Risk Factors Comparison 2024-02-21 to 2023-02-22 Form: 10-K

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Risks Related to Our Products and Our Operations We rely heavily on sales of our treprostinil- based therapies to generate revenues and support our operations. Sales of our treprostinil- based therapies — Tyvaso **DPI** , **nebulized** Tyvaso ~~DPI~~ , Remodulin, and Orenitram — comprise the vast majority of our revenues. Substantially decreased sales of any of these products could have a material adverse impact on our operations. A wide variety of events, such as withdrawal of regulatory approvals or substantial changes in prescribing practices or dosing patterns, many of which are described in other risk factors below, could cause sales of these products to materially decline, or to grow more slowly than expected. **Our net revenues could also be negatively impacted by pricing pressure as a result of competitive challenges, the IRA, and other drug price reduction initiatives.** The current and expected availability of generic versions of our products has decreased **,** and may continue to decrease **,** our revenues. The approval of new therapies may negatively impact sales of our current and potential new products. Sales may decrease if any third party that manufactures, markets, distributes, or sells our commercial products cannot do so satisfactorily, or we cannot manage our internal manufacturing processes. Finally, if demand for Tyvaso DPI does not meet our expectations, the revenue opportunity for our treprostinil products could be significantly lower than we expect. If our products fail in clinical trials, we will be unable to sell those products. To obtain approvals from the FDA and international regulatory agencies to sell new products, or to expand the product labeling for our existing products, we must conduct clinical trials demonstrating that our products are safe and effective. Regulators have substantial discretion over the approval process. Regulators may require us to amend ongoing trials or perform additional trials, which have in the past and could in the future result in significant delays and additional costs and may be unsuccessful. Delays and costs associated with regulatory requirements to change or add trials have sometimes caused us to discontinue efforts to develop a particular product, and may do so again in the future. If our clinical trials are not successful, or we fail to address identified deficiencies adequately, we will not obtain required approvals to market the new product or new indication. We cannot predict with certainty how long it will take, or how much it will cost, to complete necessary clinical trials or obtain regulatory approvals of our current or future products. The time and cost needed to complete clinical trials and obtain regulatory approvals varies by product, indication, and country. In addition, failure to obtain, or delays in obtaining, regulatory approval has in the past and could in the future require us to recognize impairment charges. Our clinical trials have been ~~(for example, the PERFECT study),~~ and in the future may be ~~,~~ discontinued, delayed, canceled, or disqualified for various reasons, including: (1) **pandemics such as** the COVID- 19 pandemic, which initially caused us to suspend enrollment of most of our clinical studies ~~, and may do so again~~ ; (2) the drug is **unsafe or** ineffective, or physicians and / or patients believe that the drug is **unsafe or** ineffective, or that other therapies are **safer,** more effective **, better tolerated,** or **more** convenient; (3) patients do not enroll in or complete clinical trials at the rate we expect **, due to the availability of alternative therapies, the enrollment of competing clinical trials, or other reasons** ; (4) we, or clinical trial sites or other third parties do not adhere to trial protocols and required quality controls under good clinical practices (GCP) regulations and similar regulations outside the United States; (5) patients experience severe side effects during treatment or die during our trials because of adverse events; and (6) the results of clinical trials conducted in a particular country are not acceptable to regulators in other countries. We may not compete successfully with established or newly developed drugs or products. Competition could negatively impact our operating results. We compete with well- established drug companies for market share, as well as, among other things, funding, licenses, expertise, personnel, clinical trial patients and investigators, consultants, and third- party collaborators. Some of these competitors have substantially greater financial, marketing, manufacturing, sales, distribution, and technical resources, and a larger number of approved products, than we do. Some of these competitors also possess greater experience in areas critical to success such as research and development, clinical trials, sales and marketing, and regulatory matters. Numerous treatments currently compete with our commercial therapies. For example, for **the** treatment of PAH, we compete with over fifteen branded and generic drugs. Sales of a generic version of Adcirca launched in August 2018 have had a material adverse impact on our sales of Adcirca. The availability of generic **treprostinil injection** ~~versions of Remodulin~~ in the United States could materially impact our revenues, and generic competition has materially impacted our Remodulin revenues outside the United States. Our competitors are also developing new products that may compete with ours. For example, Liquidia and Merck are developing Yutrepia and sotatercept, respectively, which **could be approved by the FDA during 2024 and** if successful would compete with our treprostinil- based products **, potentially materially adversely affecting our revenues. There are also two therapies approved for the treatment of IPF, and a significant number of additional therapies being developed for the treatment of IPF, which would compete with Tyvaso DPI and nebulized Tyvaso if they are ultimately approved for that indication** . Patients and doctors may discontinue use of our products if they perceive competing products as safer, more effective, less invasive, more convenient, and / or less expensive than ours. Doctors may reduce the prescribed doses of our products if they **36United Therapeutics, a public benefit corporation** prescribe them in combination with competing products. In addition, many competing therapies are less invasive or more convenient than our products, and use of these competing therapies often delays or prevents initiation of our therapies. ~~32United Therapeutics, a public benefit corporation~~ The successful commercialization of our products depends on the availability of coverage and adequacy of reimbursement from third- party payers, including governmental authorities and private health insurers. Pharmaceutical pricing and reimbursement pressures may negatively impact our sales. The commercial success of our products depends, in significant part, on coverage by governmental payers such as Medicare and Medicaid, and private insurance companies. A reduction in the availability or extent of reimbursement from

domestic or foreign government health care programs could have a material adverse effect on our business and results of our operations. Government payers and third- party payers are increasingly attempting to limit the price of medicinal products and frequently challenge the pricing of new or expensive drugs. In many markets outside the United States, governments control the prices of prescription pharmaceuticals through the implementation of reference pricing, price cuts, rebates, revenue- related taxes, and profit control. Financial pressures may cause United States government payers and / or private health insurers to implement policies that would reduce reimbursement rates for our products, limit future price increases, cap reimbursement rates for pharmaceuticals to rates paid internationally, require the automatic substitution of generic products, demand more rigorous requirements for initial coverage for new products, implement step therapy policies that require patients to try other medicines, including generic products, before using our products, or take other similar steps that could make it more difficult for patients to access our products. See, for example, the discussion of the **IRA** ~~Inflation Reduction Act~~ in the risk factor below entitled Government healthcare reform and other reforms could adversely affect our revenue, costs, and results of operations. Our prostacyclin analogue products (Tyvaso **DPI** , **nebulized** Tyvaso ~~DPI~~ , Remodulin, and Orenitram) and our oncology product (Unituxin) are expensive therapies. Specialty pharmacy distributors may not be able to obtain adequate reimbursement for our products from commercial and government payers to motivate them to support our products. Third- party payers may reduce the amount of reimbursement for our products based on changes in pricing of other therapies for the same disease or the development of new payment methodologies to cover and reimburse treatment costs, such as the use of cost- effectiveness research or value- based payment contracts. Third- party payers often encourage the use of less- expensive generic alternative therapies, which has materially impacted our Adcirca revenues and which may materially impact our Remodulin revenues **and revenues from our other products if and when generic competitors come to market. Similarly, pricing and rebating strategies for new competitive therapies could put pressure on us to reduce the prices of our products and / or offer increased rebates to third- party payers** . If commercial or government payers do not cover our products or limit payment rates, patients and physicians could choose ~~covered~~ competing products ~~and may have~~ **or products with** lower out- of- pocket costs. Our manufacturing strategy exposes us to significant risks. We must be able to manufacture sufficient quantities of our commercial products to satisfy demand. We manufacture **nebulized Tyvaso drug product,** Remodulin, Orenitram ~~, Tyvaso~~ , and Unituxin, including the active ingredient in each of these products, at our own facilities and rely on third parties for additional manufacturing capacity for **nebulized Tyvaso and** Remodulin ~~and Tyvaso~~ . We **also** ~~rely entirely on MannKind to manufacture Tyvaso DPI, Minnetronix Inc. to manufacture the Tyvaso Inhalation System, and DEKA to manufacture the Remunity Pump for Remodulin, and we~~ rely on ~~a variety of other~~ third- **parties** ~~party sole manufacturers~~ for ~~certain elements of~~ our **manufacturing, sometimes exclusively** ~~commercial and development- stage products~~ , as detailed under the risk factor below entitled, We rely in part on third parties to perform