

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.

For the fiscal year ended December 31, 2022

OR

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

For the transition period from _____ to _____
Commission file number 0-26301

United Therapeutics Corporation

(Exact Name of Registrant as Specified in Its Charter)

Delaware

(State or Other Jurisdiction of
Incorporation or Organization)

1040 Spring Street, Silver Spring, MD
(Address of Principal Executive Offices)

52-1984749

(I.R.S. Employer
Identification No.)

20910

(Zip Code)

(301) 608-9292

Registrant's Telephone Number, Including Area Code
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$.01 per share	UTHR	Nasdaq Global Select Market

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒

Non-accelerated filer ☐

Accelerated filer ☐

Smaller reporting company ☐

Emerging growth company ☐

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

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

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

The aggregate market value of the Common Stock held by non-affiliates of the registrant, based on the closing price on June 30, 2022, as reported by the Nasdaq Global Select Market was approximately \$10,532,340,521.

The number of shares outstanding of the issuer's common stock, par value \$0.01 per share, as of February 15, 2023, was 46,301,656.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for the registrant's 2023 annual meeting of shareholders scheduled to be held on June 26, 2023, are incorporated by reference in Part III of this Form 10-K.

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PART I

Item 1. Business

Overview

We build on the strength of our research and development expertise and a distinctive, entrepreneurial culture that encourages diversity, innovation, creativity, sustainability, and, simply, fun. Since inception, our mission has been to find a cure for pulmonary arterial hypertension (PAH) and other life-threatening diseases. Toward this goal we have successfully obtained approval from the U.S. Food and Drug Administration (FDA) for several medicines, we are always conducting new clinical trials, and we are working to create an unlimited supply of manufactured organs for transplantation.

We are the first publicly-traded biotech or pharmaceutical company to take the form of a public benefit corporation (PBC). Our public benefit purpose is to provide a brighter future for patients through (a) the development of novel pharmaceutical therapies; and (b) technologies that expand the availability of transplantable organs. At the same time, we seek to provide our shareholders with superior financial performance and our communities with earth-sensitive energy utilization.

We market and sell the following commercial therapies in the United States to treat PAH: Tyvaso® (treprostinil) Inhalation Solution (**Tyvaso**), which includes the Tyvaso Inhalation System; Tyvaso DPI® (treprostinil) Inhalation Powder (**Tyvaso DPI**); Remodulin® (treprostinil) Injection (**Remodulin**); Orenitram® (treprostinil) Extended-Release Tablets (**Orenitram**); and Adcirca® (tadalafil) Tablets (**Adcirca**). Tyvaso and Tyvaso DPI are also approved to treat pulmonary hypertension associated with interstitial lung disease (PH-ILD). In the United States, we market and sell an oncology product, Unituxin® (dinutuximab) Injection (**Unituxin**), which is approved for treatment of high-risk neuroblastoma, and the Remunity® Pump for Remodulin (**Remunity**). Outside the United States, we generate revenues from the sale of Tyvaso, Remodulin, and Unituxin.

We are actively advancing a pipeline of research and development projects that includes new indications, formulations, and delivery devices for our existing products, as well as new products to treat PAH and other conditions.

Our principal executive offices are located at 1040 Spring Street, Silver Spring, Maryland 20910 and at 55 T.W. Alexander Drive, Research Triangle Park, North Carolina 27709. Unless the context requires otherwise or unless otherwise noted, all references in this Annual Report on Form 10-K (this **Report**) to “**United Therapeutics**” and to the “**company**”, “**we**”, “**us**” or “**our**” are to United Therapeutics Corporation and its subsidiaries.

Our Commercial Products

Our commercial product portfolio consists of the following:

Product	Mode of Delivery	Indication	Current Status	Our Territory
Tyvaso	Inhaled solution via ultrasonic nebulizer	PAH and PH-ILD	Commercial sales in the U.S., Argentina, and Israel*	Worldwide
Tyvaso DPI	Inhaled dry powder via pre-filled, single-use cartridges	PAH and PH-ILD	Commercial sales in the U.S.	Worldwide
Remodulin	Continuous subcutaneous	PAH	Commercial sales in the U.S., most of Europe**, Argentina, Canada, Chile, Columbia, Israel, Japan, Mexico, Peru, South Korea, and Venezuela	Worldwide
Remodulin	Continuous intravenous	PAH	Commercial sales in the U.S., most of Europe**, Argentina, Canada, Columbia, Israel, Japan, Mexico, Peru, Saudi Arabia, and South Korea	Worldwide
Remunity Pump for Remodulin	Continuous subcutaneous via pre-filled and patient-filled cassettes	PAH	Commercial sales in the U.S.	Worldwide
Orenitram	Oral	PAH	Commercial sales in the U.S.	Worldwide
Unituxin	Intravenous	High-risk neuroblastoma	Commercial sales in the U.S., Canada, and Japan	Worldwide
Adcirca	Oral	PAH	Commercial sales in the U.S.	United States

* Tyvaso is only approved for PAH in Argentina. Tyvaso was also approved to treat PAH in Japan in late 2022, and we anticipate that our distributor will launch commercial sales in Japan during the second half of 2023. Tyvaso's label was expanded in Israel in late 2022 to add the PH-ILD indication.

** Remodulin is marketed and sold in most of the major European markets other than the United Kingdom.

Products to Treat Pulmonary Hypertension

Pulmonary hypertension has been classified into five groups. PAH is designated as group 1 pulmonary hypertension, which includes multiple etiologies such as idiopathic (meaning the cause is unknown) and heritable PAH, as well as PAH associated with connective tissue diseases. Pulmonary hypertension associated with lung disease, such as PH-ILD, has been classified as group 3 pulmonary hypertension. In addition, patients with PAH are classified into classes based on clinical severity, ranging from functional class I (no symptoms) through functional class IV (severe symptoms). Labeled indications for PAH therapies often note that clinical studies for the drug predominantly included patients in one or more functional classes.

Our pulmonary hypertension products were initially approved to treat only PAH. In March 2021, Tyvaso was approved to treat PH-ILD in addition to PAH. In May 2022, we also obtained FDA approval of Tyvaso DPI to treat both PAH and PH-ILD. We are engaged in further research and development for an additional indication for Tyvaso. For further details, see *Research and Development* below.

PAH is a life-threatening disease that affects the blood vessels in the lungs and is characterized by increased pressure in the pulmonary arteries, which are the blood vessels leading from the heart to the lungs. The elevated pressure in the pulmonary arteries strains the right side of the heart as it pumps blood to the lungs. This eventually leads to right heart failure and, ultimately, death. PAH is characterized by structural changes in blood vessel walls, aggregation of platelets, and alteration of smooth muscle cell function. We believe that PAH affects about 500,000 individuals worldwide. We have seen increases in the number of people diagnosed with the disease, but due to the rarity of the disease and the complexity of diagnosing it, only a small fraction of patients with PAH are being treated.

Current therapies approved by the FDA for PAH focus on three distinct molecular pathways: the prostacyclin pathway, the nitric oxide pathway, and the endothelin pathway. The classes of drugs that target these three pathways are:

- **Prostacyclin Analogues and IP Prostacyclin Receptor Agonists.** Patients with PAH have been shown to have reduced levels of prostacyclin, a naturally occurring molecule that relaxes the pulmonary blood vessels, prevents platelet aggregation, and inhibits the proliferation of smooth muscle cells in the pulmonary vessels. Drugs that mimic the action of prostacyclin, known as prostacyclin analogues, are established PAH treatments. Another class of therapy, called IP prostacyclin receptor agonists, also addresses PAH through the prostacyclin pathway. As compared with prostacyclin analogues, which broadly mimic the effect of prostacyclin, IP prostacyclin receptor agonists bind selectively to (and activate) the IP receptor, one of several prostacyclin receptors.
- **Phosphodiesterase Type 5 (PDE-5) Inhibitors and Soluble Guanylate Cyclase (sGC) Stimulators.** Patients with PAH have also been shown to have reduced levels of the enzyme responsible for producing nitric oxide, a naturally occurring substance in the body that causes relaxation of the pulmonary blood vessels. Nitric oxide produces this effect by increasing intracellular levels of cyclic guanosine monophosphate GMP (**cyclic GMP**). Therefore, another established therapeutic approach has been to inhibit the degradation of cyclic GMP using drugs known as PDE-5 inhibitors. In addition, sGC is an enzyme found in the endothelial cells and the receptor for nitric oxide. When nitric oxide binds to sGC, the enzyme enhances production of cyclic GMP. As a result, sGC stimulators are also approved to treat PAH.
- **Endothelin Receptor Antagonists.** PAH patients have also been shown to have elevated levels of endothelin-1, a naturally occurring peptide in the body that causes constriction of, and structural changes to, the pulmonary blood vessels. Therefore, another established therapeutic approach has been to block the action of endothelin with drugs that are known as endothelin receptor antagonists (**ERAs**).

Because any or all of the three pathways may be therapeutic targets in a patient, these classes of drugs are used alone or in combination to treat patients with PAH. We currently market drugs in two of these classes. Tyvaso, Tyvaso DPI, Remodulin, and Orenitram are all formulations of treprostinil, a prostacyclin analogue, and Adcirca is a PDE-5 inhibitor.

PH-ILD is also a rare condition, impacting at least 30,000 patients in the United States. Tyvaso and Tyvaso DPI are the only available therapies the FDA has approved to treat PH-ILD.

Tyvaso and Tyvaso DPI

Tyvaso was initially approved as a nebulized product by the FDA to treat PAH, and was launched commercially in the United States in 2009. Following the successful *INCREASE* phase 3 registration study of Tyvaso in patients with PH-ILD, including patients with underlying idiopathic pulmonary fibrosis (**IPF**) and combined pulmonary fibrosis and emphysema, the FDA approved our efficacy supplement to the Tyvaso new drug application (**NDA**) in March 2021. As a result, Tyvaso's label was updated to include the PH-ILD indication. In May 2022, the FDA approved our dry powder formulation of inhaled treprostinil called Tyvaso DPI, for treatment of both PAH and PH-ILD. We developed this product under an in-license from MannKind Corporation (**MannKind**), and launched this product commercially in the United States in June 2022.

We sell Tyvaso and Tyvaso DPI to specialty pharmaceutical distributors in the United States. We recognized \$873.0 million, \$607.5 million, and \$483.3 million in combined Tyvaso and Tyvaso DPI net product sales, representing 45 percent, 36 percent, and 33 percent of our total revenues for the years ended December 31, 2022, 2021, and 2020, respectively. Tyvaso (the nebulized product only) is approved and commercialized in the United States and Israel to treat PAH and PH-ILD, and in Argentina to treat

PAH. Tyvaso (the nebulized product only) was also approved to treat PAH in Japan in late 2022, and we anticipate our distributor will launch commercial sales in Japan during the second half of 2023.

Tyvaso is administered four times a day by inhaling up to twelve breaths during each treatment session, which takes approximately three minutes. Tyvaso is required to be administered using our proprietary Tyvaso Inhalation System, which consists of an ultrasonic nebulizer and related accessories. A single ampule containing Tyvaso is emptied into the Tyvaso Inhalation System once per day, so the Tyvaso Inhalation System only needs to be cleaned once daily. Tyvaso is regulated by the FDA as a drug-device combination product, consisting of Tyvaso drug product and the Tyvaso Inhalation System.

Tyvaso DPI incorporates the dry powder formulation technology and Dreamboat® inhalation device technology used in MannKind's Afrezza® (insulin human) Inhalation Powder product, which was approved by the FDA in 2014. We believe that this new inhaled treprostinil therapy provides substantial lifestyle benefits to PAH and PH-ILD patients, as compared with nebulized Tyvaso Inhalation Solution therapy, because it is: (1) less time consuming to administer and easier to maintain, as the device is provided in pre-filled, single use, disposable cassettes, eliminating the need for cleaning and filling; and (2) mobile and more convenient, as the compact design of the inhaler and drug cassettes used with Tyvaso DPI enables the device to easily fit into the patient's pocket and the device does not require electricity to function.

Ventavis® (iloprost) is the only other FDA-approved inhaled prostacyclin analogue that is available on the market. Patients need to inhale Ventavis six to nine times per day via a nebulizer. According to its package insert, each Ventavis inhalation consists of four to ten minutes of continuous inhalation via the nebulizer. We completed an open-label study in the United States to investigate the clinical effects of switching patients from Ventavis to Tyvaso. Patients in this study saved an average of approximately 1.4 hours per day when administering Tyvaso compared to Ventavis.

Studies establishing the effectiveness of Tyvaso to treat PAH included predominately PAH patients with functional class III symptoms (patients who may not have symptoms at rest but whose activities are greatly limited by shortness of breath, fatigue, or near fainting). Tyvaso was generally well tolerated in these trials. The most common side effects were transient cough, headache, nausea, dizziness, and flushing. In January and June 2021, data from the *INCREASE* study of Tyvaso for PH-ILD were published in the *New England Journal of Medicine* and *The Lancet Respiratory Medicine*, respectively.

