drug rebates to states, required drug manufacturers to provide a significant discount (70 % as of January 1, 2022) on prescriptions for branded drugs filled while the beneficiary is in the Medicare Part D coverage gap (also known as the donut hole), and imposed a significant annual fee on companies that manufacture or import branded prescription drug products. We believe it is likely that the ACA, or any legislation enacted to amend or replace it, will continue the pressure on pharmaceutical pricing, especially under the Medicare program, and also may increase our regulatory burdens and operating costs~~ . 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** ~~, as written, gives~~ **give** ~~the US Department of Health and Human Services (~~ 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 ~~will~~ also ~~require~~ **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 ~~the~~ **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 ~~. For instance, we have observed an increase in the time to fill prescriptions, particularly for patients insured through Medicare, in the first quarter of each year since we began commercializing ARIKAYCE as a result of the donut hole, and, while the situation has not extended through the entire year, this situation may recur in the first quarter of subsequent years~~ . 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 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. 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. 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. ~~We~~ **While we reported positive topline results from our ARISE trial, we** are **continuing to** ~~conducting~~ --- **conduct** our confirmatory clinical trial program for full approval of ARIKAYCE ~~, through the ARISE trial and the ENCORE trial,~~ 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 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, ~~and~~ 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. **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 ~~routinely assess regulatory strategies which could expedite the development and regulatory review of our product candidates in the US and other markets, but we may be unsuccessful in pursuing such strategies. The FDA has denied our request for orphan drug designation for brensocatib for the treatment of bronchiectasis. 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 ~~.~~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. 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 ~~a~~ **an indication within the designated** rare disease or condition generally receives marketing exclusivity for use of that drug for **that indication** ~~the designated disease or condition~~ 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** ~~disease or condition~~ 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** ~~disease or condition~~ under certain circumstances. 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. Lamira must receive separate regulatory approval or..... ability to develop and commercialize TPIP. 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 ~~and ,~~ 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 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 ~~. As additional supporting data become available, we believe the current approved shelf life for product manufactured at our CMOs will increase~~ . 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 ~~until at least 2023~~ **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 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. 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 ~~and ,~~ 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. ~~Risks generally associated~~ **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 ~~the~~ **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 ~~(ERP)~~ system ~~may materially adversely affect our business~~ , ~~financial condition~~ **which was implemented through Oracle software in 2022** , ~~results of operations~~ and **a new enterprise** ~~prospects and the value of our common stock or the effectiveness of our internal controls over financial reporting. We upgraded our company~~ - wide ~~ERP~~ **human capital management** system **, Workday, expected to be implemented** in ~~the third quarter of 2022~~ **2024** ~~, in order to enhance certain business and financial operations and processes and increase data security~~ . If ~~the~~ **we are unable to successfully continue** ~~upgrade~~ **upgrading** ~~to our~~ - **or** ~~ERP system does~~ **expanding our technological capabilities to support our growth or if there are deficiencies in the design or implementation of such capabilities, we may** not ~~enhance our business and financial operations or increase our data security as we expect, our business could~~ be **able** ~~adversely affected. The upgrade~~ to **take advantage** ~~our ERP system has required and will continue to require capital and human resources, changes to our business processes and the attention~~ of **market opportunities** ~~many of our employees. Any deficiencies in the design and implementation of the upgraded ERP system could result in potentially significantly more expenses than already incurred and could adversely affect our ability to operate our business~~ , ~~including~~ **manage** our ~~ability to~~ **costs effectively,** manage our inventory, maintain a secure data environment, file timely reports with the SEC, or otherwise ~~affect~~ **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 ~~of~~ **failure by such vendors to do so, or any disruption in our ability to access** ~~these~~ -- **the** ~~consequences~~ **Internet,** could materially **and** adversely affect our **ability to manage our** ~~business, financial condition, results of~~ operations ~~and prospects and the value~~ **. We have limited experience operating internationally, are subject to a number** of ~~our common stock~~ **risks associated with** ~~or~~ **our** ~~the effectiveness of our internal~~ **international** ~~controls over financial reporting~~ **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, ~~2022~~ **2023** , we had ~~85~~ **124** employees located in Europe and ~~72~~ **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 ~~geopolitical events, such as war and terrorism,~~ foreign currency fluctuations and inflation, ~~which~~ 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** ~~disruption~~ **disruptions** ~~to~~ **in** our international operations, including planned or ongoing clinical studies ~~, reduced revenue, increased or unpredictable operating expenses and other obligations incident to doing business in, or with a company located in, another country~~ ; 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. 