activities that are critical to our business. If any of our internal or third- party manufacturing and supply arrangements are interrupted ~~for compliance issues, issues related to pandemics, or other reasons~~ , we may not have sufficient inventory to meet future demand. Changes in suppliers and / or service providers could interrupt the manufacturing of our commercial products and impede the progress of our commercial launch plans and clinical trials. Our internal manufacturing process subjects us to risks as we engage in increasingly complex manufacturing processes. We manufacture our entire supply of Orenitram and Unituxin without an FDA- approved back- up manufacturing site, and do not plan to engage a third party to manufacture these ~~materials~~ **products** . Our ~~long- term~~ organ manufacturing programs will involve exceptionally complicated manufacturing processes, many of which have never been attempted on a clinical or commercial scale. It will take substantial time and resources to develop and implement such manufacturing processes, and we may never be able to do so successfully. Additional risks of our manufacturing strategy include the following: • We, our third- party manufacturers, and other third parties involved in the manufacturing process, such as third parties that operate testing and storage facilities, are subject to the **cGMP requirements of the** FDA ~~' s current good manufacturing practices regulations~~ **and its international counterparts, as applicable** , current good tissue practices, and similar international regulatory standards, and other quality standards related to device manufacturing. Our ability to exercise control over regulatory compliance by our third- party manufacturers is limited. **• We believe we and our third- party manufacturers need to increase our respective manufacturing capacity by constructing new facilities, and / or expanding existing facilities, in order to continue meeting anticipated demand for our products. These efforts are often costly and time- consuming, and must meet rigorous regulatory requirements. For example, we are engaged in significant efforts to expand MannKind' s capacity to manufacture Tyvaso DPI in the near term, at our expense. Longer- term, we are constructing our own facility to manufacture Tyvaso DPI. These efforts could be unsuccessful or take longer or cost more than we anticipate, due to a variety of factors including the lead time needed to procure, install, and qualify the highly specialized equipment necessary to manufacture the product. If these plans are not successfully and timely implemented, we could be unable to meet the growing demand for Tyvaso DPI, which would negatively impact our Tyvaso DPI revenues. 2023 Annual Report37** • We may experience difficulty designing and implementing processes and procedures to ensure compliance with applicable regulations as we develop manufacturing operations for new products. • Natural and man- made disasters (such as fires, contamination, power loss, hurricanes, earthquakes, flooding, terrorist attacks, and acts of war), disease outbreaks, and pandemics such as COVID- 19 impacting our internal and third- party manufacturing sites could cause a supply disruption. • **The** ~~Even if we, our third- party manufacturers, and other third parties involved in the manufacturing process comply with applicable drug and device manufacturing regulations, the~~ sterility and quality of our products could be substandard and such products could not be sold or used or could be subject to recalls. • The FDA and its international counterparts would require new testing and compliance inspections of new manufacturers of our products, or new manufacturing facilities we operate. • ~~The~~ **If we produce products that do not meet** FDA **- approved specifications** and **we fail to detect these issues prior to distribution of these products, our products may be the subject of safety alerts, product recalls, or** other **corrective actions, and we may be charged in product liability claims and lawsuits which, regardless of their ultimate outcome,**

could have a material adverse effect on our business and reputation and on our ability to attract and retain customers. • ~~regulatory~~ **Regulatory** agencies may not be able to timely inspect our facilities, or those of our third- party manufacturers, which could result in delays in obtaining necessary regulatory approvals for our products. ~~2022 Annual Report33~~ • We may be unable to contract with needed manufacturers on satisfactory terms or at all. • The supply of materials and components necessary to manufacture and package our products may become scarce or unavailable, which could delay the manufacturing and subsequent sale of such products. For example, supply disruptions caused by COVID- 19 impacted DEKA' s ability to secure certain components and raw materials necessary to manufacture sufficient quantities of Remunity Pumps and accessories, delaying our ability to commence commercial sales, and ongoing global semiconductor supply disruptions could impact our third- party manufacturers' ability to secure semiconductor chips necessary to manufacture sufficient quantities of devices required to ~~deliver~~ **administer nebulized** Tyvaso and Remodulin, which would have a material impact on our operations. Products manufactured with substituted materials or components must be approved by the FDA and applicable international regulatory agencies before they ~~could~~ **can** be sold. • ~~Our business partners who manufacture~~ **Manufacturers of** the devices **used** to ~~deliver~~ **administer** our ~~products~~ **inhaled and infused therapies** are subject to ~~the FDA' s~~ medical device requirements **of the FDA and its international counterparts, as applicable** . Any non- compliance, recall, or enforcement action issued against them could adversely impact our sales and operations. • The infrastructure of our internal manufacturing facilities, along with certain facilities of our third- party manufacturers, is aging. These facilities have highly sophisticated and complex utility systems. If any of these systems require long- term repair or replacement, the impacted facility may not be able to manufacture product for a substantial period of time. • We **and** ~~, along with~~ our third- party manufacturers ~~,~~ rely upon local municipalities to supply our facilities with clean water, which is processed into high purity water and used as a key ingredient for ~~three~~ **several** of our commercial drug products. If local municipalities are unable to supply water that meets relevant quality standards, we and our third- party manufacturers may be unable to manufacture **these** ~~product~~ **products** until such a situation is remediated. • Our supply chain for raw materials and consumables extends worldwide and is complex. Suppliers based in China and Taiwan play a substantial role in our supply chain. Political unrest or trade disputes involving China, Taiwan, or other countries in our supply chain could impact our ability and the ability of our third- party manufacturers to source raw materials and consumables. We also have limited visibility into the supply chains on which our primary suppliers rely; as such, we rely on our primary suppliers to have robust risk mitigation strategies to detect issues and prevent supply disruption. • We are closely monitoring the military ~~conflict~~ **conflicts** in Ukraine **and Israel** . Although we do not directly source any raw materials or consumables from Ukraine, Russia, ~~or~~ Belarus, **Gaza, or Israel,** our European **- and Middle East** - based suppliers and service providers could be impacted by ~~an~~ extended ~~conflict~~ **conflicts** or an escalation of ~~the~~ **these** ~~conflict~~ **conflicts** into neighboring countries. **• The cost of many key raw materials and consumables used in the manufacture of our products has increased due to significant inflationary pressure. Should inflation continue to grow above historical averages, we could see higher than average year- over- year increases in cost of goods sold. • Any of our third- party manufacturers could undergo a change of control, causing a change in our business relationship with the relevant manufacturer. Such a change could impact our long- term supply outlook and cause us to seek alternatives that could require a lengthy regulatory approval process. Due to the nature of our products, alternative suppliers may not be readily available, causing us to rely solely on internal capabilities to meet future demand. • In 2024, we plan to begin operating a clinical scale, designated pathogen- free facility (DPF) to produce our xenotransplantation products for human clinical studies. This facility will house genetically modified pigs in a highly controlled containment environment. This facility is a first of its kind, and unforeseen operational issues or disease outbreak amongst its herd could significantly impact the clinical development timelines for our xenotransplantation products. We will need to construct additional commercial- scale DPF facilities at significant expense in order to support the commercialization of our xenotransplantation products. 38United Therapeutics, a public benefit corporation** Any of these factors could disrupt sales of our commercial products, delay clinical trials or commercialization of new products, result in product liability claims and product recalls, and entail higher costs. Interruptions in our manufacturing process could be significant given the length of time and complexity involved in obtaining necessary regulatory approvals for alternative arrangements, through either third parties or internal manufacturing processes. Third parties assist us in activities critical to our operations, such as: (1) manufacturing our clinical and commercial products; (2) conducting clinical trials, preclinical studies, and other research and development activities; (3) obtaining regulatory approvals; (4) conducting pharmacovigilance and product complaint activities, including **adverse event** ~~drug safety,~~ reporting ~~adverse events~~ , and handling product complaints; (5) obtaining medical device clearances and approvals for the devices used to ~~deliver~~ **administer** our drugs; and (6) marketing and distributing our products. Any disruption in the ability of third parties to continue to perform these critical activities ~~, including as a result of the COVID- 19 pandemic,~~ could materially adversely impact our business and results of operations. Any change in service providers could interrupt the manufacture and distribution of our products and services, and impede the progress of our clinical trials, commercial launch plans, and related revenues. We rely on various distributors to market, distribute, and sell our commercial products. If they are unsuccessful in, or reduce or discontinue, their sales efforts, our revenues may decline materially. Outside the United States, we rely substantially on our international distributors to obtain and maintain regulatory approvals for our products and to market and sell our products in compliance with applicable laws and regulations. In the United States, we derive **substantially** all of our treprostinil- based revenues from sales to two distributors, Accredo and CVS Specialty. If either of these two distributors places significantly larger or smaller orders in a given time period, our revenues can be materially impacted in a way that does not reflect patient demand. We rely entirely on third parties to supply pumps and other supplies necessary to ~~deliver~~ **administer** Remodulin. There are a limited number of pumps available in the market, and the discontinuation of any particular pump could have a material, adverse impact on our Remodulin revenues if a viable supply of an alternate pump is not available. Smiths Medical **(which has since been acquired by ICU Medical)** discontinued manufacturing the MS- 3 system used to ~~deliver~~ **administer** subcutaneous Remodulin, and specialty pharmacy