We completed two clinical studies of Tyvaso DPI. One was a study in healthy volunteers, comparing the pharmacokinetics of Tyvaso DPI to Tyvaso Inhalation Solution. We completed the study in October 2020 and announced in January 2021 that the study demonstrated comparable systemic treprostinil exposure between Tyvaso DPI and Tyvaso Inhalation Solution. In December 2020, we completed a clinical study called *BREEZE*, which evaluated the safety and pharmacokinetics of switching PAH patients from Tyvaso Inhalation Solution to Tyvaso DPI. The *BREEZE* study demonstrated the safety and tolerability of Tyvaso DPI in subjects with PAH transitioning from Tyvaso Inhalation Solution, and comparable systemic treprostinil exposure between Tyvaso DPI and Tyvaso Inhalation Solution.

In August 2018, we settled patent litigation with Watson Laboratories, Inc. (**Watson**) related to its abbreviated new drug application (**ANDA**) seeking FDA approval to market a generic version of nebulized Tyvaso in the United States. Under the terms of this settlement, Watson may launch its generic version of nebulized Tyvaso in the United States beginning in January 2026, although Watson may be permitted to enter the market earlier under certain circumstances. For further detail, see the section below entitled *Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity—Generic Competition and Challenges to our Intellectual Property Rights*.

Remodulin

Remodulin was approved by the FDA for subcutaneous and intravenous administration in 2002 and 2004, respectively, and has been sold commercially in the United States since 2002. We sell Remodulin to specialty pharmaceutical distributors in the United States and to pharmaceutical distributors internationally. We recognized \$500.2 million, \$513.7 million, and \$516.7 million in Remodulin net product sales, representing 26 percent, 31 percent, and 35 percent of our total revenues for the years ended December 31, 2022, 2021, and 2020, respectively. Remodulin is indicated to treat patients with PAH to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with functional class II-IV (moderate to severe) symptoms. Outside of the United States, Remodulin is marketed and sold for treatment of PAH throughout most of Europe, Canada, Mexico, and various countries throughout Asia, the Middle East, and South America, as noted in the table above.

We believe that Remodulin has many qualities that make it an appealing alternative to competitive therapies. Remodulin is stable at room temperature, so it does not need to be cooled during infusion and patients do not need to use cooling packs or refrigeration to keep it stable. Treprostinil is highly soluble under certain circumstances and highly potent, which enables us to manufacture Remodulin in concentrated solutions. This allows therapeutic concentrations of Remodulin to be delivered at very low flow rates via miniaturized infusion pumps for both subcutaneous and intravenous infusion. Remodulin can be continuously infused for up to 48 hours before refilling the external infusion pump. This profile contrasts favorably with non-treprostinil based, continuously infused prostacyclin therapies on the market—Flolan®, Veletri®, and generic epoprostenol.

Flolan and generic epoprostenol are not stable at room temperature (and therefore require refrigeration or the use of cooling packs), but Veletri may be stable at room temperature depending on its concentration. Flolan, generic epoprostenol, and Veletri have shorter half-lives than Remodulin, requiring mixing prior to pump refills. None of these competitive products may be administered via subcutaneous infusion, and therefore may only be delivered intravenously which, unlike subcutaneous infusion, requires intravenous infusion line placement and carries the risk of serious bloodstream infection.

We also face competition from manufacturers of generic versions of Remodulin in the United States and abroad. See the section below entitled *Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity—Generic Competition and Challenges to our Intellectual Property Rights*.

Patients must use external pumps manufactured by third parties to deliver Remodulin. Smiths Medical, Inc. (**Smiths Medical**, now a subsidiary of ICU Medical, Inc.) manufactures the pumps used by most patients in the United States to administer Remodulin, including the CADD-MS[®] 3 (**MS-3**) pump used to deliver subcutaneous Remodulin, and the CADD-Legacy[®] pump to deliver intravenous Remodulin. In 2015, Smiths Medical notified us that it was planning to discontinue the manufacture of the MS-3 pumps and associated cartridges. In response, we funded Smiths Medical's manufacture of several thousand additional MS-3 pumps and, in parallel, pursued development of the Remunity Pump to help ensure that PAH patients would not experience a delay or disruption in their Remodulin therapy. The inventory of MS-3 pumps held by specialty pharmacy distributors (including the additional pumps we funded the manufacture of) is now exhausted, or nearly so. Smiths Medical has also announced plans to discontinue the CADD Legacy system, and to make an alternative pump, the CADD Solis, available for administration of intravenous Remodulin. In addition to Remunity, we are developing another next-generation delivery system for Remodulin.

There are serious side effects associated with Remodulin. For example, when infused subcutaneously, Remodulin causes varying degrees of infusion site pain and reaction (redness and swelling) in most patients. Patients who cannot tolerate the infusion site pain related to the use of subcutaneous Remodulin may instead use intravenous Remodulin. Intravenous Remodulin is delivered continuously through a surgically implanted central venous catheter, similar to Flolan, Veletri, and generic epoprostenol. Patients who receive therapy through implanted venous catheters have a risk of developing bloodstream infections and a serious systemic infection known as sepsis. Other common side effects associated with both subcutaneous and intravenous Remodulin include headache, diarrhea, nausea, jaw pain, vasodilation, and edema. As noted below under *Research and Development*, we are working on a prodrug version of Remodulin called RemoPro[™] to reduce the infusion site pain associated with subcutaneous administration of treprostinil.

Remunity Pump

In February 2021, we launched limited commercial sales of the Remunity Pump, which is a semi-disposable system for subcutaneous delivery of treprostinil that we developed in collaboration with DEKA Research & Development Corp (**DEKA**) under an exclusive development and license agreement. The Remunity Pump consists of a small, lightweight, durable pump and controller designed to have a service life of at least three years. The Remunity Pump uses disposable cassettes filled with Remodulin, which can be connected to the pump with less patient manipulation than is typically involved in filling other currently-available subcutaneous pumps. In November 2019, we entered into a supply agreement with an affiliate of DEKA to manufacture and supply the Remunity Pump to us. Under the terms of the agreement, we reimburse all of DEKA's and its affiliates' costs to manufacture the Remunity Pump.

The Remunity Pump was initially made available to patients in weekly shipments of disposable cassettes pre-filled with Remodulin. In September 2022, we launched a patient-filled version of the Remunity Pump, which enables patients to receive monthly shipments of empty, ready-to-fill Remunity cassettes and Remodulin.

Orenitram

Orenitram is the only FDA-approved, orally-administered prostacyclin analogue, and is the only oral PAH prostacyclin class therapy approved in the United States that is titratable to a maximum tolerated dose without a dose ceiling. We sell Orenitram to the same specialty pharmaceutical distributors in the United States that distribute Tyvaso, Tyvaso DPI, and Remodulin. We recognized \$325.1 million, \$306.1 million, and \$293.1 million in Orenitram net product sales, representing 17 percent, 18 percent, and 20 percent of our total revenues for the years ended December 31, 2022, 2021, and 2020, respectively. In 2013, the FDA approved Orenitram for treatment of PAH patients to improve exercise capacity. The primary study that supported efficacy of Orenitram was a 12-week monotherapy study in which PAH patients were not on any approved background PAH therapy. In August 2018, we announced that our clinical study of Orenitram called *FREEDOM-EV* had met its primary endpoint of delayed time to first clinical worsening event. In particular, the preliminary results showed that Orenitram, when taken with an oral PAH background therapy, decreased the risk of a clinical worsening event versus placebo by 25 percent ($p=0.0391$), driven by a 61 percent decrease in the risk of disease progression for patients taking Orenitram, when compared to placebo ($p=0.0002$). In October 2019, the FDA approved a supplement to the Orenitram NDA to update the product's label to reflect the *FREEDOM-EV* results. As a result, Orenitram is indicated to delay disease progression and improve exercise capacity. Mortality rates were similar between Orenitram and placebo groups at the end of randomized treatment. However, in participants for whom data are available (89 percent), Orenitram was associated with a 37 percent decreased risk of mortality compared with placebo at study closure ($p=0.0324$). These mortality data are not reflected in the FDA-approved label because they include data accrued in the open-label extension study.

Secondary endpoints in the *FREEDOM-EV* study included changes from baseline in six-minute walk distance (**6MWD**), Borg dyspnea score (shortness of breath test), functional class, NT-proBNP levels, and combined 6MWD and Borg dyspnea score. Secondary endpoint data, which are not included in the updated FDA-approved labeling, are summarized below:

- *Change in 6MWD*: The median 6MWD trended toward improvement at week 24 (Hodges-Lehmann treatment estimate: seven meters). Median 6MWD improved with Orenitram at weeks 36 (13 meters) and 48 (21 meters) compared to placebo.

- *Change in Borg dyspnea score and WHO functional class:* When classified categorically as “improved,” “no change,” or “deteriorated,” participants in the Orenitram group exhibited a significantly positive shift in Borg dyspnea score and WHO functional class compared to placebo at weeks 24, 36, and 48.
- *Change in NT-proBNP levels:* NT-proBNP levels were significantly improved with Orenitram at weeks 24 and 36. Per the study protocol, NT-proBNP was not assessed at week 48.
- *Change in combined 6MWD and Borg dyspnea score:* Combined 6MWD and Borg dyspnea score was significantly improved with Orenitram when assessed at week 24 compared to placebo.

In 2020, we published the results of a retrospective study in which a competing therapy, selexipag, was associated with 67 percent higher PAH-associated healthcare costs on average, during the first six months of therapy, compared to Orenitram. Selexipag and Orenitram are the only FDA-approved oral prostacyclin-class therapies.

The studies that established efficacy included predominately patients with functional class II-III symptoms and etiologies of idiopathic or heritable PAH (66 percent) or PAH associated with connective tissue disease (26 percent). The most common side effects observed in our clinical studies were headache, nausea, and diarrhea. Orenitram is currently only approved in the United States.

In February 2018, we settled patent litigation with Actavis Laboratories FL, Inc. (**Actavis**) related to its ANDA seeking FDA approval to market a generic version of Orenitram in the United States. Under the terms of this settlement, Actavis may launch its generic version of Orenitram in the United States beginning in June 2027, although Actavis may be permitted to enter the market earlier under certain circumstances. In May 2022, we settled litigation with ANI Pharmaceuticals, Inc. (**ANI**) regarding its ANDA seeking FDA approval to market a generic version of Orenitram. Under the settlement agreement, ANI can market its generic version of Orenitram in the United States beginning in December 2027, although it may be permitted to enter the market earlier under certain circumstances. For further detail, see the section below entitled *Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity—Generic Competition and Challenges to our Intellectual Property Rights*.

Adcirca

Adcirca is a PDE-5 inhibitor, the active pharmaceutical ingredient of which is tadalafil. Tadalafil is also the active pharmaceutical ingredient in Cialis®, which is marketed by Eli Lilly and Company (**Lilly**) for treatment of erectile dysfunction. We acquired the commercial rights to Adcirca for treatment of PAH in the United States from Lilly in 2008. We sell Adcirca at prices established by Lilly, which are at parity with Cialis pricing. We recognized \$41.3 million, \$55.9 million, and \$67.3 million in Adcirca net product sales, representing two percent, three percent, and four percent of our total revenues for the years ended December 31, 2022, 2021, and 2020, respectively.

In 2009, the FDA approved Adcirca with a recommended dose of 40 mg, making it the only once-daily PDE-5 inhibitor for treatment of PAH. Adcirca is indicated to improve exercise ability in patients with PAH. Studies establishing effectiveness included predominately patients with functional class II-III symptoms. Headaches were the most commonly reported side effect.

In August 2018, Mylan N.V. announced the launch of its generic version of Adcirca, which resulted in a material adverse impact on Adcirca net product sales. Additional companies launched generic versions of Adcirca in February 2019. In June 2020, we amended our Adcirca license agreement to extend its term through December 31, 2023. For further detail, see the section below entitled *Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity—Generic Competition and Challenges to our Intellectual Property Rights*.

Product to Treat Cancer — Unituxin

In March 2015, the FDA approved our Biologics License Application (**BLA**) for Unituxin, in combination with granulocyte-macrophage colony-stimulating factor, interleukin-2, and 13-cis-retinoic acid, for treatment of patients with high-risk neuroblastoma (a rare form of pediatric cancer) who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Unituxin is a chimeric monoclonal antibody composed of a combination of mouse and human DNA that induces antibody-dependent cell-mediated cytotoxicity, a mechanism of cell-mediated immunity whereby the immune system actively targets a cell that has been bound by specific antibodies. Unituxin therapy is associated with severe side effects, including infections, infusion reactions, hypokalemia, hypotension, pain, fever, and capillary leak syndrome. In November 2018, we received approval from Health Canada to market Unituxin, and we launched commercial sales of the product in Canada in late 2019. In June 2021, our Japanese distributor obtained approval to market Unituxin in Japan, and launched commercial sales shortly thereafter.

We recognized \$182.9 million, \$202.3 million, and \$122.9 million in Unituxin net product sales, representing nine percent, 12 percent, and eight percent of our total revenues for the years ended December 31, 2022, 2021, and 2020, respectively.