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. Our three largest customers as of December 31, ~~2022~~ **2023** accounted for **88 % and** 90 ~~% and 75~~ % of our total gross product revenue for the years ended December 31, **2023 and** 2022 ~~and 2021~~ , 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. ~~The degree to which~~ **A pandemic, including a resurgence of** COVID- 19 ~~affects us will depend on developments that are highly uncertain and beyond our knowledge or control~~ , ~~including, but not limited to, the duration and severity of the pandemic, the actions taken to reduce its transmission, and the speed with which and the extent to which normal economic and operating conditions resume. We are committed to the safety and well- being of our workforce. Our employees (other than our laboratory personnel) have been provided a flexible approach to where and how they work to enable them to more easily manage business and personal responsibilities. We have enhanced our internal communications and touch points to ensure connectivity to our workforce. We will continue to manage this situation with a focus on the safety of our employees, ARIKAYCE physicians, caregivers and patients. 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. ~~The~~ **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 ~~COVID- 19~~ illness, concerns about ~~the~~ **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** ~~amikacin liposome inhalation suspension~~ 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 ~~active pharmaceutical ingredient for~~ **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** ~~rely upon~~ 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~~ **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 ~~licensing agreement with PARI, with respect to NTM lung disease and bronchiectasis, we have specific obligations to use commercially reasonable efforts to achieve certain developmental and regulatory milestones by set deadlines. Additionally, for NTM lung disease, we are obligated to use commercially reasonable efforts to achieve certain commercial milestones in Europe. The consequences of our failing to use commercially reasonable efforts to achieve certain commercial milestones are context- specific, but include ending PARI' s non- compete obligation, making the license non- exclusive and terminating the license, in each case with respect to the applicable indication. Similarly, 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 ~~. Finally, if we do not proceed with the development of our ARIKAYCE program in the NTM lung disease or CF indications, certain of our contract counterparties may elect to proceed with the development of these indications~~ . Risks Related to Government Regulation 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 ~~federal privacy regulations under the~~ Health Insurance Portability and Accountability Act of 1996 (HIPAA), state, and foreign ~~medical record~~ privacy laws may limit access to information identifying those individuals who may be prospective users **or limit the ability to market to them** . ~~There~~ **Some of these laws** are ~~ambiguities~~ **new or ambiguous** as to what is required to comply with ~~these~~ **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 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, ~~2022~~ **2023** , our accumulated deficit was $ ~~2~~ **3** . ~~7~~ **4** billion. For the years ended December 31, **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , our consolidated net loss was $ **749. 6 million, $** 481. 5 million ~~,~~ **and** $ 434. 7 ~~million and $ 294. 1~~ 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. 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 ~~than in 2021~~ , 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. In October 2022, we entered into a loan agreement (the Loan Agreement) with certain funds managed by Pharmakon ~~Advisors, LP (Pharmakon)~~ and a revenue interest purchase agreement (the Royalty Financing Agreement) with OrbiMed ~~Royalty & Credit Opportunities IV, LP (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 ~~. Accounting guidance requires that we separately account for the liability and equity components of the Convertible Notes because they may be settled entirely or partially in cash upon conversion in a manner that reflects our economic interest cost. As a result, the equity component of the Convertible Notes is required to be included in the additional paid- in capital section of shareholders' equity on our consolidated balance sheet, and the value of the equity component is treated as original issue discount for purposes of accounting for the debt component of the Convertible Notes. We may report greater net loss (or lower net income) in our financial results because this guidance requires interest to include both the current period' s amortization of the debt discount and the instrument' s coupon interest, which could adversely affect our reported or future financial results, the market price of our common stock and the trading prices of the Convertible Notes~~ . 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 have substantial tax loss carry forwards ~~for~~ **in the** US **(both** federal ~~income tax~~ and state **)** ~~income tax purposes~~ , ~~and beginning in 2015, we had tax loss carry forwards in~~ Ireland ~~as well~~ **, 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** . 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 ~~balance sheets~~ **financial statements** , which could adversely affect our business, results of operations and financial condition. Risks Related to Ownership of Our Common Stock 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. 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 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. ~~We previously had a shareholder rights plan, or " poison pill, " which expired in May 2011.~~ Under Virginia law, our board of directors may implement a ~~new~~ shareholders' rights plan **or" poison pill"** without shareholder approval. Our board of directors ~~intends to~~ regularly ~~consider~~ **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.