distributors ~~have~~ informed us that supplies of MS- 3 pumps are ~~nearly~~ **fully** exhausted. ~~Smiths~~ **In 2022, ICU** Medical ~~has also announced plans to discontinue~~ **discontinued manufacturing and distribution of** the CADD **-** Legacy system used to ~~deliver~~ **administer** intravenous Remodulin. Historically, these ~~are~~ **were** the pumps primarily used to ~~deliver~~ **administer** Remodulin to patients in the United States. In 2021, we launched the Remunity Pump to ~~deliver~~ **administer** subcutaneous Remodulin, and ~~Smiths~~ **in 2022 ICU** Medical ~~plans to make~~ **made** an alternative pump, the CADD **-** Solis, available for intravenous Remodulin. We **rely entirely on DEKA and its affiliates to manufacture the Remunity Pump for Remodulin. We** are also engaged in further efforts to develop alternative pumps to ~~deliver~~ **administer** Remodulin. However, if these alternative systems are not seen as adequate substitutes, or are not developed on a timely basis, our sales of Remodulin could be materially, adversely impacted. Lilly manufactures and supplies Adcirca for us. We use Lilly' s pharmaceutical wholesaler network to distribute Adcirca. If Lilly is unable to manufacture or supply Adcirca or its distribution network is disrupted, it could delay, disrupt, or prevent us from selling ~~34United Therapeutics, a public benefit corporation~~ Adcirca. We rely ~~entirely~~ on **two contract manufacturers —** Minnetronix Inc. ~~as the sole~~ **and Phillips- Medisize Corp. — to** ~~manufacturer~~ **manufacture** ~~of~~ the Tyvaso Inhalation System **for nebulized Tyvaso** . As **nebulized** Tyvaso is a drug- device combination, we cannot sell **nebulized** Tyvaso without the Tyvaso Inhalation System. We **also rely on various third parties to supply the monthly disposable device accessories that are used with the Tyvaso Inhalation System to administer nebulized Tyvaso. We currently** rely entirely on MannKind to manufacture Tyvaso DPI **finished drug product and inhalers** for us. If MannKind is unable to manufacture Tyvaso DPI **in sufficient quantities** for us for any reason, our commercial sales of Tyvaso DPI ~~would~~ **could** be materially and adversely impacted ~~. We rely entirely on DEKA and its affiliates for the manufacture of the Remunity Pump for Remodulin~~ . Finally, we also rely on various sole- source suppliers for manufacturing activities related to ralinepag ~~, RemoPro,~~ and other pumps we are developing for **Remodulin. We also rely entirely on Gilero to manufacture cartridges that were recently cleared by the FDA for use with the MS- 3 pump to administer** Remodulin. For a further discussion of risks created by the use of third- party contract manufacturers, see the risk factor above entitled, Our manufacturing strategy exposes us to significant risks. We rely heavily on third- party contract research organizations, contract laboratories, clinical investigative sites, and other third parties to conduct our clinical trials, preclinical studies, and other research and development activities. In addition, the success of certain products we are developing will depend on clinical trials sponsored by third parties. Third- party failure to conduct or assist us in conducting clinical trials in accordance with study protocols, quality controls, GCP, or other applicable requirements or to submit associated regulatory filings, could limit or prevent our ability to rely on results of those trials in seeking regulatory approvals. Reports of actual or perceived side effects and adverse events associated with our products could cause our sales to decrease or regulatory approvals to be revoked. Reports of side effects and adverse events associated with our products could affect a physician' s decision to prescribe or a patient' s willingness to use our products, which may have a significant adverse impact on sales of our products. An example of a known risk associated with the ~~delivery~~ **pump** system used for intravenous Remodulin is sepsis, which is a serious and potentially life- threatening infection of the bloodstream caused by a wide variety of bacteria. In addition, Unituxin is associated with severe side effects, and its label contains a boxed warning related to potential infusion reactions and neurotoxicity. We are required to report certain adverse events to the FDA **and its international counterparts** . Development of new products, and **2023 Annual Report39** new formulations and indications for existing products, could result in new side effects and adverse events which may be serious in nature. If the use of our products harms patients or is perceived to harm patients, regulatory approvals could be revoked or otherwise negatively impacted. Negative attention from special interest groups may impair our business. Our early- stage research and development involves animal testing required by regulatory authorities, which we conduct both directly and through contracts with third parties. Our xenotransplantation and regenerative medicine programs rely heavily on the use of animals to manufacture and test our products. Certain special interest groups categorically object to the use of animals for research purposes. Any negative attention, threats or acts of vandalism directed against our animal research activities could impede the operation of our business. We may not maintain adequate insurance coverage to protect us against significant product liability claims. The testing, manufacturing, marketing, and sale of drugs and diagnostics involve product liability risks. We may not be able to maintain our current product liability insurance at an acceptable cost, if at all. In addition, our insurance coverage may not be adequate for all potential claims. If losses significantly exceed our liability insurance coverage, we may experience financial hardship or potentially be forced out of business. Clinical testing and eventual marketing and sale of new products, reformulated versions of existing products, or use of existing products in new indications could expose us to new product liability risks that are not covered by our existing policies. If we fail to attract and retain key management and qualified scientific and technical personnel, we may not be able to achieve our business objectives. Members of our management team, including our founder, Chairperson and Chief Executive Officer, Dr. Martine Rothblatt, play a critical role in defining our business strategy and maintaining our corporate culture. The loss of the services and leadership of Dr. Rothblatt or any other members of our senior management team could have an adverse effect on our business. We do not maintain key person life insurance on our senior management team members. Failure to identify, hire, and retain suitable successors for members of our senior management team and to transfer knowledge effectively could impede the achievement of our business objectives. Our future success also depends on our ability to attract and retain qualified scientific and technical personnel. Competition for such personnel in our industries is intense. If we fail to attract and retain such employees, ~~whom we call " Unitherians ",~~ we may not be successful in developing and commercializing new therapies. Risks Related to Legal Compliance We must comply with extensive laws and regulations in the United States and other countries. Failure to obtain approvals on a timely basis or to comply with these requirements could delay, disrupt, or prevent commercialization of our products. The products we develop must be approved for marketing and sale by regulatory agencies. Our research and development efforts must comply with extensive regulations, including those promulgated by the FDA ~~and~~ **,** the U. S. Department of Agriculture **, and their international counterparts, as applicable** . The process of obtaining and maintaining regulatory approvals for new drugs, biologics, and medical devices is lengthy, expensive, and

uncertain. The regulatory approval process is particularly uncertain for our transplantation programs, which include the development of xenotransplantation, regenerative medicine, 3- D organ bioprinting, and cell- based products. Once approved, the ~~2022 Annual Report35~~ manufacture, distribution, advertising, and marketing of our products are subject to extensive regulation, including **requirements related to** product labeling, ~~strict~~ pharmacovigilance and adverse event and medical device reporting, complaint processing, storage, distribution, and record- keeping ~~requirements~~. Our product candidates have in the past and may in the future fail to receive regulatory approval. If granted, product approvals can be conditioned on the completion of post- marketing clinical studies, accompanied by significant restrictions on the use or marketing of a given product and withdrawn for failure to comply with regulatory requirements, such as post- marketing requirements and post- marketing commitments, or upon the occurrence of adverse events subsequent to commercial introduction. Our ability to obtain ~~FDA~~ **regulatory** ~~approval~~ **approvals** for our products has been, and in the future may be, materially impacted by the outcome and quality of our clinical trials and other data submitted to regulators, as well as the quality of our manufacturing operations and those of our third- party contract manufacturers and contract laboratories. In addition, third parties may submit citizen petitions to the FDA seeking to delay approval of, or impose additional approval conditions for, our products. If successful, citizen petitions can significantly delay, or even prevent, the approval of our products. For example, a third party submitted a citizen petition