Research and Development

We focus our research and development efforts on the following pipeline programs. We also engage in a variety of additional research and development efforts, including technologies designed to increase the supply of transplantable organs and tissues and improve outcomes for transplant recipients through regenerative medicine, 3-D organ bioprinting, xenotransplantation, and *ex vivo* lung perfusion.

Select Pipeline Programs

Product	Mode of Delivery	Indication	Current Status STUDY NAME	Our Territory
RemoPro™ (subcutaneous prodrug)	Continuous subcutaneous	PAH	Phase 1	Worldwide
Tyvaso (treprostinil)	Inhaled	IPF	Phase 3 <i>TETON</i> studies	Worldwide
Ralinepag (IP receptor agonist)	Oral	PAH	Phase 3 <i>ADVANCE</i> studies	Worldwide, subject to out-licenses granted in certain Asian countries

RemoPro

We are conducting a series of phase 1 studies to develop a new prodrug called RemoPro, which is intended to enable subcutaneous delivery of treprostinil analog therapy without the site pain currently associated with subcutaneous Remodulin. As a prodrug, RemoPro is designed to be inactive in the subcutaneous tissue, which is intended to decrease or eliminate site pain, and to metabolize into treprostinil or a treprostinil analog once it is absorbed into the blood.

Tyvaso — *TETON* studies

We are enrolling two phase 3 studies, called *TETON 1* and *TETON 2*, of Tyvaso for the treatment of IPF. *TETON 1* is being conducted in the United States and Canada, and *TETON 2* is being conducted outside the United States and Canada. The primary endpoint of both studies is the change in absolute forced vital capacity (**FVC**) from baseline to week 52. The *TETON 1* study enrolled its first patient in June 2021, and the *TETON 2* study enrolled its first patient in October 2022.

The *TETON* studies were prompted by data from the *INCREASE* study of Tyvaso in PH-ILD, which demonstrated improvements in certain key parameters of lung function in pulmonary hypertension patients with fibrotic lung disease (improved absolute FVC and reduced exacerbations of underlying lung disease). Specifically, in the *INCREASE* study, treatment with Tyvaso resulted in significant improvements in percent predicted FVC at weeks 8 and 16, with subjects having an underlying etiology of IPF showing the greatest improvement (week 8: 2.5%; $p=0.0380$ and week 16: 3.5%; $p=0.0147$). Consistent positive effects were also observed in patients with chronic hypersensitivity pneumonitis and environmental/occupational lung disease. In May 2022, data from the *INCREASE* open-label, long-term extension trial were presented at a medical conference, indicating that improvements in FVC were sustained for at least 64 weeks for PH-ILD patients with underlying IPF. For those patients who received placebo during the *INCREASE* study, marked improvements in FVC were observed following transition to active Tyvaso during the open-label extension study. These data points, combined with substantial preclinical evidence of antifibrotic activity of treprostinil, suggest that Tyvaso may offer a treatment option for patients with IPF.

In December 2020, the FDA granted orphan designation for treprostinil to treat IPF. In March 2022, the European Medicines Agency (**EMA**) also granted orphan designation for treprostinil to treat IPF.

If the *TETON* studies are successful, we also plan to seek FDA approval to expand the Tyvaso DPI label to include IPF.

Ralinepag

Ralinepag is a next-generation, oral, selective, and potent prostacyclin receptor agonist that we are developing for treatment of PAH. We are enrolling two phase 3 studies of ralinepag: (1) *ADVANCE OUTCOMES*, which is an event-driven study of ralinepag in PAH patients with a primary endpoint of time to first clinical worsening event; and (2) *ADVANCE CAPACITY*, studying the effect of ralinepag on exercise capacity in PAH patients with a primary endpoint of change in peak oxygen uptake via cardiopulmonary exercise test. Both of these studies are global, multi-center, placebo-controlled trials of patients on approved oral background PAH therapies.

Organ Manufacturing

Each year, end-stage organ failure kills millions of people. A significant number of these patients could have benefited from an organ transplant. Unfortunately, the number of usable, donated organs available for transplantation has not grown significantly over the past half century while the need has soared. Our long-term goals are aimed at addressing this shortage. With advances in technology, we believe that creating an unlimited supply of tolerable manufactured organs is now principally an engineering challenge, and we are dedicated to finding engineering solutions. We are engaged in research and development of a variety of technologies designed to increase the supply of transplantable organs and tissues and to improve outcomes for transplant recipients through regenerative medicine, 3-D organ bioprinting, xenotransplantation, and ex vivo lung perfusion.

In 2019, we entered into a collaboration agreement with the University of Alabama at Birmingham (**UAB**) to develop a pilot-scale, designated pathogen-free facility to house genetically-modified pigs, with a goal of commencing human clinical trials of xenotransplanted kidneys we call UKidneys™ from pigs to humans in the near term. In August 2020, UAB began to conduct operations at the facility with the first introduction of genetically modified pigs, and in March 2021, the facility received its recertification of compliance from the American Association for Accreditation of Laboratory Animal Care. We also have sponsored research agreements with Johns Hopkins University, New York University (**NYU**), and University of Maryland Baltimore to conduct preclinical testing of our porcine xenografts, which have been generating data regarding our UKidneys, UThymoKidneys™, and UHearts™.

While we continue to develop and commercialize therapies for rare and life-threatening conditions, we view organ manufacturing as a complementary solution for a broad array of diseases, many of which (such as PAH) have proven incurable to date through more traditional pharmaceutical and biologic therapies. For this reason, in 2015 we created a wholly-owned PBC called Lung Biotechnology PBC, chartered with the express purpose of “address[ing] the acute national shortage of transplantable lungs and other organs with a variety of technologies that either delay the need for such organs or expand the supply.” It is also why we included the development of “technologies that expand the availability of transplantable organs” as part of our express public benefit purpose when we converted United Therapeutics to a PBC in 2021.

Recently, we and our collaborators announced several key achievements in our organ manufacturing program:

- **First Successful Xenotransplantation of a Porcine Heart:** In January 2022, University of Maryland School of Medicine surgeons successfully transplanted an experimental, genetically-modified UHeart into a living human under an expanded access authorization by the FDA. The patient survived for approximately two months with the UHeart. In June 2022, data from this procedure were published in the *New England Journal of Medicine*.
- **Successful UKidney and UHeart Tests in Preclinical Human Models:** In September 2021, collaborators at NYU and UAB tested UThymoKidneys and UKidneys from our genetically modified pigs in brain-dead organ donors, providing preclinical evidence that genetically modified pig organs could transcend the most proximate immunological barriers to xenotransplantation. Results of the UAB experiment were published in the *American Journal of Transplantation* in January 2022, and results of the NYU experiments were published in the *New England Journal of Medicine* in May 2022.

In June and July 2022, collaborators at NYU tested two UHearts from our genetically modified pigs in brain-dead organ donors. In each case, normal function was observed for our UHearts over a three-day study period, without signs of early rejection.

- **Ex Vivo Lung Perfusion:** To date, nearly 300 patients have received lung transplants following use of our centralized ex vivo lung perfusion service. Ex vivo lung perfusion technology increases the number of transplantable lungs by giving surgeons the ability to assess the function of marginal lungs to determine if the lungs are suitable for transplantation. This allows for the use of lungs that would have otherwise not been transplanted.
- **Drone Delivery of Organs:** In October 2021, we successfully completed the first-ever drone delivery of a lung for transplant at Toronto General Hospital, demonstrating the feasibility of our goal of delivering our manufactured organs with zero carbon footprint aircraft.

Aurora-GT

Our affiliate, Northern Therapeutics, Inc. (**Northern Therapeutics**), is conducting a Canadian clinical study (called *SAPPHIRE*) of a gene therapy product called Aurora-GT, in which a PAH patient's own endothelial progenitor cells are isolated, transfected with the gene for human endothelial nitric oxide synthase, expanded ex vivo, and then delivered back to the same patient. This therapy is intended to rebuild the blood vessels in the lungs that are compromised by PAH. Northern Therapeutics is a Canadian entity in which we have a 49.7 percent voting stake and a 71.8 percent financial stake. Northern Therapeutics discontinued enrollment of new patients at the end of 2022 when we ceased funding the *SAPPHIRE* program. After reviewing the data from the *SAPPHIRE* study, which enrolled 12 patients and is expected to unblind in early 2024, we will decide whether to pursue a BLA for Aurora-GT, and Northern Therapeutics will consider whether to initiate further studies. We have the exclusive right to pursue this technology in the United States. Under our agreement with Northern Therapeutics, we funded all of the expenses of the *SAPPHIRE* program through the end of 2022; thereafter, Northern Therapeutics is solely responsible for all future costs of developing Aurora-GT outside the United States.

Sales and Marketing

Our marketing strategy for our commercial PAH and PH-ILD products is to use our sales and marketing teams to reach out to the prescriber community to: (1) increase PAH and PH-ILD awareness; (2) increase understanding of the progressive nature of PAH and the importance of early treatment; and (3) increase awareness of our commercial products and how they fit into the various stages of disease progression and treatment.

Distribution of Commercial Products

United States Distribution of Tyvaso, Tyvaso DPI, Remodulin, Remunity Pump, Orenitram, and Unituxin

We distribute Tyvaso, Tyvaso DPI, Remodulin, the Remunity Pump, and Orenitram throughout the United States through two contracted specialty pharmaceutical distributors: Accredo Health Group, Inc. and its affiliates (**Accredo**) and Caremark, L.L.C. (**CVS Specialty**). These distributors are required to maintain certain minimum inventory levels in order to ensure an uninterrupted supply to patients who are prescribed our therapies. We compensate Accredo and CVS Specialty on a fee-for-service basis for certain ancillary services in connection with the distribution of these products. If any of our distribution agreements expire or terminate, we may, under certain circumstances, be required to repurchase any unsold inventory held by our distributors.

These specialty pharmaceutical distributors are responsible for assisting patients with obtaining reimbursement for the cost of our treprostinil-based products and providing other support services. Under our distribution agreements, we sell each of our treprostinil-based products to these distributors at a transfer price that we establish. We have also established patient assistance programs in the United States, which provide our treprostinil-based products to eligible uninsured or under-insured patients at no charge. Accredo and CVS Specialty assist us with the administration of these programs.

We distribute Unituxin throughout the United States through an exclusive distribution agreement with ASD Specialty Healthcare, Inc. (**ASD**), an affiliate of AmerisourceBergen Corporation. Under this agreement, we sell Unituxin to ASD at a transfer price that we establish, and we pay ASD fees for services provided in connection with the distribution and support of Unituxin.

To the extent we increase the price of any of these products, increases are typically in the single-digit percentages per year.

United States Distribution of Adcirca

Under our manufacturing and supply agreement with Lilly, Lilly manufactures and distributes Adcirca on our behalf through its wholesaler network in the same manner that it distributes its own pharmaceutical products. Under the terms of this agreement, we take title to Adcirca upon completion of its manufacture by Lilly. Adcirca is shipped to customers in accordance with purchase orders received by Lilly. Upon shipment, Lilly sends an invoice and collects the amount due from the customer subject to customary discounts and rebates, if any. Although Lilly provides these services on our behalf, we maintain the risk of loss as it pertains to inventory, product returns, and non-payment of invoices. The manufacturing and supply agreement will continue in effect until the December 31, 2023 expiration or earlier termination of our license agreement for Adcirca. Lilly retains authority under the license agreement for all regulatory activities with respect to Adcirca, as well as its retail pricing, which has been and is expected to remain at price parity with Cialis. We have also established a patient assistance program in the United States, which provides Adcirca to eligible uninsured or under-insured patients at no charge.

International Distribution of Tyvaso, Remodulin, Orenitram, and Unituxin

We currently sell Remodulin outside the United States to various distributors, each of which has exclusive distribution rights in one or more countries within Europe, the Middle East, Asia, and South and Central America. Our primary distributor outside the United States is Grupo Ferrer Internacional, S.A. (**Ferrer**), which holds Remodulin marketing authorization rights in many of these territories. We sell nebulized Tyvaso commercially to distributors that have exclusive distribution rights in Argentina and Israel. We also plan to sell nebulized Tyvaso through an exclusive distributor in Japan, where the product was approved in late 2022. We also distribute Remodulin and Unituxin in Canada through a specialty pharmaceutical wholesaler. In some of the markets where we are not licensed to market Remodulin, such as Taiwan, Turkey, and the United Kingdom, Remodulin is available, but not marketed, on a named patient basis in which therapies are approved for individual patients by a national medical review board, hospital, or health plan on a case-by-case basis. Similar named-patient programs are also available for Tyvaso in certain countries. We entered into exclusive agreements with Ferrer to distribute Orenitram and Tyvaso throughout the territories where it also has distribution rights for Remodulin. Initial feedback from the EMA has indicated that approval of either Orenitram or Tyvaso would require another large clinical trial of the applicable product. As such, the likelihood of commercially launching these products in Europe is remote. We distribute Unituxin in Japan through a third-party distributor that obtained Japanese marketing authorization during the second quarter of 2021.

Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity

Our success depends in part on our ability to obtain and maintain patent protection for our products, preserve trade secrets, prevent third parties from infringing upon our proprietary rights, and operate without infringing upon the proprietary rights of others in the United States and worldwide. Many of these proprietary rights stem from licenses and other strategic relationships with third parties. In addition to intellectual property rights, U.S. and international regulatory authorities often provide periods of market exclusivity for manufacturers of biopharmaceutical products.