to the FDA requesting that the FDA refuse to approve Tyvaso DPI, and / or impose additional requirements in order to approve the product. While the petition was denied by the FDA, it delayed ~~the~~ FDA ~~'s~~ approval of our NDA for Tyvaso DPI. Regulatory approval for our currently marketed products is limited by the FDA and other regulators to those specific indications and conditions for which clinical safety and efficacy have been demonstrated. Any regulatory approval of our products is limited to specific diseases and indications for which our products have been deemed safe and effective ~~by the FDA~~. ~~FDA~~ **Regulatory** approval is also required for new formulations and new indications for an approved product. While physicians may prescribe drugs for uses that are not described in the product' s labeling and for uses that differ from those approved by regulatory authorities (called " off- label " uses), our ability to promote our products is limited to those indications that are specifically approved by the FDA **and its international counterparts**. Failure to follow ~~FDA~~ **applicable 40United Therapeutics, a public benefit corporation** rules and guidelines related to promotion and advertising can result in the **adverse regulatory actions by the** FDA ~~'s refusal to approve a product, suspension or withdrawal of an~~ **and** ~~approved product from the market, product recalls~~ **its international counterparts — such as warning letters**, enforcement ~~action~~ **actions**, civil lawsuits, or criminal prosecution. We must comply with various laws in jurisdictions around the world that restrict certain marketing practices. Our business activities may be subject to challenge under laws in jurisdictions around the world restricting particular marketing practices, such as: • Anti- kickback and false claim statutes, the Foreign Corrupt Practices Act, and the United Kingdom Bribery Act. In the United States, the ~~AKS~~ **Federal Anti- Kickback Statute** prohibits, among other activities, knowingly and willfully offering, paying, soliciting, or receiving remuneration (i. e., anything of value) to induce, or in return for, the purchase, lease, order or arranging the purchase, lease or order of any health care product or service reimbursable under any federally financed healthcare program like Medicare or Medicaid. This statute is interpreted broadly to apply to arrangements between pharmaceutical manufacturers and prescribers, purchasers, specialty pharmacies, formulary managers, patients, and others. Our practices may not always qualify for safe harbor protection under this statute. • The Federal False Claims Act, which prohibits any person from knowingly presenting or causing to be presented a false or fraudulent claim for payment of government funds, or making or causing a false statement material to a false or fraudulent claim. Pharmaceutical and health care companies have faced liability under this law for causing false claims to be submitted because they marketed a product for unapproved and non- reimbursable uses. • Analogous state laws and regulations, including anti- kickback and false claims laws, which apply to items and services reimbursed under Medicaid or, in several states, regardless of the payer, including private payers. **We are also subject to numerous other laws and regulations that, while not specific to the healthcare industry, apply to the healthcare industry in important ways. For example, we are subject to antitrust regulations with respect to interactions with other participants in the markets we currently serve or may serve in the future. These antitrust laws are vigorously enforced in the U. S. and in other jurisdictions in which we operate.** Compliance with these and similar laws on a state- by- state basis is difficult, time consuming, and requires substantial resources. Any investigation, inquiry, or other legal proceeding under these laws related to our operations, even if we successfully defend against it, or any penalties imposed upon us for failure to comply, could have a material adverse effect on our business and financial condition or reputation. Sanctions under these federal and state laws may include treble civil monetary penalties, payment of damages, fines, exclusion of our products from reimbursement under federal health care programs, imprisonment, and the curtailment or restructuring of our operations. Our industry is highly regulated and changes in law or government health care programs may adversely impact our business, operations, or financial results. We cannot predict how future federal or state legislative or administrative changes related to healthcare reform will affect our business. Political, economic, and regulatory influences may lead to fundamental changes in the U. S. healthcare industry, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U. S. We expect there will continue to be legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to commercialize and to sell our products profitably. ~~At the federal level, there have been and continue to be a number of healthcare- related legislative and regulatory initiatives and reforms that significantly affect the pharmaceutical industry. For example, the PPACA, enacted in 2010, substantially changed the way healthcare is financed by both governmental and commercial payers, and has significantly impacted the U. S. pharmaceutical industry. The PPACA is a broad measure intended to expand healthcare coverage within the United States, 36United Therapeutics, a public benefit corporation primarily through the imposition of health coverage- related mandates on employers and individuals and expansion of the Medicaid program. Additionally, there has been increasing legislative, regulatory, and enforcement interest in the United States regarding drug pricing practices.~~ Among other things, there have been several U. S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other

things: bring more transparency to drug pricing; reduce the cost of prescription drugs under government payer programs; review the relationship between pricing and manufacturer patient programs; and reform government program reimbursement methodologies for drugs. **Most** ~~Significantly~~ **significantly** , on August 16, 2022, President Biden signed the IRA into law. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the PPACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Medicare Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. **HHS has issued guidance** ~~For that and other reasons~~ , ~~it~~ **and** is ~~currently unclear how~~ **expected to continue to issue guidance, even while lawsuits challenging** the IRA **remain pending.** ~~will be effectuated, and while~~ **While** the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant. Orenitram and Tyvaso DPI are both reimbursed under Medicare Part D **, and the reimbursement amount will be impacted by the IRA discounting program that will replace the coverage gap discount program in 2025** . ~~We anticipate paying increased rebates for~~ **Under the new program, manufacturers must give a 10 percent discount on** Part D **drugs** ~~utilization of Tyvaso DPI and Orenitram when the Part D discounting program under the IRA is fully implemented~~ in ~~2025, principally driven by~~ the ~~requirement for manufacturers to pay~~ **initial coverage phase, and** a 20 percent ~~rebate~~ **discount** on Part D drugs in the so- called " catastrophic phase " (the phase after the patient incurs costs above the initial phase out- of- pocket threshold, which will be $ 2, 000 beginning in 2025). ~~This~~ **We anticipate that these increased discounts** will ~~have~~ **impact Tyvaso DPI and Orenitram revenues, while also having** an industry- wide impact on the cost of Part D drugs ~~, including~~ **. The impact on** Tyvaso DPI and Orenitram **revenues** . ~~This~~ could be offset ~~, to some degree or to a large degree,~~ by an ~~expansion~~ **increase** in the number of patients able to afford these ~~medicines~~ **therapies** , but ~~these~~ -- **the** ~~impacts are~~ **amount of offset, if any, is** inherently uncertain and difficult to predict. **The IRA allows the 10 and 20 percent discounts to be 2023 Annual Report41 phased in over time for certain drugs for " specified small manufacturers. " In January 2024, CMS provided a preliminary, non- binding notification that we were deemed a specified small manufacturer. We are still evaluating the potential impact of this status on our revenues. The IRA discounting program that will replace the coverage gap discount program will also increase financial obligations of Part D prescription drug plans with respect to beneficiaries in the catastrophic coverage phase. This may incentivize Part D prescription drug plans to seek greater price concessions from us in order to include our products on their formularies.** In addition, Congress ~~has recently~~ enacted other statutes that could adversely affect our ability to successfully commercialize our products. **The** ~~Under the~~ American Rescue Plan Act of 2021 **eliminated** ~~, effective January 1, 2024,~~ the statutory cap on Medicaid Drug Rebate program rebates that manufacturers pay to state Medicaid programs ~~will be eliminated~~ , ~~which~~ **effective January 1, 2024. Previously, the rebate was capped at the drug' s average manufacturer price. Removal of the rebate cap** could increase our Medicaid rebate liability. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement limitations, marketing cost disclosure, and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. We anticipate that the IRA and other healthcare reform measures that may be adopted in the future may result in additional downward pressure on ~~coverage and~~ the payment that we receive for any approved product, and adversely impact our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payment from commercial payers. ~~The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.~~ Further state and federal healthcare reform measures adopted in the future could limit the amounts that state and federal governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressure. In October 2020, ~~the~~ HHS and the FDA issued a final rule and guidance concerning two new pathways for importing lower- cost drugs into the United States. The final rule allows certain prescription drugs to be imported from Canada, and the guidance describes procedures for drug manufacturers to facilitate the importation of FDA- approved drugs and biologics manufactured abroad and originally intended for sale in a foreign country into the United States. **The FDA recently approved Florida' s drug importation plan.** More recently, the Biden administration reaffirmed its goal of taking further action with respect to the pharmaceutical industry, beyond implementation of the IRA. It is difficult to predict the impact, if any, of any such legislation or executive actions on the use of and reimbursement for our products in the United States, including the potential for the importation of generic versions of our products. If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions, and fines, which could adversely impact our business, financial condition, results of operations, and prospects. We participate in, and have certain price reporting obligations to, the Medicaid Drug Rebate program and other governmental programs that require us to pay rebates or offer discounts on our products. Certain programs, such as the 340B program ~~and the VA FSS pricing program~~ , impose limits on the price we are permitted to charge certain entities for our products or for any future products for which we receive regulatory approval. ~~Statutory and regulatory changes~~ **Changes** ~~regarding~~ **to** these programs ~~and their requirements~~ could negatively affect the coverage and reimbursement by these programs of our products or any future products for which we receive regulatory approval and could negatively impact our results of operations. Our failure to comply with these price reporting, rebate payment, or pricing requirements could adversely impact our financial results. Applicable laws and regulations, including the IRA, could affect our obligations in ways we cannot anticipate. ~~2022 Annual Report37~~ Pricing and rebate

calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. If we must restate or recalculate information provided under these programs, our costs of compliance could increase. **We** ~~Additionally, we~~ could be held liable for errors **in** ~~associated with~~ our ~~submission of~~ pricing data, including retroactive rebates and program refunds. We may incur significant civil monetary penalties if we are found to have knowingly ~~submitted false average manufacturer price or best price information to the government, to have made a misrepresentation in our reporting of average sales price figures, to have knowingly~~ provided false information **to the government** ~~in connection with a non- federal average manufacturing price filing,~~ or to have charged 340B covered entities more than the statutorily mandated ceiling price. Certain failures to timely submit required data also could result in a civil monetary penalty for each day the information is late. We could also become subject to allegations under the False Claims Act and other laws and regulations. In addition, misreporting and failure to timely report data to CMS also can be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid Drug Rebate program. **If** ~~In the event that~~ CMS terminates our rebate agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs. CMS, the VA, the Office of Inspector General of the Department of Health and Human Services (OIG), and other governmental agencies have pursued manufacturers that were alleged to have failed to report data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that any submissions we are required to make under governmental drug pricing programs will not be found to be incomplete or incorrect. **42United Therapeutics, a public benefit corporation** Similar political, economic, and regulatory developments are occurring in other countries ~~, including within the EU,~~ and may affect **our** ~~the ability of pharmaceutical companies to profitably~~ **profitability** ~~commercialize their products~~ . In ~~particular in the EU, and in~~ addition to continuing pressure on prices and cost containment measures, legislative developments at the **European Union (** EU **)** or member state level may result in significant additional requirements or obstacles that may increase operating costs. ~~The delivery of healthcare~~ **Healthcare** ~~in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines and medical devices, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare~~ budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines and medical devices by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval or certification of our product candidates, restrict or regulate post- approval activities, and affect our ability to commercialize our product candidates, if approved or certified. In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We may be subject to enforcement action or penalties in connection with the contract pharmacy policy we have implemented pursuant to the 340B program. We participate in the 340B program and have implemented a policy regarding the distribution of our drugs at 340B ceiling prices through third- party pharmacies that contract with 340B covered entities, known as " 340B contract pharmacies ". ~~Our policy responds to the increasing use of 340B contract pharmacies which, coupled with a lack of oversight and transparency, has resulted in increased risks of 340B statutory violations by 340B covered entities, such as the diversion of 340B- purchased drugs to individuals who are not patients of the 340B covered entity, and prohibited " duplicate discounts " when 340B- purchased drugs trigger a Medicaid rebate. These program integrity risks have been exacerbated by the exponential growth in the use of 340B contract pharmacies over the past decade.~~ Under our 340B contract pharmacy policy, which we adopted to address ~~these~~ **program integrity** risks, our drugs are only shipped at the 340B ceiling price to those 340B contract pharmacies that meet certain criteria. Our policy has no impact on 340B purchases by 340B covered entities themselves. Our contract pharmacy policy preserves patient access, while addressing compliance and integrity concerns resulting from the proliferation of contract pharmacies. Nonetheless, certain 340B covered entities and ~~the~~ HHS, in a non- binding (and now- retracted) Advisory Opinion, stated that, in their view, manufacturers in the 340B program are obligated to sell 340B drugs at the 340B ceiling prices to all contract pharmacies acting as agents of a covered entity. We and certain other manufacturers initiated litigation challenging the Advisory Opinion and HRSA' s position on contract pharmacies generally. HHS subsequently withdrew the Advisory Opinion, but HRSA issued letters to manufacturers, including us, threatening enforcement action if the manufacturers do not abandon their 340B contract pharmacy policies. We filed suit against HHS and HRSA ~~on~~ **in** June ~~23,~~ 2021 in the U. S. District Court for the District of Columbia. ~~On~~ **In** September ~~22,~~ 2021, HRSA sent to us, along with the other manufacturers challenging HRSA' s 340B interpretation, letters stating that HRSA was referring this issue to the OIG for potential enforcement action. We have not had any communication from the OIG regarding our 340B contract pharmacy policy. ~~On~~ **In** November ~~5,~~ 2021, the court granted our motion for summary judgment, ruling that the letters threatening enforcement action " contain legal reasoning that rests upon an erroneous reading of Section 340B. " HRSA ~~filed a notice of appeal on December 28, 2021. That appeal~~ has **appealed** ~~been fully briefed~~ , and ~~we are awaiting~~ the **appellate** court' s decision **is pending** . If HRSA prevails on appeal or develops a new theory of liability, we may face enforcement action or penalties as well as adverse publicity. **Such an outcome may also prompt other parties to challenge our policies.** We expect the compliance of policies like ours will continue to be litigated **. We may also face enforcement action under the laws of certain states that are seeking to impose their own 340B requirements** . If we are unable to curb the proliferation of abuses caused by 340B contract pharmacies, we could see increased sales at 340B ceiling prices, which could have a material adverse impact on our revenues. ~~38United Therapeutics, a public benefit corporation~~ Patient assistance programs for pharmaceutical products have come under increasing scrutiny by governments, legislative bodies, ~~and~~ enforcement agencies **, and other third- parties** . These activities may result in actions that effectively reduce prices or demand for our products, harm our business or reputation, or subject us to fines or penalties. Company- sponsored patient assistance

programs, including insurance premium and co- pay assistance programs and manufacturers' donations to third- party charities that provide such assistance, are subject to heightened scrutiny. The Department of Justice (DOJ) has taken enforcement action against pharmaceutical companies alleging violations of the Federal False Claims Act and other laws in connection with patient assistance programs. In December 2017, we entered into a civil Settlement Agreement with the U. S. Government to resolve a DOJ investigation of our support of non- profit patient assistance programs and paid $ 210. 0 million, plus interest, to the U. S. Government upon settlement. We also entered into a Corporate Integrity Agreement (the CIA) with the OIG, which required us to maintain our corporate compliance program and to undertake a set of defined corporate integrity obligations for five years ending December 2022 **. As discussed in Note 14 — Litigation, to our consolidated financial statements, we have been sued by Humana Inc., United Healthcare Services, Inc., and various parties in the MSP Recovery litigation for allegedly violating RICO and various state laws in connection with our donations to a charity. These lawsuits, or other lawsuits in the future, could result in significant monetary judgements and the imposition of other penalties against us** . Members of Congress have called upon the OIG to issue revised guidance about patient assistance programs. Actions taken by the OIG, the DOJ or other agencies as a result of this industry- wide inquiry could reduce demand for our products and / or coverage of our products by federal and state health care. If any or all of these events occur, our business, prospects, and stock price could be materially and adversely affected. Payers and pharmacy benefit managers have developed mechanisms to limit the benefits patients receive under co- pay assistance programs through imposing so- called co- pay accumulator or maximizer programs. These programs do not allow a patient using co- pay assistance to count the manufacturer' s co- payment contribution toward their annual out- of- pocket payment maximum / deductible. Once the co- pay benefit has been exhausted, patients are faced with paying the full out- of- pocket maximum / deductible. Some states have passed legislation to limit the use of co- pay accumulator programs, while some other states have indicated that these programs should be allowed to limit cost of care and encourage patients to use lower cost generics. In addition, some states have imposed restrictions on manufacturer co- pay programs when therapeutic **2023 Annual Report43** equivalents are available. Growing use of such