Patents provide the owner with a right to exclude others from practicing an invention. Patents may cover the active ingredients, uses, formulations, doses, administrations, delivery mechanisms, manufacturing processes, and other aspects of a product. The period of patent protection for any given product generally depends on the expiration date of various patents and may differ from country to country according to the type of patents, the scope of coverage, and the remedies for infringement available in a country. Most of our commercial products and investigational products are protected by patents that expire on varying dates.

Significant legal questions exist concerning the extent and scope of patent protection for biopharmaceutical products and processes in the United States and elsewhere. Accordingly, there is no certainty that patent applications owned or licensed by us will be issued as patents, or that our issued patents will afford meaningful protection against competitors. Once issued, patents are subject to challenge through both administrative and judicial proceedings in the United States and other countries. Such proceedings include re-examinations, *inter partes* reviews (IPR), post-grant reviews, and interference proceedings before the U.S. Patent and Trademark Office, as well as opposition proceedings before the European Patent Office. Litigation may be required to enforce, defend, or obtain our patent and other intellectual property rights. Any administrative proceeding or litigation could require a significant commitment of our resources and, depending on outcome, could adversely affect the scope, validity, or enforceability of certain of our patent or other proprietary rights.

Tyvaso, Tyvaso DPI, Remodulin, and Orenitram Proprietary Rights

We have a number of issued patents and pending patent applications covering our treprostinil-based products, Tyvaso, Tyvaso DPI, Remodulin, and Orenitram. We have two unexpired patents related to the manufacture of treprostinil that expire in 2028 and are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the **Orange Book** (see *Orange Book* below), for Tyvaso, Tyvaso DPI, Remodulin, and Orenitram. Both of these patents are subject to the IPR proceedings discussed below under *Generic Competition and Challenges to our Intellectual Property Rights*.

In addition to the treprostinil patents noted above, we have other patents specific to our individual treprostinil-based products, including the following:

- **Tyvaso.** We have been granted two patents directed to a method of treating pulmonary hypertension and a kit for treating pulmonary hypertension. These two patents expire in 2028 and are listed in the Orange Book. Counterparts to these two patents are issued in several other countries. We have also been granted two patents on methods of treating pulmonary hypertension by administering treprostinil by inhalation, which expire in 2024. These two patents are also listed in the Orange Book.
- **Tyvaso DPI.** We have three Orange Book-listed patents that we license from MannKind directed to the composition of Tyvaso DPI drug product, which expire in 2025, 2030, and 2035, respectively. We have another issued patent listed in the Orange Book directed to a method of treating pulmonary hypertension, which expires in 2027. Counterparts to these patents are issued in several other countries. Additionally, our license agreement with MannKind includes rights to a substantial portfolio of additional issued U.S. and international patents related to a component of the drug product and methods of making the drug product, which expire at various dates through 2035, and pending applications that, if issued, could extend protection to 2042 or beyond.
- **Remodulin.** We have been granted three U.S. patents covering an improved diluent for Remodulin, which expire in 2028 and 2029. We have another patent covering intravenous administration of Remodulin with certain diluents, which expires in 2024. We have been granted two patents covering a treprostinil formulation with a citrate buffer, which expire in 2024. We have been granted another patent covering a method of treating pulmonary hypertension by administering treprostinil at a certain rate intravenously, which expires in 2024. All seven of these patents are listed in the Orange Book.
- **Orenitram.** Our patents for Orenitram cover methods of use for treating PAH, orally administered formulations, controlled moisture storage and manufacturing methods, as well as those covering controlled release formulations licensed to us by Supernus Pharmaceuticals Inc. (**Supernus**). These patents will expire in the United States between 2024 and 2031 and in various countries throughout the world between 2024 and 2030.

We have additional pending U.S. and international patent applications related to Tyvaso, Tyvaso DPI, Remodulin, and Orenitram.

Orange Book

In seeking approval of a drug through an NDA or upon issuance of new patents following approval of an NDA, applicants are required to submit to the FDA each patent that has claims covering the applicant's product or a method of using the product. Each of the patents submitted is then published in the Orange Book. See *Governmental Regulation—Patent Term and Regulatory Exclusivity* below for further details. Remodulin currently has nine unexpired Orange Book-listed patents with expiration dates ranging from 2024 to 2029. Tyvaso currently has six unexpired Orange Book-listed patents expiring in 2028. Tyvaso DPI currently has six unexpired Orange Book-listed patents with expiration dates ranging from 2025 to 2035. Orenitram currently has twelve unexpired Orange Book listed patents with expiration dates ranging from 2024 to 2031. Additional patent applications are pending, and if granted, may be eligible for listing in the Orange Book.

Regulatory Exclusivity

- *Tyvaso and Tyvaso DPI*. In 2010, the FDA granted orphan drug designation for Tyvaso, which resulted in an orphan exclusivity period that expired in July 2016. In March 2021, the FDA granted Tyvaso three-year clinical trial exclusivity for PH-ILD as a result of the *INCREASE* study and the expansion of the Tyvaso label to include a PH-ILD indication. This exclusivity period will extend through March 2024, and also covers Tyvaso DPI for PH-ILD. In 2004, the European Commission designated Tyvaso an orphan medicinal product for treatment of both PAH and chronic thromboembolic pulmonary hypertension, which would confer a ten-year exclusivity period commencing if and when we obtain marketing approval. In December 2020, the FDA granted orphan designation for treprostinil for treatment of IPF. Thus, if our *TETON* studies are successful and the FDA approves a supplemental NDA to update the Tyvaso and/or Tyvaso DPI labeling to include an IPF indication, the FDA should grant seven-year orphan drug exclusivity for this new indication. The EMA has also granted orphan drug designation for treprostinil to treat IPF.
- *Remodulin*. Regulatory exclusivity for Remodulin in the United States and Europe has expired.
- *Orenitram*. In November 2019, following approval of our supplemental NDA to reflect the *FREEDOM-EV* results in the Orenitram label, the FDA granted orphan exclusivity for the new indication that Orenitram delays disease progression in PAH patients. This exclusivity expires in October 2026.

Supernus License

In 2006, we entered into an exclusive license agreement with Supernus to use certain of its technologies in manufacturing Orenitram. Under the agreement, we paid Supernus certain amounts upon the achievement of specified milestones based on the development and commercial launch of Orenitram for PAH, and we would be obligated to make additional milestone payments if we develop Orenitram for a second indication. In addition, the agreement provides that we will pay a single-digit percentage royalty based on net worldwide sales. The term of this royalty expires during the second quarter of 2026.

Generic Competition and Challenges to our Intellectual Property Rights

Remodulin—Generic Competition

We settled litigation with Sandoz, Inc. (**Sandoz**) related to its ANDA seeking FDA approval to market a generic version of Remodulin and in March 2019, Sandoz announced the availability of its generic product in the United States. We have also entered into similar settlement agreements with other generic companies, some of which have also launched sales of generic versions of Remodulin. Through December 31, 2022, we have seen limited erosion of Remodulin sales as a result of generic treprostinil competition in the United States. We are currently engaged in litigation with Sandoz and its marketing partner, RareGen (now a subsidiary of Liquidia Corporation, the parent company of Liquidia Technologies, Inc. (**Liquidia**)), related to the infusion devices used to deliver Remodulin subcutaneously. We understand that generic treprostinil was initially launched by Sandoz/RareGen for use only by intravenous administration. In May 2021, Sandoz/Liquidia Corporation announced that Sandoz's generic treprostinil has been made available for subcutaneous use, following FDA clearance of a cartridge that can deliver the product via the Smiths Medical CADD MS-3 pump. See Note 14—*Litigation*, to our consolidated financial statements included in this Report.

Regulatory authorities in various European countries began approving generic versions of Remodulin in 2018, followed by pricing approvals and commercial launches in most of these countries in 2019 and 2020. As a result, our international Remodulin revenues have decreased compared to the period prior to generic launch, due to increased competition and a reduction in our contractual transfer price for Remodulin sold by certain international distributors for sales in countries in which the pricing of Remodulin is impacted by the generic competition.

Tyvaso and Orenitram—Potential Future Generic Competition

We settled litigation with Watson and Actavis related to their ANDAs seeking FDA approval to market generic versions of nebulized Tyvaso and Orenitram, respectively, before the expiration of certain of our U.S. patents. Under the settlement agreements, Watson and Actavis can market their generic versions of nebulized Tyvaso and Orenitram in the United States beginning in January 2026 and June 2027, respectively, although they may be permitted to enter the market earlier under certain circumstances. In May 2022, we settled litigation with ANI regarding its ANDA seeking FDA approval to market a generic version of Orenitram. Under the settlement agreements, ANI can market its generic version of Orenitram in the United States beginning in December 2027, although it may be permitted to enter the market earlier under certain circumstances. Competition from

these generic companies could reduce our net product sales and profits. See Note 14—*Litigation*, to our consolidated financial statements included in this Report.

Liquidia—Yutrepia

We are engaged in patent litigation with Liquidia concerning three patents related to Tyvaso and Tyvaso DPI. The litigation is proceeding in parallel in two fora: (1) federal court; and (2) the Patent Trial and Appeal Board (**PTAB**) of the U.S. Patent and Trademark Office.

As background, in January 2020 Liquidia submitted its initial NDA to the FDA for approval of Yutrepia™, a dry powder formulation of treprostinil for inhalation. The Yutrepia NDA was submitted under the 505(b)(2) regulatory pathway with Tyvaso as the reference listed drug and received tentative approval from the FDA in November 2021. If and when Liquidia launches commercial sales of Yutrepia, it would compete directly with Tyvaso, Tyvaso DPI, and our other treprostinil-based products.

Following the initial submission of the Yutrepia NDA, we filed a lawsuit in federal district court against Liquidia for infringement of three of our patents: U.S. Patent Nos. 9,604,901 (the '**901 patent**'), 9,593,066 (the '**066 patent**'), and 10,716,793 (the '**793 patent**'). In December 2021, we filed a stipulation that the '901 patent would not be infringed by Liquidia based on the court's claim construction ruling. Trial was held during March 2022 on the '066 patent and the '793 patent, and we received the court's decision in August 2022. The court found that Liquidia's product would infringe the '793 patent and that Liquidia had not proved that any claim of that patent is invalid. The court also determined that Liquidia had proved that certain claims of the '066 patent were invalid and that we had not proved Liquidia's infringement of another '066 patent claim. Accordingly, the court issued a final judgment that bars the FDA from approving Liquidia's approved product until expiration of the '793 patent in May 2027. The parties have each appealed portions of the decision adverse to them, and those appeals are pending.

Separately, Liquidia has been attempting to invalidate these patents by filing petitions for IPR with the PTAB. Challengers in IPR proceedings have a lower burden of proof (preponderance of the evidence) relative to district court litigation (clear and convincing evidence) to successfully challenge the validity of patent claims.

- '**066 patent**': In October 2020, the PTAB declined to institute IPR proceedings relating to this patent because Liquidia failed to establish a reasonable likelihood of prevailing on any claim of this patent.
- '**901 patent**': In October 2021, the PTAB issued a final written decision on Liquidia's IPR relating to this patent. The PTAB upheld the patentability of two of the claims of this patent, one of which was being asserted against Liquidia in the district court litigation, and found that seven other claims of this patent were unpatentable. We have appealed the PTAB's decision, and the appeal is pending. All claims of this patent remain valid until any IPR appeals are exhausted. In December 2021, we filed a stipulation in the district court litigation that the '901 patent would not be infringed by Liquidia based on the court's claim construction ruling.
- '**793 patent**': In August 2021, the PTAB instituted IPR proceedings related to this patent. In July 2022, the PTAB issued a final written decision finding all claims of this patent to be unpatentable. We filed a request for rehearing and for precedential opinion panel review. On October 26, 2022, the PTAB denied our request for precedential opinion panel review, but "determine[d] that the Board's Final Written Decision did not address adequately whether the [references relied upon as the basis for canceling claims] qualify as prior art." Thus, the PTAB directed the original panel "in its consideration on rehearing, to clearly identify whether the ... references qualify as prior art." The original panel issued its decision on our request for rehearing on February 2, 2023. The original panel agreed that it had overlooked our arguments and its rationale for determining that certain references are prior art was erroneous. Nonetheless, the original panel determined the references qualify as prior art under a new rationale. Thus, the original panel maintained that the claims of this patent are not valid. We have until April 6, 2023 to appeal. All claims of this patent remain valid until any IPR appeals are exhausted.

Liquidia could obtain final FDA approval for its proposed product prior to May 2027 in two circumstances: (1) Liquidia could prevail on appeal, either from the district court judgment or IPR proceedings, such that its product is not found to infringe any valid claims of our patents; or (2) the district court or appeals court could stay the district court order barring FDA approval of its product during the pendency of its appeals. Liquidia has filed a motion with the district court to stay the bar against final FDA approval, and that motion is fully briefed and pending.

For further details, please see Note 14—*Litigation*, to our consolidated financial statements.