programs, or new laws limiting manufacturer ability to provide co- pay assistance, could affect patient access to our products and limit product utilization, which may, in turn, adversely affect our business, prospects, and stock price. Improper handling of hazardous materials used in our activities could expose us to significant remediation liabilities. Our research and development and manufacturing activities involve the controlled use of chemicals and hazardous substances. We are expanding these activities in both scale and location. Patients may dispose of our products using means we do not control. Such activities subject us to numerous federal, state, and local environmental and safety laws and regulations that govern the management, storage, and disposal of hazardous materials. Compliance with current and future environmental laws and regulations can require significant costs. The risk of accidental contamination or injury from these materials cannot be completely eliminated. Once chemical and hazardous materials leave our facilities, we cannot control the manner in which such hazardous waste is disposed of by our contractors. We could be liable for substantial civil damages or costs associated with the cleanup of the release of hazardous materials and such liability could have a material adverse effect on our business. The increasing use of social media platforms presents new risks and challenges. Social media is increasingly being used to communicate information about our products and the diseases that our therapies are designed to treat. Social media practices in our industry continue to evolve and regulations related to such use are not always clear. This evolution creates uncertainty and risk of noncompliance. For example, patients and others may use social media channels to comment on the effectiveness of a product or to report an alleged adverse event. When such disclosures occur, we may fail to monitor and comply with applicable adverse event reporting obligations or we may not be able to defend against political and market pressures generated by social media due to restrictions on what we may say about our products. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate comments about us on any social networking website. If any of these events occur or we otherwise fail to comply with applicable regulations, we could incur liability, face overly restrictive regulatory actions, or incur other harm to our business. Risks Related to Our Intellectual Property and Data Privacy If any of the agreements under which we license or acquired intellectual property rights are breached or terminated, we could lose our rights to continue to develop, manufacture, and sell the products covered by such agreements. Our business depends upon our continuing ability to exploit our intellectual property rights acquired from third parties under product license and purchase agreements covering drugs or other products or technology. We may be required to license additional intellectual property owned by third parties to continue to develop and commercialize our products. This dependence on intellectual property developed by others involves the following risks: • We may be unable to obtain rights to intellectual property that we need for our business at a reasonable cost or at all; • If any of our product licenses or purchase agreements are terminated, we may lose our rights to develop, make, and sell the products to which such licenses or agreements relate; • Our rights to develop and market products to which the intellectual property relates are frequently limited to specific territories and fields of use (such as **the** treatment of particular diseases); and ~~2022 Annual Report39~~ • If a licensor of intellectual property fails to maintain the intellectual property licensed, we may lose any ability to prevent others from developing or marketing similar products covered by such intellectual property. In addition, we may be forced to incur substantial costs to maintain the intellectual property ourselves or take legal action seeking to force the licensor to do so. Our intellectual property rights may not effectively deter competitors from developing competing products that, if successful, could have a material adverse effect on our revenues and profits. The period under which our commercial and developmental therapies are protected by our patent rights is limited. Three of our U. S. patents covering our current methods of synthesizing and producing treprostinil ~~, the active ingredient in Tyvaso, Tyvaso DPI, Remodulin, and Orenitram,~~ expired in October 2017, and three more will expire in 2028. Our patents related to our individual treprostinil- based products expire at various times between 2024 and ~~2035~~ **2042** . We entered into settlement agreements with **certain** ~~a number of~~ generic drug companies permitting **them** ~~certain companies~~ to launch generic versions of Remodulin in the United States and other companies to launch generic versions of **nebulized Tyvaso and** Orenitram ~~and Tyvaso~~ in the United States **. In some instances, the FTC has brought actions**

against brand and generic companies that have entered into such agreements, alleging that they violate antitrust laws. Even in the absence of an FTC challenge, other governmental or private litigants may assert antitrust or other claims against us relating to such agreements. We have been sued by Sandoz for violating our settlement agreement with them. This action or other actions against us in the future could result in significant monetary judgements and the imposition of other penalties against us . A U. S. patent for Adcirca for **the** treatment of pulmonary hypertension expired in November 2017, and FDA- conferred regulatory exclusivity expired in May 2018, leading to the launch of a generic version of Adcirca in August 2018. We have no issued patents or pending patent applications covering Unituxin. For further details, ~~please~~ see Part I, Item 1 ~~.~~ — Business — Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity — Generic Competition and Challenges to our Intellectual Property Rights. **44United Therapeutics, a public benefit corporation** We cannot be sure that our existing or any new patents will effectively deter or delay competitors' efforts to bring new products to market, or that additional patent applications will result in new patents. When our patents expire, competitors may develop generic versions of our products and market them at a lower price ~~to compete with our products~~ . Competitors may also seek to design around our patents or exclude patented methods of treatment, such as patent- protected indications, from the label for generic versions of our products in an effort to develop competing products that do not infringe our patents. In addition, patent laws of foreign jurisdictions may not protect our patent rights to the same extent as the ~~patent laws of the~~ United States **' laws** . Third parties have challenged, and may in the future challenge, the validity of our patents, through patent litigation and / or initiating proceedings, including re- examinations, IPRs, post- grant reviews, and interference proceedings, before the USPTO or other applicable patent filing offices, or other means. For example, Liquidia is challenging various patents related to **nebulized** Tyvaso and our other treprostinil- related patents. Patent litigation can be time consuming, distracting, and costly, and the outcome may be difficult to predict and unfavorable to us. If we are unsuccessful in the defense of our patents, our business could be negatively impacted. ~~Even if our patents are determined to be valid or enforceable, a competitor could circumvent our patents by effectively designing around the claims of our patents. Accordingly, our patents may not provide us with any competitive advantage.~~ We also rely on trade secrets to protect our proprietary know- how and other **confidential** technological advances ~~that we do not publicly disclose~~ . Our confidentiality agreements with our ~~Unitherians~~ **employees** and others to whom we disclose trade secrets and confidential information may not necessarily prevent our trade secrets from being used or disclosed without our authorization. These agreements may be difficult, time- consuming, and expensive to enforce or may not provide an adequate remedy in the event of unauthorized disclosure. If our trade secrets were ~~to be~~ lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us, and our business and competitive position could be harmed. Third parties may allege that our products or services infringe their patents and other intellectual property rights, which could result in the payment of royalties that negatively affect our profits, subject us to costly and time- consuming litigation, or cause us to lose the ability to sell the related products. To the extent third- party patents to which we currently do not hold licenses are necessary for us to manufacture, use, or sell our products, we would need to obtain necessary licenses to prevent infringement. For products or services that utilize intellectual property of strategic collaborators or other suppliers, such suppliers may have an obligation to secure the needed license to these patents at their cost; if not, we would be responsible for the cost of these licenses. Royalty payments and other fees under these licenses would erode our profits from the sale of related products and services. Moreover, we may be unable to obtain these licenses on acceptable terms or at all. If we fail to obtain a required license or are unable to alter the design of the product to avoid infringing a third- party patent, we would be unable to continue to manufacture or sell related products. If a third party commences legal action against us for infringement, we may incur significant costs to defend **ourselves against the claims made in** the action and our management' s attention could be diverted from our day- to- day business operations, whether or not the action has merit. An adverse judgment or settlement resulting from the action could require us to pay substantial amounts in damages for infringement or to obtain a license to continue to use the intellectual property that is the subject of the infringement claim, or could result in injunctive relief limiting our ability to develop, manufacture, or sell our products. ~~Information technology security~~ **Cybersecurity** ~~breaches~~ **incidents** and other disruptions ~~could compromise~~ **impacting our networks, systems,** ~~our~~ **or data may have a material adverse effect on** ~~information and expose us to legal responsibility which would cause~~ our business ~~and reputation to suffer~~ . We are increasingly dependent on information technology systems and infrastructure, much of which is outsourced to third parties including in " cloud " **-** based platforms. We collect, store, and use sensitive or confidential data, including intellectual property, our proprietary business information and that of our suppliers, customers, and business partners, and personally identifiable information. ~~The secure maintenance~~ **Actual or alleged cybersecurity incidents, including those caused by employee error, malfeasance, system failures, malware, ransomware, viruses, distributed denial** of ~~this~~ **services attacks, credential harvesting, social engineering, and other forms of unauthorized access or disclosure to, or disrupting the operation of, our networks and systems or those of our customers, suppliers, vendors, and other service providers, can cause the loss, destruction, or unauthorized access or disclosure of data, including personal** information ~~is critical to~~ **of employees or confidential or proprietary information, disruption of** our operations **,** and **damage to our reputation, any of which could be costly to address and remediate and adversely affect our** business ~~strategy~~ **, financial condition, or results of operations** . We are **also** ~~40United Therapeutics, a public benefit corporation~~ subject to laws and regulations in the United States and abroad, such as ~~HIPAA~~ **the Health Insurance Portability** and ~~EU~~ **Accountability Act of 1996 and European Union** regulations related to data privacy, which require us to protect the privacy and security of certain types of information. **Therefore** ~~Our information technology and infrastructure may be vulnerable to attacks by hackers~~ , **cybersecurity incidents** ~~breached due to employee error, malfeasance, or other disruptions, or subject to system failures. Because the techniques used to obtain unauthorized access, disable, or degrade service, or sabotage systems change frequently and may be difficult to detect for long periods of time, we may be unable to anticipate these techniques or implement adequate preventive measures. Any breaches~~

~~or failures~~ could ~~compromise sensitive and confidential information stored on our networks or those of third parties and~~ expose **us** ~~such information~~ to **significant civil and /** ~~public disclosure, loss, or theft. Any actual or alleged unauthorized access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disruption of our~~ **or** ~~operations~~ **criminal penalties** , ~~and damage to our reputation~~ **as well as private litigation** , ~~any~~ **all** of which could adversely affect our business, financial condition, or results of operations. ~~Costs~~ **In the past** we **have experienced, and in the future we** may ~~incur~~ **again experience, data security incidents. The preventive actions we take to reduce exposure to, and the risks associated with, cybersecurity incidents may be insufficient to prevent or mitigate the effects of material cybersecurity incidents in the future. Because the tools and methods used by threat actors to damage or obtain unauthorized access to networks, systems, and data change frequently, and are often not known until used against a target, we may be unable to anticipate these tools or methods or implement adequate preventative measures. It is impossible to eliminate all cybersecurity threats and exposure to cybersecurity incidents, and thus our networks and systems,** as **well as** ~~a result of any of the~~ **those of** ~~foregoing, could adversely affect our business, financial condition, or~~ **our** ~~results of operations~~ **service providers, suppliers, customers and other third parties, remain potentially vulnerable to known or unknown threats** . **2023 Annual Report45** Risks Related to Our Financing Capacity, Indebtedness, and Investments If we need additional financing and cannot obtain it, our product development and sales efforts may be limited. We may be required to seek additional sources of financing to meet unplanned or planned expenditures. Unplanned expenditures could be significant and may result from necessary modifications to product development plans or product offerings in response to difficulties encountered with clinical trials. We may also face unexpected costs in preparing products for commercial sale, or in maintaining sales levels of our currently marketed therapeutic products. Our ~~2022~~ Credit Agreement contains affirmative and negative covenants that, among other things, limit our ability to incur additional indebtedness. If we are unable to obtain additional funding on commercially reasonable terms or at all, we may be compelled to delay clinical studies, curtail operations, or obtain funds through collaborative arrangements that may require us to relinquish rights to certain products or potential markets. We may not be able to generate sufficient cash to service or repay our indebtedness, which may have a material adverse effect on our financial position, results of operations, and cash flows. We may borrow up to $ 2. 0 billion under our ~~2022~~ Credit Agreement, which matures in March ~~2027~~ **2028** . Currently, our outstanding principal balance is $ ~~800~~ **700** . 0 million. Our ability to repay or refinance our debt obligations under our ~~2022~~ Credit Agreement and any future debt that we may incur will depend on our financial condition and operating performance, which are subject to a number of factors beyond our control. We may be unable to maintain a level of cash flows from operating activities sufficient to permit us to pay the principal and interest on our indebtedness. Our inability to generate sufficient cash flows to satisfy our debt obligations would materially and adversely affect our financial position and results of operations. If we cannot repay or refinance our debt as it becomes due, we may be forced to take disadvantageous actions, including reducing or delaying investments and capital expenditures, disposing of material assets or operations, seeking additional debt or equity capital, or restructuring or refinancing our indebtedness. We may not be able to effect any such alternative measures on commercially reasonable terms or at all and, even if successful, such actions may not enable us to meet any such debt service obligations. In addition, our ability to withstand competitive pressures and to react to changes in our industry could be impaired. Our portfolio of investments is subject to market, interest, operational, and credit risk that may reduce its value. We maintain a portfolio of investments that includes: (1) corporate debt securities; (2) strategic investments in publicly- traded equity securities; and (3) strategic ~~debt and~~ equity investments in privately- held companies. These investments are subject to general economic conditions, volatility in the financial marketplace, market- and industry- wide dynamics, **the current elevated interest rate environment and** changes in interest rates, industry- and company- specific developments impacting the business, prospects, and credit ratings of the issuer of the securities, and other factors, each of which has affected, and may in the future affect, the income that we receive from our investments, the net realizable value of our investments, and our ability to sell them. These factors have caused, and could in the future cause, us to: (a) experience a decline in our investment income; (b) record impairment charges to reduce the carrying value of our investment portfolio; or (c) sell investments for less than our acquisition cost; each of which in turn could negatively impact our liquidity and our earnings. Our efforts to mitigate these risks through diversification of our investments and monitoring of our portfolio' s overall risk profile may not be successful and the value of our investments may decline. The privately- held companies we have invested in may be particularly susceptible to the factors described above as these companies are typically in the early stages of developing technologies or products that may never materialize, which could result in a loss of all or a substantial part of our investment in these companies. **If we are not able to successfully identify, finance, consummate and / or integrate acquisitions, our business operations and financial position could be adversely affected. During the fourth quarter of 2023, we acquired IVIVA and Miromatrix. We may continue to seek to expand in part through acquisitions of complementary businesses, products, and technologies. The success of this strategy will depend on our ability to identify, and the availability of, suitable acquisition candidates. We may incur costs related to an acquisition but may be unable or unwilling to consummate the proposed transaction. Acquisitions involve numerous risks, including: the ability to realize anticipated synergies and manage the integration of personnel, products, and acquired infrastructure and controls; potential increases in operating costs; managing geographically remote operations; the diversion of management' s attention from other business concerns; potential disruptions in ongoing operations during integration; risks inherent in entering markets and sectors in which we have limited or no direct experience; and the potential loss of key employees, customers, or vendors and other business partners of the acquired companies. External factors, such as compliance with law, may also impact the successful integration of an acquired business. Acquisitions could involve dilutive issuances of equity securities, the incurrence of debt, one- time write- offs of goodwill, and substantial amortization expenses of other intangible assets. We may be unable to obtain financing on favorable terms, or at all, if necessary to finance future acquisitions, which may make acquisitions impossible or more costly. The terms of financing we obtain may be onerous**