Adcirca—Generic Competition

A U.S. patent for Adcirca for 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 by Mylan N.V. in August 2018, and by additional companies in February 2019. Generic competition for Adcirca has had a material adverse impact on Adcirca net product sales.

General

We intend to vigorously enforce our intellectual property rights related to our products. However, we may not prevail in defending our patent rights, and additional challenges from other ANDA filers or other challengers may surface with respect to our products. Our patents could be invalidated, found unenforceable, or found not to cover one or more generic forms of our products. If any ANDA filer or filer of a 505(b)(2) NDA for a branded treprostinil product were to receive approval to sell its treprostinil product and/or prevail in any patent litigation, our affected product(s) would become subject to increased

competition. Patent expiration, patent litigation, and competition from generic or other branded treprostinil manufacturers could have a significant, adverse impact on our treprostinil-based product revenues (including the anticipated revenues from new products such as Tyvaso DPI), our profits, and our stock price. These potential effects are inherently difficult to predict. For additional discussion, refer to the risk factor entitled, *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*, contained in *Part I, Item 1A—Risk Factors* included in this Report.

Adcirca License Agreement

In 2008, Lilly granted us an exclusive license to develop, market, promote, and commercialize Adcirca for treatment of pulmonary hypertension in the United States. We agreed to pay Lilly royalties based on our net product sales of Adcirca. Lilly retained the exclusive rights to develop, manufacture, and commercialize pharmaceutical products containing tadalafil, the active pharmaceutical ingredient in Adcirca, for treatment of pulmonary hypertension outside of the United States and for treatment of other diseases worldwide. Lilly retained authority for all regulatory activities with respect to Adcirca and for setting the wholesale price of Adcirca, which has been and is expected to continue to be at price parity with Cialis. In May 2017, we amended our Adcirca license agreement with Lilly in order to clarify and extend the term of the agreement and to amend the economic terms of the agreement following a patent expiry in November 2017. As a result, we are required to make milestone payments to Lilly equal to \$325,000 for each \$1.0 million in net product sales, plus a royalty equal to ten percent of our net product sales. In June 2020, we amended our Adcirca license agreement to extend its term through December 31, 2023. Following expiration, we will remain obligated to refund the purchase price of any Adcirca that we previously sold to distributors that expires unsold. For additional discussion, refer to our *Adcirca* product description included in *Part I, Item 1—Business Overview—Products to Treat Pulmonary Arterial Hypertension*.

We also agreed to purchase Adcirca at a fixed manufacturing cost. The agreement provides a mechanism, generally related to the increase in the national cost of pharmaceutical manufacturing, pursuant to which Lilly may raise the manufacturing cost of Adcirca.

Unituxin Proprietary Rights and Regulatory Exclusivity

Approval of our biologics license application (**BLA**) for Unituxin conferred a 12-year data exclusivity period through March 2027, during which the FDA may not approve a biosimilar for Unituxin. Our orphan drug exclusivity in the United States for Unituxin expired in March 2022. Under a non-exclusive license agreement with The Scripps Research Institute, we pay a royalty of one percent of Unituxin net product sales. We have no patents covering Unituxin.

DEKA Agreements

In December 2014, we entered into an exclusive agreement with DEKA to develop a semi-disposable system for subcutaneous delivery of Remodulin, which we refer to as the Remunity Pump. Our agreement with DEKA expires on the last to occur of 25 years from the first product launch under the agreement, or upon the expiration of the last valid claim of a patent licensed from DEKA under the agreement that covers the Remunity Pump. Under the terms of the agreement, we funded the development costs related to the Remunity Pump, and will continue to fund further development costs associated with new versions of the pump. We pay product fees and a single-digit royalty to DEKA based on commercial sales of the Remunity Pump and the Remodulin drug product sold for use with the system. Either party may terminate the agreement immediately upon a material breach by the other party that is uncured following the relevant cure period, or in the event of the other party's bankruptcy or insolvency. In November 2019, we entered into a supply agreement with an affiliate of DEKA to manufacture and supply the Remunity Pump. Under this supply agreement, we are responsible for all costs associated with manufacturing the Remunity Pump. The Remunity Pump is covered by issued patents and pending patent applications both in the U.S. and other countries. The expiration dates of currently issued U.S. patents range from 2027 through 2033.

Tyvaso DPI and the MannKind Agreement

In September 2018, we entered into a worldwide, exclusive license and collaboration agreement with MannKind for the development and commercialization of Tyvaso DPI for treatment of PAH. The agreement became effective on October 15, 2018.

Under our agreement with MannKind, we are responsible for global development, regulatory, and commercial activities related to Tyvaso DPI, and we share manufacturing responsibilities with MannKind. Under the terms of the agreement, we paid MannKind \$45.0 million following the effectiveness of the agreement in October 2018, and we paid \$25.0 million in each of 2019 and 2020 following the achievement of specific development targets. We also pay MannKind low double-digit royalties on our net sales of the product. In addition, we have the option, in our sole discretion, to expand the license to include other active ingredients for treatment of pulmonary hypertension. We will pay MannKind up to \$40.0 million in additional option exercise and development milestone payments for each product (if any) added to the license pursuant to this option, as well as a low double-digit royalty on our net sales of any such product.

Under our license agreement with MannKind, we have an exclusive license to a variety of granted and pending patents and patent applications related to treprostinil inhalation powder and the Dreamboat device, including multiple patent families covering the U.S. and other major market countries. These patents cover drug formulation, devices and device components, and manufacturing processes and intermediates. For additional detail concerning these patents, refer to *Tyvaso*, *Tyvaso DPI*, *Remodulin*, and *Orenitram Proprietary Rights* above.

In August 2021 we entered into a commercial supply agreement with MannKind (as amended, the **Supply Agreement**). Pursuant to the Supply Agreement, MannKind is responsible for manufacturing and supplying Tyvaso DPI to us on a cost-plus basis. Unless earlier terminated, the initial term of the Supply Agreement continues until December 31, 2031 and will thereafter be renewed automatically for additional, successive two-year terms unless we give 24 months' written notice of non-renewal, or MannKind gives 48 months' written notice of non-renewal, prior to the end of the initial term or any additional renewal term. In addition, each party has customary termination rights, including termination for the other party's material breach that is not cured within a specific timeframe or in the event of liquidation, bankruptcy or insolvency of the other party.

Ralinepag and the Arena Agreement

On November 15, 2018, we entered into an exclusive license agreement with Arena Pharmaceuticals, Inc. (**Arena**) related to ralinepag. On January 24, 2019, in connection with the closing of the transactions contemplated by the license agreement: (1) Arena granted to us perpetual, irrevocable, and exclusive rights throughout the universe to develop, manufacture, and commercialize ralinepag; (2) Arena transferred to us certain other assets related to ralinepag, including, among others, related domain names and trademarks, permits, certain contracts, inventory, regulatory documentation, Investigational New Drug (**IND**) Application No. 109021 (related to ralinepag), and non-clinical, preclinical, and clinical trial data; (3) we assumed certain limited liabilities from Arena, including, among others, all obligations arising after the closing under the assumed contracts and the IND described above; and (4) we paid Arena \$800.0 million, which we expensed as acquired in-process research and development and included within research and development expenses in our consolidated statements of operations for the year ended December 31, 2019. We will also pay Arena: (1) a one-time payment of \$250.0 million for the first, if any, marketing approval we receive in the United States for an inhaled version of ralinepag to treat PAH; (2) a one-time payment of \$150.0 million for the first, if any, marketing approval we receive in any of Japan, France, Italy, the United Kingdom, Spain, or Germany for an oral version of ralinepag to treat any indication; and (3) low double-digit, tiered royalties on net sales of any pharmaceutical product containing ralinepag as an active ingredient, subject to certain adjustments for third-party license payments. Under our license agreement with Arena, we have an exclusive license to a variety of granted and pending patents and applications related to ralinepag covering drug formulation, manufacturing and dosage, among others. Many of these patents and patent applications would be eligible for listing in the Orange Book. In March 2022, Arena was acquired by Pfizer Inc. Based on potential patent term extensions and additional patent filings, we believe that U.S. patent protection for ralinepag will likely last through at least the mid-2030s.

Other

We are party to various other license agreements related to therapies and technologies under development. These license agreements require us to make payments based on a percentage of sales if we are successful in commercially developing these therapies, and may require other payments upon the achievement of certain milestones.

Manufacturing and Supply

We synthesize treprostinil, the active ingredient in Tyvaso, Tyvaso DPI, and Remodulin, and treprostinil diolamine, the active ingredient in Orenitram, at our facility in Silver Spring, Maryland. We produce dinutuximab, the active ingredient in Unituxin, at our Silver Spring facility. We manufacture drug product for nebulized Tyvaso, Remodulin, and Unituxin at our Silver Spring facility. We manufacture Orenitram drug product and we package, warehouse, and distribute Tyvaso, Remodulin, Orenitram, and Unituxin at our facility in Research Triangle Park, North Carolina.

We maintain, at a minimum, a two-year inventory of Tyvaso (nebulized only), Remodulin, and Orenitram based on expected demand, and we contract with third-party contract manufacturers to supplement our capacity for some products, in order to mitigate the risk that we might not be able to manufacture internally sufficient quantities to meet patient demand. For example, Baxter Pharmaceutical Solutions, LLC is approved by the FDA, the EMA, and various other international regulatory agencies to manufacture Remodulin for us. We rely on Woodstock Sterile Solutions to serve as an additional manufacturer of nebulized Tyvaso. We have no plans to develop a redundant manufacturing source for dinutuximab, the active ingredient in Unituxin, or for finished Unituxin or Orenitram drug product.

DEKA and its affiliates are currently entirely responsible for manufacturing the Remunity Pump. We rely entirely on Minnetronix Inc. to manufacture the nebulizer used in our Tyvaso Inhalation System. MannKind is the sole manufacturer of finished drug product and devices for Tyvaso DPI. We currently rely on third-party contract manufacturers to produce ralinepag.

Although we believe that additional third parties could provide similar products, services, and materials, there are few companies that could replace our existing third-party manufacturers and suppliers. A change in supplier or manufacturer could cause a

delay in the manufacturing, distribution, and research efforts associated with our respective products or result in increased costs. See also *Item 1A—Risk Factors* included in this Report.

Competition

Many drug companies engage in research, development, and commercialization of products to treat cardiopulmonary diseases and cancer. For treatment of PAH, we compete with many approved products in the United States and the rest of the world. In the U.S., these competitive therapies include oral ERAs (Letairis® (ambrisentan), Opsumit® (macitentan), Tracleer® (bosentan), generic bosentan, and generic ambrisentan); prostacyclin-class therapies (Flolan (intravenous epoprostenol), Uptravi® (oral selexipag), Veletri® (intravenous epoprostenol), Ventavis® (inhaled epoprostenol), generic epoprostenol, and generic treprostinil injection); PDE-5 inhibitors (Revatio® (sildenafil), generic sildenafil, and generic tadalafil); and Adempas® (riociguat), an sGC stimulator that targets a similar vasodilatory pathway as PDE-5 inhibitors. These therapies are manufactured and marketed by large pharmaceutical companies such as Johnson & Johnson, Gilead Sciences, Inc., and Bayer Schering Pharma AG, as well as a variety of large generic drug manufacturers.

There are also a wide variety of investigational PAH therapies undergoing development. Therapies undergoing registration-phase studies, or which have completed registration-phase studies, include the following:

- *Yutrepia*, a dry powder formulation of treprostinil developed by Liquidia, which is designed for pulmonary delivery using a disposable inhaler. In November 2021, Liquidia announced the FDA granted tentative approval for its NDA for Yutrepia to treat PAH, with final approval pending resolution of the regulatory stay triggered by the litigation described above under *Patent and Other Property Rights, Strategic Licenses, and Market Exclusivity—Generic Competition and Challenges to our Intellectual Property Rights*. In late 2020, Liquidia completed a business combination with RareGen, LLC, which markets a generic version of Remodulin manufactured by Sandoz. Liquidia has indicated that it plans to seek approval to expand Yutrepia's label to include PH-ILD, following expiration of Tyvaso's regulatory exclusivity in that indication in March 2024.
- *Sotatercept*, an injected TGF-beta modulator being developed by Acceleron Pharma, Inc. (**Acceleron**), which was acquired by Merck & Co., Inc. (**Merck**). Merck announced positive top-line results of a phase 3, registration trial in PAH called *STELLAR* in October 2022. Acceleron indicated it may also study sotatercept in PH-ILD.
- *Imatinib*, a drug currently used to treat cancer under the trade name Gleevec®, is being developed separately for treatment of PAH by three companies. Tenax Therapeutics, Inc. announced plans to initiate a phase 3 study of an oral formulation during 2023. Aerovate Therapeutics, Inc. is conducting a phase 2/3 clinical study of an inhaled, dry powder formulation of imatinib. Aerami Therapeutics Holdings, Inc. is conducting a phase 1 trial of an inhaled formulation of imatinib.
- *MK-5475*, an inhaled soluble guanylate cyclase stimulator being developed by Merck for PAH in a phase 2/3 trial. Phase 1 results were published in *Respiratory Medicine* in November of 2022.
- *L606*, an inhaled, liposomal form of treprostinil being developed by Pharmosa Biopharm Inc. (**Pharmosa**) for PAH, which completed a phase 1 study in healthy volunteers. Pharmosa initiated a phase 3 study in August 2021.