and restrict our operations. Further, certain acquisitions may be subject to regulatory approval, which can be time consuming and costly to obtain or may be denied, and if obtained, the terms of such regulatory approvals may limit our ongoing operations or require us to divest assets. 46United Therapeutics, a public benefit corporation Risks Related to Our Common Stock The price of our common stock can be highly volatile and may decline. The price of common stock can be highly volatile within the pharmaceutical and biotechnology sector. Consequently, significant price and volume fluctuations in the market may not relate to operating performance. The price of our common stock could decline sharply due to general market conditions as well as the following factors, among others: ~~2022 Annual Report41~~ • quarterly and annual financial results and any failure to meet our expectations or those of securities analysts; • timing of enrollment and results of our clinical trials; • announcements regarding generic or other challenges to the intellectual property related to our products, the launch of generic versions of our products or other competitive products, such as sotatercept or Yutrepia, and the impact of competition from generic and other products on our revenues; • announcements regarding litigation matters, including our ongoing ~~patent~~ litigation with Liquidia ~~related to its NDA for Yutrepia~~ , among others; • announcements regarding our efforts to obtain ~~FDA~~ **regulatory** approval of, and to launch commercial sales of, new products; • physician, patient, investor, or public concerns regarding the efficacy and / or safety of products marketed or being developed by us or by others; • changes in, or new laws and regulations affecting reimbursement of, our therapeutic products by government payers, changes in reimbursement policies of private insurance companies **, including the implementation and impacts of the IRA** , and negative publicity surrounding the cost of high- priced therapies; • announcements of technological innovations or new products or announcements regarding our existing products, including in particular the development of new, competing therapies; • substantial sales of our common stock by us or our existing shareholders, or concerns that such sales may occur; • future issuances of common stock by us or other activity which could be viewed as being dilutive to our shareholders; • rumors or incorrect statements by investors and / or analysts concerning our company, our products, or our operations; • failures or delays in our efforts to obtain or maintain domestic or international regulatory approvals; • discovery of previously unknown problems with our marketed products, or problems with our manufacturing, regulatory, compliance, promotional, marketing **,** or sales activities that result in regulatory penalties or restrictions on our products, up to the withdrawal of our products from the market; and • accumulation of significant short positions in our common stock by hedge funds or other investors or the significant accumulation of our common stock by hedge funds or other institutional investors with investment strategies that may lead to short- term holdings. Provisions of Delaware law, our charter, bylaws and employment and license agreements, among other things, could prevent or delay a change of control or change in management that may be beneficial to our public shareholders. Certain provisions of Delaware law, our restated certificate of incorporation, and ~~our ninth amended and restated~~ bylaws may prevent, delay, or discourage a merger, tender offer, or proxy contest; the assumption of control by a holder of a large block of our securities; and / or the replacement or removal of current management by our shareholders. For example, as a result of our conversion to a PBC, our Board is required to consider and balance the financial interests of shareholders, the interests of stakeholders materially affected by our conduct, and the pursuit of our specific public benefit purpose when evaluating takeover offers. This requirement of Delaware ~~PBC~~ law may make our company a less attractive takeover target than a traditional for- profit corporation. Non-competition and all other restrictive covenants in most of our employment agreements will terminate upon a change of control that is not approved by our Board. Similarly, a change of control, under certain circumstances, could accelerate the vesting of outstanding stock options, and restricted stock units. Any increase in our stock price resulting from the announcement of a change of control, and our broad- based change of control severance program, under which ~~Unitherians~~ **our employees** may be entitled to severance benefits if they are terminated without cause (or they terminate their employment for good reason) following a change of control, could make an acquisition of our company significantly more expensive to the purchaser. We enter into certain license agreements that generally prohibit our counterparties or their affiliates from taking necessary steps to acquire or merge with us, directly or indirectly throughout the term of the agreements, plus a specified period thereafter. We are also party to certain license agreements that restrict our ability to assign or transfer the rights licensed to us to third parties, including parties with whom we wish to merge, or those attempting to acquire us. These agreements often require that we obtain prior consent of the counterparties if we contemplate a change of control. If these counterparties withhold consent, related agreements could be terminated and we would lose related license rights. For example, Lilly and MannKind have the right to terminate our license agreements related to Adcirca and Tyvaso DPI, respectively, in the event of certain change of control transactions. These restrictive change of control provisions could impede or prevent mergers or other transactions that could benefit our shareholders. **2023 Annual Report47** Our shareholders must rely on stock appreciation for any return on their investment in us. We have never paid, and do not intend to pay, cash dividends. ~~Our 2022 Credit Agreement~~ **The terms of our current or future debt arrangements we may enter into** may restrict us from doing so. As a result, the return on an investment in our common stock depends entirely upon the future appreciation, if any, in the price of our common stock. ~~42United Therapeutics, a public benefit corporation~~ Our exclusive forum bylaw may limit our shareholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers, or other ~~Unitherians~~ **employees** . Our bylaws provide that, to the fullest extent permitted by law, unless we agree in writing to an alternative forum, (~~a~~ **1**) the Delaware Court of Chancery (or, if such court does not have, or declines to accept, jurisdiction, another state court or a federal court located in Delaware) will be the exclusive forum for any complaint asserting any internal corporate claims, including claims in the right of the corporation based upon a violation of a duty by a current or former director, officer, ~~Unitherian~~ **employee** , or stockholder in such capacity, or as to which the Delaware General Corporation Law confers jurisdiction upon the Court of Chancery, and (~~b~~ **2**) the federal district courts will be the exclusive forum for any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. The choice of forum provision may limit our shareholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers, or other ~~Unitherians~~ **employees** , and may discourage such lawsuits. There is uncertainty as to whether a court would enforce this provision. If a court ruled the choice

of forum provision was inapplicable or unenforceable in an action, we may incur additional costs to resolve such action in other jurisdictions. Our choice of forum provision is intended to apply to the fullest extent permitted by law to the above- specified types of actions and proceedings, including any derivative actions asserting claims under state law or the federal securities laws. Our shareholders will not be deemed, by operation of the choice of forum provision, to have waived our obligation to comply with all applicable federal securities laws and the rules and regulations thereunder. In 2021, we converted to a Delaware PBC. Conversion may not result in the benefits that we anticipate, requires our directors to balance the interest of shareholders with other interests, and may subject us to additional litigation and other risks. **We** ~~In 2021, our shareholders approved an amendment to our restated certificate of incorporation to become a PBC, and we completed the conversion to a PBC that same day. While our Board believes that our conversion to a PBC is in the best interest of shareholders, our status as a PBC may not result in the benefits that we anticipate. For example, we~~ may not be able to achieve our public benefit purpose or realize the expected positive impacts from being a PBC. One of the primary distinctions between a PBC and a traditional Delaware for- profit corporation is that, in making decisions, the directors of a PBC have an obligation to balance the financial interests of shareholders, the interests of stakeholders materially affected by the PBC' s conduct, and the pursuit of the corporation' s specific public benefit purpose. The application of this balancing obligation may allow our directors to make decisions that they could not have made pursuant to the fiduciary duties applicable prior to PBC conversion. There is no guarantee that our Board will resolve conflicts among the financial interests of our shareholders, our ~~specific~~ public benefit purpose, or stakeholders materially affected by our conduct, in favor of our shareholders' financial interests. For instance, in a sale of control transaction, our Board would be required to consider and balance the factors listed above and might choose to accept an offer that does not maximize short- term shareholder value due to its consideration of other factors. This requirement of Delaware ~~PBC~~ law may make our company a less attractive takeover target than a traditional for- profit corporation. A Delaware PBC must also provide its shareholders with a statement, at least every other year, as to the PBC' s assessment of the success of its efforts to promote its public benefit purpose and the best interests of those materially affected by the PBC' s conduct. If the public perceives that we are not successful in promoting our public benefit purpose, or that our pursuit of our public benefit purpose is having a negative effect on the financial interests of our shareholders, that perception could negatively affect our reputation, which could adversely affect our business, results of operations and stock price. In addition, Delaware' s PBC statute may be amended to require more explicit or burdensome reporting requirements that could increase the time and expense required to comply. As a Delaware PBC, we may be subject to increased litigation risk. Shareholders of a Delaware PBC (if they, individually or collectively, own the lesser of (1) two percent of the PBC' s outstanding shares; or (2) shares with a market value of $ 2 million or more on the date the lawsuit is instituted) can file a derivative lawsuit claiming the directors failed to balance shareholder and public benefit interests. Traditional Delaware for- profit corporations are not subject to this potential liability. As a PBC, we may be subject to increased derivative litigation, which may be costly and require management' s attention, which may adversely affect our financial condition and results of operations. In addition, there is currently limited case law involving PBCs (including case law interpreting and applying the balancing obligation of PBC directors), which may expose us to additional litigation risk generally until additional case law develops or additional legislative action is taken.