Additional therapies being studied for PAH include Insmed Incorporated's TPIP (INS1009, an inhaled version of treprostinil) (phase 2); PhaseBio Pharmaceuticals, Inc.'s pemziviaptadil (PB1046) (phase 2); Enzyvant Therapeutics GmbH's rodatristat ethyl (RVT-1201) (phase 2); Gossamer Bio, Inc.'s seralutinib (GB002) (phase 2); SoniVie's TIVUS™ (pivotal trial); Respira Therapeutics' vardenafil (RT234) (phase 2b); Cereno Scientific's valproic acid (CS1) (phase 2); and Bial Portela C.S.A.'s zamicastat (BIA 5-1058) (phase 2).

Oral non-prostacyclin therapies (such as PDE-5 inhibitors and ERAs) are commonly prescribed as first-line treatments for less severely ill PAH patients. As patients progress in their disease severity, additional advanced approved therapies, such as inhaled prostacyclin analogues (including Tyvaso and Tyvaso DPI) or infused prostacyclin analogues (including Remodulin) are then commonly added. Orenitram was the first approved oral prostacyclin-class therapy for PAH in the United States, and offers a more convenient alternative therapy to Remodulin, Tyvaso, and Tyvaso DPI. The use of available oral therapies could delay many patients' need for inhaled or infused prostacyclin therapy. As a result, the availability of oral therapies affects demand for our inhaled and infused products.

Orenitram faces direct competition from Uptravi, which is indicated to delay disease progression and reduce the risk of hospitalization for PAH. Orenitram's initial indication was limited to the improvement of exercise capacity, which may have led physicians to prescribe Uptravi instead of Orenitram. However, Uptravi is an oral IP prostacyclin receptor agonist. While prostacyclin analogues such as Orenitram broadly mimic the effect of prostacyclin, IP prostacyclin receptor agonists bind selectively to the IP receptor, one of several prostacyclin receptors. In addition, Orenitram's label allows physicians flexibility to titrate each patient's dosing up to a level according to tolerability, without any stated maximum. By contrast, Uptravi's label specifies a specific maximum dose. Given the progressive nature of PAH, many patients initiate Orenitram or another one of our treprostinil-based therapies after their disease progresses while taking Uptravi. In August 2018, we announced the results of our *FREEDOM-EV* clinical study, which demonstrated that Orenitram delays time to clinical worsening, demonstrated improvement across key clinical measures, and, at study closure, indicated a positive impact on survival rates. In October 2019, the FDA approved a supplement to our Orenitram NDA expanding the Orenitram label to indicate that it also delays disease progression, in addition to improving exercise capacity. We believe that these clinical results and updated labeling have resulted in increased use of Orenitram.

We have faced generic competition for Adcirca since the launch of generic tadalafil in the United States in August 2018, which has significantly reduced our Adcirca revenues. We have also faced generic competition for Remodulin in the United States and certain European countries since 2019. Finally, we have entered into settlement agreements with Actavis and ANI permitting them to launch generic versions of Orenitram in June 2027 and December 2027, respectively, and with Watson permitting it to launch a generic version of nebulized Tyvaso in January 2026, or in each case earlier under certain circumstances. For details regarding these and other potential generic competitors, see the section above entitled *Patents and Other Proprietary Rights, Strategic Licenses, and Market Exclusivity—Generic Competition and Challenges to our Intellectual Property Rights*.

Tyvaso, Tyvaso DPI, and our other treprostinil-based products may face competition from Liquidia if it obtains final approval of Yutrepia, a dry powder inhaled version of treprostinil.

Aside from Tyvaso and Tyvaso DPI, there are no approved therapies to treat PH-ILD. Several PAH drug candidates are also being developed for PH-ILD (e.g., Yutrepia, sotatercept, MK-5476, and TPIP). Other companies are now developing, or may in the future develop, therapies to treat group 3 pulmonary hypertension, including INOpulse®, an inhaled nitric oxide delivery system being developed by Bellerophon Therapeutics, Inc. for fibrotic interstitial lung disease (fILD) patients at risk of pulmonary hypertension, as well as pulmonary hypertension associated with other indications such as COPD and sarcoidosis. A phase 3 study in fILD is ongoing.

In addition, the use of antifibrotic therapies to treat underlying lung disease (such as the IPF therapies discussed below) could delay the onset of group 3 pulmonary hypertension.

Following the results of the *INCREASE* study, we expanded our investigational efforts with inhaled treprostinil to examine its use to treat the lung diseases underlying PH-ILD, including our *TETON* studies of Tyvaso in IPF patients. If the *TETON* program is successful, we anticipate seeking an IPF indication for Tyvaso and Tyvaso DPI. There are currently two therapies that are approved to treat IPF: Ofev® (nintedanib), which is marketed by Boehringer Ingelheim International GmbH, and Esbriet® (pirfenidone), which is marketed by F. Hoffman-La Roche Ltd. (Roche). However, clinical studies have indicated that these therapies only slow lung function decline in IPF patients, resulting in a significant unmet need for therapies that halt or reverse lung function decline in IPF. There are a number of potentially competing therapies in advanced clinical development for IPF. These therapies include, but are not limited to, FibroGen, Inc.'s pamrevlumab (phase 3), Galacto, Inc.'s GB0139 (phase 2), Sanofi S.A.'s belumosudil (KD025) (phase 2), MediciNova, Inc.'s tipelukast (MN-001) (phase 2), Nitto Biopharma's ND-L02-s0201 (phase 2), Bristol Myers Squibb Company's Orenicia® (abatacept) (phase 2), BMS-986278 (phase 2), and CC-90001 (phase 2), and Horizon Therapeutics plc's HZN-825 (phase 2).

Unituxin may face competition from Qarziba® (dinutuximab beta), an antibody product developed by Apeiron Biologics AG that is approved in Europe to treat high-risk neuroblastoma, but is not approved in the United States. In October 2016, EUSA Pharma (UK) Ltd. (which was acquired by Recordati Group in 2022) announced it had acquired global commercialization rights to Qarziba. In addition, Y-mAbs Therapeutics, Inc. (Y-mAbs), is developing several GD-2 targeting drug candidates, and in November 2020 obtained FDA approval for Danyelza® (naxitamab-gqqgk) to treat pediatric and adult patients with relapsed and refractory (second line) high-risk neuroblastoma in bone or bone marrow. Y-mAbs launched commercial sales of Danyelza in 2021. Y-mAbs is also conducting studies of naxitamab for frontline high-risk neuroblastoma.

We compete with the developers, manufacturers, and distributors of all of the products noted above for customers, funding, access to licenses, personnel, third-party collaborators, product development, and commercialization. Some of these companies have substantially greater financial, marketing, sales, distribution and technical resources, and more experience in research and development, product development, manufacturing and marketing, clinical trials, and regulatory matters, than we have.

Governmental Regulation

Pharmaceutical Product Approval Process

The research, development, testing, manufacture, promotion, marketing, distribution, sampling, storage, approval, labeling, record keeping, post-approval monitoring and reporting, and import and export of pharmaceutical products are extensively regulated by governmental agencies in the United States and in other countries. In the United States, failure to comply with requirements under the Federal Food, Drug, and Cosmetic Act (**FDC Act**), the Public Health Service Act (**PHSA**), and other federal statutes and regulations, may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs or BLAs, warning letters, product recalls, product seizures, total or partial suspension of manufacturing or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Satisfaction of FDA pre-market approval requirements is extremely costly and typically takes many years. The actual cost and time required may vary substantially based upon the type, complexity, and novelty of the product or disease. Drugs are subject to rigorous regulation and requirements by the FDA in the United States, the EMA in the European Union (**EU**), and similar regulatory authorities in other countries. The steps ordinarily required before a new drug may be marketed in the United States, which are similar to steps required in most other countries, include: (1) preclinical testing; (2) submission to the FDA of an IND; (3) clinical studies, including well-controlled clinical trials, in healthy volunteers and patients to establish safety, efficacy, and dose-response characteristics for each drug indication; (4) submission of an NDA to the FDA; and (5) FDA acceptance, review, and approval of the NDA.

Preclinical Testing

Preclinical tests include laboratory evaluation of product chemistry and formulation, as well as animal studies to explore toxicity and for proof-of-concept. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices.

Submission of IND

The results of preclinical testing are submitted to the FDA as part of an IND, along with other information including information about product chemistry, manufacturing, and controls, and a proposed clinical trial protocol. Absent FDA objection within 30 days after submission of an IND, the IND becomes effective and the clinical trial proposed in the IND may begin.

Clinical Studies

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (1) in compliance with federal regulations; (2) in compliance with good clinical practices (**GCP**), an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; and (3) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be approved by an institutional review board (**IRB**). An IRB may also require the clinical trial at a site to be halted temporarily or permanently for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials in support of an NDA typically are conducted in sequential phases, but the phases may overlap.

- *Phase 1* involves the initial introduction of the drug into healthy human subjects or patients to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness.
- *Phase 2* usually involves studies in a limited patient population to assess the efficacy of the drug in specific, targeted indications, explore tolerance and optimal dosage, and identify possible adverse effects and safety risks.
- *Phase 3* trials, also called pivotal studies, major studies or advanced clinical trials, demonstrate clinical efficacy and safety in a larger number of patients, typically at geographically diverse clinical study sites, and permit the FDA to evaluate the overall benefit-risk relationship of the drug and provide adequate information for drug labeling.
- *Phase 4* studies are often conducted following marketing approval, in order to meet regulatory requirements or to provide additional data related to drug use.

FDA Approval Process

After successful completion of the required clinical testing, an NDA is typically submitted to the FDA in the United States, and a marketing authorization application is typically submitted to the EMA in the EU. FDA approval of the NDA is required before the product may be marketed in the United States. The NDA must include the results of all preclinical, clinical, and other testing and a compilation of data related to the product's pharmacology, chemistry, manufacture, and controls.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing. If the FDA determines that the application is not sufficiently complete to permit substantive review, it may request additional information and decline to accept the application for filing until the information is provided. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most applications for non-priority drugs are reviewed within ten to twelve months. Special pathways, including "accelerated approval," "fast track" status, "breakthrough therapy" status, and "priority review" status are granted for certain drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. These special pathways can significantly reduce the time it takes for the FDA to review an NDA, but do not guarantee that a product will receive FDA approval. In May 2018, the Right to Try Act established a new regulatory pathway to increase access to unapproved, investigational treatments for patients diagnosed with life-threatening diseases or conditions who have exhausted approved treatment options and who are unable to participate in a clinical trial. The Food and Drug Omnibus Reform Act (**FDORA**), which was passed as part of the Consolidated Appropriations Act, 2023, expands the FDA's authority in regulating accelerated approval requirements for drugs and biologics, including allowing the FDA to require initiation of a post-approval study before granting accelerated approval and to expedite withdrawal of approval if conditions are not satisfied.

The FDA may refer applications for novel pharmaceutical products or pharmaceutical products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. During the review process, the FDA also reviews the drug's product labeling to ensure that appropriate information is communicated to health care professionals and consumers. In

addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and the facility or the facilities at which the drug is manufactured to ensure they are in compliance with the FDA's current Good Manufacturing Practices (cGMP).

After the FDA evaluates the NDA and the manufacturing facilities, the FDA may issue either an approval letter or a complete response letter, which generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those conditions have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even after a resubmission, the FDA may decide that the application does not satisfy the regulatory criteria for approval.

Post-Approval Regulatory Requirements

Once an NDA is approved, the product is subject to continuing regulation. For instance, pharmaceutical products may be marketed only for their approved indications and in accordance with the provisions of their approved labeling. The FDA closely regulates the post-approval marketing, labeling, and advertising of prescription drugs, including direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the Internet.

Adverse event reporting and submission of periodic reports continue to be required following FDA approval of an NDA. In addition, as a condition of NDA approval, the FDA may require post-marketing testing, including phase 4 clinical studies, and/or a risk evaluation and mitigation strategy (REMS) to help ensure that the benefits of the drug outweigh the potential risks. A REMS can include medication guides, communication plans for healthcare professionals, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. Additionally, quality control as well as drug manufacture, packaging, and labeling procedures must continue to conform to cGMP requirements. Manufacturing facilities are subject to continual review and periodic inspections by the FDA and certain state agencies.

Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards or if previously unrecognized problems are subsequently discovered. Discovery of previously unknown problems with a product, including adverse events or problems with manufacturing processes of unanticipated severity or frequency, or failure to comply with regulatory requirements, may also result in (1) revisions to the approved labeling; (2) imposition of post-market studies or clinical trials to assess new safety risks; or (3) imposition of distribution or other restrictions under a REMS program. Other potential consequences include: (1) restrictions on the marketing or manufacturing of the product; (2) fines, warning letters, or holds on post-approval clinical trials; (3) refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals; (4) product seizure or detention, or refusal to permit the import or export of products; or (5) injunctions or the imposition of civil or criminal penalties.

Approval of Changes to an Approved Product

Certain changes to the conditions established in an approved application, including changes in indications, labeling, equipment, or manufacturing processes or facilities, require submission and FDA approval of an NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing supplements as it does in reviewing NDAs.

Orphan Drugs

Under the Orphan Drug Act, an applicant can request the FDA to designate a product as an "orphan drug" in the United States if the drug is intended to treat a rare disease or condition affecting fewer than 200,000 people in the United States, or for which there is no reasonable expectation that U.S. sales will be sufficient to recoup the development and production costs. Orphan drug designation must be requested before submitting an NDA or BLA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA or BLA applicant to receive orphan drug designation and FDA approval for a particular active ingredient to treat a particular disease via a particular delivery method is entitled to a seven-year exclusive marketing period in the United States. During the seven-year period, the FDA may not approve any other application to market the same drug for the same disease, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity, meaning that it has greater effectiveness or safety, or provides a major contribution to patient care (such as a change in delivery system). The FDA's interpretation of the scope of orphan drug exclusivity remains the subject of scrutiny. Historically, exclusivity was specific to the orphan indication for which the drug was actually approved. As a result, the scope of exclusivity was interpreted as preventing approval of a competing product. However, in September 2021, the federal court in *Catalyst Pharmaceuticals, Inc. v. Becerra*, suggested that orphan drug exclusivity covers the full scope of the orphan-designated "disease or condition" regardless of whether a drug obtained approval for a narrower use. In January 2023, the FDA clarified in a Federal Register notice that it intends to continue limiting exclusivity to the specific orphan indication. The reach and impact of this decision beyond the Eleventh Circuit is not yet known. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. The 21st Century Cures Act (**Cures Act**), which became law in December 2016, expanded the types of studies that qualify for orphan drug grants. Orphan drug designation also may qualify an applicant for federal tax credits related to research and development costs.

Patent Term and Regulatory Exclusivity

In 1984, the Hatch-Waxman Act created a faster approval process for generic drugs, called the ANDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strength(s), route of administration, and dosage form as an approved drug and has been shown through bioequivalence testing to be therapeutically equivalent to the approved drug, which is known as the reference listed drug (**RLD**). ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as “generic equivalents” to the approved drug, and can often be substituted by pharmacists under prescriptions written for the original approved drug. In 2018, the FDA advanced policies aimed at promoting drug competition and patient access to generic drugs, such as issuing guidance about making complex generic drugs and the circumstances in which approval of a generic product application may be delayed.

NDA applicants are required to identify each patent with claims that cover the drug (drug substance or drug product) or FDA-approved method of using the drug. Upon product approval, these patents are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Every ANDA applicant must make one of several certifications to the FDA with regard to each Orange Book listed patent for the RLD. A Paragraph III certification states that the ANDA applicant seeks approval after the patent expires. A Paragraph IV certification asserts that the patent does not block approval of the ANDA, either because the patent is invalid or unenforceable or because the patent, even if valid, is not infringed by the new product. If the applicant does not challenge the listed patents, the ANDA will not be approved until all the listed patents claiming the referenced product have expired. Alternatively, for a method of use patent covering an approved indication, an ANDA applicant may submit a statement to the FDA that the company is not seeking approval for the covered indication. As a practical matter, this is available only if the RLD is approved for multiple indications, at least one of which is not patent protected.

If the ANDA applicant has submitted a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The Hatch-Waxman Act also provides that patent terms may be extended to compensate for some of the patent life that is lost during the FDA regulatory review period for a product. This extension period is generally one-half of the time between the effective date of an IND and the submission date of an NDA, plus all of the time between the submission date of an NDA and its approval, subject to a maximum extension of five years, and the limitation that the patent term cannot be extended more than 14 years after approval. Generally, patent term extension is available if the product represents the first permitted commercial marketing of a drug containing the active ingredient. Similar patent term extensions are available under European laws.

An ANDA also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of an NDA for a new chemical entity, has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredient, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV certification, in which case the submission may be made four years following the original product approval. Following approval of an application to market a drug that contains previously approved active ingredients in a new dosage form, route of administration or combination, or for a new condition of use that was required to be supported by new clinical trials conducted by or for the sponsor, the FDC Act provides three years of exclusivity during which the FDA cannot grant effective approval of an ANDA for such new condition of use, dosage form, or strength that meets certain statutory requirements.

Section 505(b)(2) New Drug Applications

Most drug products (other than biological products) obtain FDA marketing approval pursuant to an NDA submitted under Section 505(b)(1) of the FDC Act, or an ANDA. A third alternative is a special type of NDA submitted under Section 505(b)(2) of the FDC Act, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the FDA's finding of safety and efficacy data for an existing product, or published literature, in support of its application.

Section 505(b)(2) NDAs may provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA in which the applicant relies, at least in part, on information from studies made to show whether a drug is safe or effective that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. A Section 505(b)(2) applicant may eliminate the need to conduct certain preclinical or clinical studies, if it can establish that reliance on studies conducted for a previously-approved product is scientifically appropriate. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication for which the Section 505(b)(2) NDA applicant has submitted data.

To the extent that the Section 505(b)(2) applicant relies on prior FDA findings of safety and efficacy, the applicant is required to certify to the FDA concerning any patents listed for the previously approved product in the Orange Book to the same extent that an ANDA applicant would. Thus, approval of a Section 505(b)(2) NDA can be delayed until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new active

ingredient, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Marketing Pharmaceutical Products Outside the United States

Outside of the United States, our ability to market our products is also contingent upon receiving marketing authorizations from regulatory authorities. The foreign regulatory approval process may include some or all of the risks associated with the FDA review and approval process set forth above, and the requirements governing the conduct of clinical trials and marketing authorization may vary widely from country to country.

Biologics

Biological products used for the prevention, treatment, or cure of a disease, or condition, of a human being are subject to regulation under the FDC Act and the PHSA. Biological products are approved for marketing via a BLA that follows an application process and carries approval requirements that are very similar to those for NDAs. To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there is a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction, or spread, of communicable diseases in the United States.

After a BLA is approved, the product may also be subject to official lot release, meaning the manufacturer must submit samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. As with drugs, after approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

The Biologics Price Competition and Innovation Act of 2009 (**BPCI Act**) created an abbreviated approval pathway for biological products shown to be "biosimilar" to an FDA-licensed reference biological product to minimize duplicative testing. Biosimilarity requires the absence of clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, which, absent a waiver, must be shown through analytical studies, animal studies, and at least one clinical study. Intricacies associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation that are still being addressed by the FDA. In July 2018, the FDA announced an action plan to encourage the development and efficient review of biosimilars, including the establishment of a new office within the agency that will focus on therapeutic biologics and biosimilars. On December 20, 2020, Congress amended the Public Health Services Act as part of the COVID-19 relief bill to further simplify the biosimilar review process by making it optional to show that conditions of use proposed in labelling have been previously approved for the reference product, which used to be a requirement of the application. In September 2021, the FDA issued two guidance documents, one final and one draft, intended to inform prospective applicants and facilitate the development of proposed biosimilars and interchangeable biosimilars, as well as to describe the FDA's interpretation of certain statutory requirements added by the BPCIA.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is approved as a biosimilar and also meets additional standards for interchangeability with the reference product, has exclusivity against other biologics submitted under the abbreviated approval pathway for a set period. Effective March 2020, certain products that were approved as drugs under the FDC Act, such as insulin and human growth hormone, are now deemed to be biologics under the PHSA, which means they may face competition through the biosimilars pathway and they may not be eligible for the twelve-year period of exclusivity granted to new BLAs. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries. FDORA now provides for multiple first interchangeable biosimilars to qualify for exclusivity if they are approved on the same day.

Cell-Based and Tissue-Based Products

Manufacturers of cell- and tissue-based products must comply with the FDA's current good tissue practices (**cGTP**), which are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of such products. The primary intent of the cGTP requirements is to ensure that cell- and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable diseases. Cell and tissue-based products may also be subject to the same approval standards, including demonstration of safety and efficacy, as other biologic and drug products, if they meet certain criteria such as if the cells or tissues are more than minimally manipulated or if they are intended for a non-homologous use (a use different from the cell's origin).

The Cures Act established a new FDA Office of Tissues and Advanced Therapies and Regenerative Advanced Therapy (**RAT**) designation, which makes a product eligible for FDA priority review and accelerated approval. Therapies that are eligible for RAT designation include cell therapies, therapeutic tissue engineering products, human cell and tissue products, or any combination product using these therapies, with certain exceptions. For RAT designation, the product also must be intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and the preliminary clinical evidence must indicate that the product has the potential to address unmet medical needs for the disease or condition.

Regulation of Medical Devices

We currently do not hold any stand-alone medical device authorizations, but we do hold FDA authorization for the Tyvaso Inhalation System and the Dreamboat inhaler as part of the drug-device combination NDAs for Tyvaso and Tyvaso DPI, respectively. In addition, our business partners have the medical device clearances required to deliver our drugs, including, for example, the Remunity Pump. Medical devices may also be subject to FDA approval and extensive regulation under the FDC Act. Medical devices are classified into one of three classes: Class I, Class II, or Class III. A higher class indicates a greater degree of risk associated with the device and a greater amount of control needed to ensure safety and effectiveness.

All devices, unless exempt by FDA regulation, must adhere to a set of general controls, including compliance with the applicable portions of the FDA's Quality System Regulation (**QSR**), which sets forth good manufacturing practice requirements; facility registration and product listing; reporting of adverse medical events; truthful and non-misleading labeling; and promotion of the device consistent with its cleared or approved intended uses. Class II and III devices are subject to additional special controls and may require FDA clearance of a premarket notification (**510(k)**) or approval of a premarket approval application (**PMA**).

Most Class I devices are exempt from FDA premarket review or approval. Class II devices, with some exceptions, must be "cleared" by the FDA through the 510(k) process, which requires a company to show that the device is "substantially equivalent" to certain "predicate" devices already on the market. To be substantially equivalent, the proposed device must have the same intended use as the predicate device, and either have the same technological characteristics as the predicate device or have different technological characteristics and not raise different questions of safety or effectiveness than the predicate device. Once a 510(k) is cleared, any change that could significantly affect the safety or effectiveness of the device requires the submission and clearance of a new 510(k) before the change can be implemented. In November 2018, the FDA announced plans to significantly revise the 510(k) program to encourage reliance on modern predicates (e.g., predicates that are less than 10 years old). In January 2019, the FDA also finalized guidance on the alternative 510(k) pathway for well-known device types, the "Safety and Performance Based Pathway," which relies on modern performance-based criteria and current technological principles to demonstrate substantial equivalence.

Devices deemed by the FDA to pose the greatest risks, such as life-sustaining, life-supporting, or some implantable devices, or devices that have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally-marketed device, are placed in Class III, requiring approval of a PMA application. A PMA generally requires data from clinical trials that establish the safety and effectiveness of the device. Once approved, certain changes, such as changes to manufacturing facilities, methods, or quality control procedures, or changes in the design specifications, which affect the safety or effectiveness of the device, require the submission of a PMA Supplement. Some "pre-amendment" devices (devices that were legally marketed prior to May 28, 1976) are unclassified, but are subject to FDA's premarket notification and clearance process in order to be commercially distributed. A 510(k) application also sometimes requires clinical data.

The FDA also allows the submission of a direct *de novo* petition. This procedure allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents low or moderate risk, rather than requiring the submission and approval of a PMA. Prior to the enactment of the Food and Drug Administration Safety and Innovation Act of 2012 (**FDASIA**), a medical device could only be eligible for *de novo* classification if the manufacturer first submitted a 510(k) premarket notification and received a determination from the FDA that the device was not substantially equivalent. FDASIA streamlined the *de novo* classification pathway by permitting manufacturers to request *de novo* classification directly without first submitting a 510(k) premarket notification to the FDA and receiving a not substantially equivalent determination.

The 510(k), *de novo*, and PMA processes can be expensive, lengthy, and unpredictable. The FDA's 510(k) clearance process usually takes from three to 12 months, but can last longer. The process of obtaining a PMA approval is much more costly and uncertain than the 510(k) clearance process and generally takes from one to three years, or even longer, from the time the application is filed with the FDA. In addition, a PMA approval generally requires the performance of one or more clinical trials. Despite the time, effort, and cost invested by a sponsor, a device may not be approved or cleared by the FDA. The Cures Act requires the FDA to establish a program that would expedite access to devices that provide more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, for which no approved or cleared treatment exists or which offer significant advantages over existing approved or cleared alternatives. In December 2018, the FDA published final guidance on this "breakthrough" devices pathway which allows for sponsors to interact directly with the FDA during the development process and to receive prioritized review of their submission. In January 2021, the FDA released final guidance on the Safer Technologies Program (**STeP**), to encourage the innovation and market entry of device technologies that are safer than current alternatives but that do not otherwise satisfy the breakthrough device criteria, including device technologies to treat non-life-threatening or reasonably reversible conditions. STeP is modeled after the breakthrough device program and is intended to provide similar benefits, including increased communication with the FDA and prioritized review. In October 2022, the FDA issued

a draft guidance entitled “Select Updates for the Breakthrough Devices Program Guidance: Reducing Disparities in Health and Health Care.” The draft guidance clarifies how the Breakthrough Device Program may apply to certain medical devices that provide more effective treatment or diagnosis methods for life-threatening or irreversibly debilitating diseases or conditions in groups with health or health care disparities.

Clinical trials for medical devices are subject to similar requirements as clinical trials with respect to drugs or biologics. Clinical trials involving significant risk devices (e.g., devices that present a potential for serious risk to the health, safety, or welfare of human subjects) are required to obtain both FDA approval of an investigational device exemption (IDE) application and IRB approval before study initiation. Clinical trials involving non-significant risk devices are not required to submit an IDE for FDA approval but must obtain IRB approval before study initiation. During a study, the sponsor is required to comply with the applicable FDA requirements, including, for example, trial monitoring, selecting clinical investigators and providing them with the investigational plan, ensuring IRB review, adverse event reporting, record keeping requirements, and prohibitions on the promotion of investigational devices or on making safety or effectiveness claims about them. The clinical investigators in the clinical study are also subject to FDA regulations and must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of the investigational device, and comply with all reporting and recordkeeping requirements. Additionally, after a trial begins, the sponsor, the FDA, or the IRB could suspend or terminate a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits.

After a device is cleared or approved for marketing, numerous and pervasive regulatory requirements continue to apply. These include:

- establishment registration and device listing with the FDA;
- QSR requirements, which require manufacturers, including third-party manufacturers, to follow stringent design, testing, control, documentation, and other quality assurance procedures during all aspects of the design and manufacturing process;
- labeling regulations and FDA prohibitions against the promotion of investigational products, or the promotion of “off-label” uses of cleared or approved products;
- requirements related to promotional activities;
- clearance or approval of product modifications to 510(k)-cleared devices that could significantly affect safety or effectiveness or that could constitute a major change in intended use of one of our cleared devices, or approval of certain modifications to PMA-approved devices;
- medical device reporting regulations, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur;
- correction, removal, and recall reporting regulations, which require that manufacturers report to the FDA field corrections and product recalls or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FDCA that may present a risk to health;
- the FDA’s recall authority, whereby the agency can order device manufacturers to recall from the market a product that is in violation of governing laws and regulations; and
- post-market surveillance activities and regulations, which apply when deemed by the FDA to be necessary to protect the public health or to provide additional safety and effectiveness data for the device.

The FDA has broad regulatory and enforcement powers with respect to medical devices, similar to those for drugs and biologics. The regulations are complex and have tended to become more stringent over time. Regulatory changes could result in additional restrictions or requirements. The FDA enforces these regulatory requirements through, among other means, periodic unannounced inspections. FDORA gives the FDA authority to request medical device facility records in advance of, or in lieu of, inspections. Any failure to comply with applicable regulatory requirements could result in enforcement action by the FDA, which may include any of the following sanctions:

- adverse publicity, warning letters, untitled letters, it has come to our attention letters, fines, injunctions, consent decrees, and civil penalties;
- repair, replacement, refunds, recall, or seizure of products;
- operating restrictions, partial suspension, or total shutdown of production;
- denial of requests for regulatory clearance or PMA approval of new products or services, new intended uses, or modifications to existing products or services;
- withdrawal of regulatory clearance or PMA approvals that have already been granted; or
- criminal prosecution.

States also impose regulatory requirements on medical device manufacturers and distributors. The FDA also administers certain controls over the import and export of medical devices to and from the United States. Additionally, each foreign country subjects medical devices to its own regulatory requirements. States also impose regulatory requirements on medical device manufacturers and distributors. Failure to comply with the applicable federal or state requirements could result in, among other things: (1) fines, injunctions, and civil penalties; (2) recall or seizure of products; (3) operating restrictions, partial suspension, or

total shutdown of manufacturing; (4) refusing requests for approval of new products; (5) withdrawing approvals already granted; and (6) criminal prosecution.

The FDA also administers certain controls over the import and export of medical devices to and from the United States. Additionally, each foreign country subjects medical devices to its own regulatory requirements. In the EU, there is no authorization process for medical devices. Medical devices are CE marked and placed on the market in the EU at the discretion and on the liability of their manufacturer following a conformity assessment process that may include the participation of a notified body.

Combination Products

A combination product is a product composed of a combination of two or more FDA-regulated product components or products, e.g., drug-device or device-biologic. A combination product can take a variety of forms, such as a single entity made by physically or chemically combining components, or a single unit made of separately packaged products. Each combination product is assigned a lead FDA Center, which has jurisdiction for the premarket review and regulation, based on which constituent part of the combination product provides the primary mode of action, i.e., the mode of action expected to make the greatest contribution to the overall intended therapeutic effect of the product. If the classification as a combination product or the lead Center assignment is unclear or in dispute, a sponsor may request a meeting, submit a Request for Designation (**RFD**), and the FDA will issue a designation letter within 60 calendar days of the filing of the RFD. Depending on the type of combination product, the FDA may require a single application for approval, clearance, or licensure of the combination product, or separate applications for the constituent parts. During the review of marketing applications, the lead Center may consult or collaborate with other FDA Centers. In 2017, the FDA released final documents addressing the application of cGMP requirements and classification issues related to combination products.

The Cures Act sets forth a number of provisions pertaining to combination products, such as procedures for negotiating disagreements between sponsors and the FDA and requirements intended to streamline FDA premarket reviews of combination products that contain an already-approved component. For drug-device combination products, comprised of an FDA-approved drug and device primary mode of action, the Cures Act applies Hatch Waxman requirements to the premarket review process such that a patent dispute regarding the listed drug may result in the delay of the 510(k) clearance or PMA approval of the combination product. Furthermore, the Cures Act applies exclusivity provisions (e.g., new chemical entity and orphan drug exclusivities) to the device clearance and approval process for combination products with a device primary mode of action.

Government Reimbursement of Pharmaceutical Products

In the United States, many independent third-party health plans, and government health care programs, such as Medicaid and Medicare, pay for patient use of our commercial products. A material portion of our product sales are reimbursed under these government programs. The availability of adequate government reimbursement for our products is subject to regulatory changes and controls affecting these programs.

Medicaid is a joint federal and state program that is administered by the states for low-income and disabled beneficiaries. We participate in the Medicaid Drug Rebate program, pursuant to which, as a condition of having federal funds made available for our drugs under Medicaid and Medicare Part B, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are reimbursed by Medicaid. Medicaid rebates are based on pricing data we report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services (**CMS**), the federal agency that administers the Medicaid and Medicare programs. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all applicable sales and associated rebates, discounts, and other price concessions. If we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data to CMS for up to three years after those data originally were due.

Medicare is a federal program that is administered by the federal government that provides covered health care benefits to individuals age 65 or over and to certain disabled and chronically ill persons. We are required to provide average sales price (**ASP**) information for certain of our products to CMS on a quarterly basis. The ASP we report must be calculated based on a statutorily-defined formula as well as regulations and interpretations of the statute by CMS. The ASP information is used by CMS to compute Medicare reimbursement rates for our drugs that are covered by Medicare Part B, which covers physician-administered drugs, physician services, and outpatient care. Medicare Part A covers inpatient hospital benefits, while Medicare Part D is a voluntary outpatient prescription drug benefit to Medicare beneficiaries.

Our drugs are covered under these various programs:

- Unituxin is administered entirely as an in-patient therapy and would typically be reimbursed under Medicare Part A. However, because Unituxin is indicated for the treatment of a pediatric cancer, Medicare is unlikely to cover treatment, but Medicaid may cover pediatric patients requiring care.
- Remodulin and nebulized Tyvaso are reimbursable under Medicare Part B. The Medicare Part B contractors who administer the program cover Remodulin and Tyvaso under local coverage determinations and provide reimbursement according to statutory guidelines.

- Tyvaso DPI, Orenitram, and Adcirca are reimbursed under Medicare Part D, and we pay rebates to Part D plans that cover these products.
- Medicaid also covers Remodulin, Tyvaso, Tyvaso DPI, Adcirca, Orenitram, and Unituxin, and, as noted above, we must pay Medicaid rebates on this utilization.

The Inflation Reduction Act of 2022 (**IRA**) will have significant impacts on prices and reimbursement rates, as discussed below under *U.S. Healthcare Reform*.

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

We are required to report our 340B ceiling prices to HRSA on a quarterly basis, which HRSA then publishes to 340B covered entities. HRSA has promulgated a regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. Moreover, HRSA established an administrative dispute resolution (**ADR**) process for claims by covered entities that a manufacturer engaged in overcharging, and by manufacturers that a 340B covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. An ADR proceeding could potentially subject us to discovery by covered entities and other onerous procedural requirements and could result in additional liability. Further, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities, expand manufacturer ceiling price obligations to so-called "contract pharmacies," or require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount could affect our 340B ceiling price calculations and negatively impact our results of operations.

In order to be eligible to have our products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we also participate in the U.S. Department of Veterans Affairs (**VA**) Federal Supply Schedule (**FSS**) pricing program. Under this program, we are obligated to make our products available for procurement under an FSS contract under which we must comply with standard government terms and conditions and charge a price to certain federal agencies that is no higher than the statutory federal ceiling price (**FCP**). The FCP is based on the non-federal average manufacturer price (**Non-FAMP**), which we calculate and report to the VA on a quarterly and annual basis. We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies, and the courts, which can change and evolve over time. CMS, the Department of Health & Human Services Office of Inspector General and other governmental agencies have pursued manufacturers that were alleged to have failed to report these data to the government in a timely or accurate 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 the Medicaid Drug Rebate program, the 340B program, the VA/FSS program, the Tricare Retail Pharmacy Program, and other governmental drug pricing programs will not be found to be incomplete or incorrect.

In addition, in the U.S., drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny, including with respect to companies that have increased the price of products after acquiring those products from other companies. There are numerous ongoing efforts at the federal and state level seeking to indirectly or directly regulate drug prices to reduce overall healthcare costs using tools such as price ceilings, value-based pricing, and increased transparency and disclosure obligations. Several states have passed or are considering legislation that requires or purports to require companies to report pricing information, including proprietary pricing information. For example, in 2017, California adopted a prescription drug price transparency state bill requiring advance notice of and an explanation for price increases of certain drugs that exceed a specified threshold. Similar bills have been introduced previously at the federal level and also enacted in other states, and additional legislation could be introduced in the future.

U.S. Healthcare Reform

Our industry is highly regulated and changes in law or government health care programs may adversely impact our business, operations, or financial results. 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 Patient Protection and Affordable Care Act (**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. Among other things, the PPACA establishes annual fees and taxes on manufacturers of certain branded prescription drugs. The PPACA is a broad measure intended to expand healthcare coverage within the United States, primarily through the imposition of health coverage-related mandates on employers and individuals and expansion of the Medicaid program. The PPACA and certain of its provisions have been subject to judicial challenges as well as efforts to repeal or replace them or to alter their interpretation or implementation.

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, 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. For that and other reasons, it is currently unclear how the IRA will be effectuated, and while the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant.

In addition, Congress has recently enacted other statutes that could adversely affect our ability to successfully commercialize our products. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate program rebates that manufacturers pay to state Medicaid programs will be eliminated, which could result in increased Medicaid rebate liability for us.

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.

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. More recently, the Biden administration has reaffirmed its aim to take further action with respect to the pharmaceutical industry, beyond implementation of the IRA.

Anti-Kickback, False Claims Laws, and The Prescription Drug Marketing Act

The federal Anti-Kickback Statute (**AKS**) prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of, or referring an individual for the furnishing of, any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted broadly to apply to arrangements between pharmaceutical manufacturers and prescribers, purchasers, formulary managers, and others. The term “remuneration” has been broadly interpreted to apply to anything of value including, for example, gifts, cash payments, donations, waivers of payment, ownership interests, and providing any item, service, or compensation for something other than fair market value. Liability under the AKS may be established without proving actual knowledge of the statute or specific intent to violate it. Although there are a number of statutory exceptions and regulatory safe harbors to the AKS protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors, and speakers, may be subject to scrutiny if they do not fit squarely within an exception or safe harbor. Moreover, some common practices do not have dedicated safe harbors. The regulatory safe harbors also are subject to regulatory revision and interpretation by a number of government agencies. Violations of the AKS are punishable by imprisonment, criminal fines, damages, civil monetary penalties, exclusion from participation in federal healthcare programs, and liability under the federal civil False Claims Act (**FCA**).

The FCA prohibits any person from, among other things, presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or making, or causing to be made, a false statement material to a false or fraudulent claim.

Actions under the FCA may be brought by the Attorney General or as a *qui tam* action by a private individual in the name of the government. Such private individuals may share in amounts paid by the defendant to the government in recovery or settlement. Many pharmaceutical and other healthcare companies have been prosecuted under the FCA for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates; allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product; violating the AKS; materially deviating from statutorily required manufacturing standards; and on the basis of allegations related to certain marketing practices, including off-label promotion. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per violation, as well as potential exclusion from participation in federal healthcare programs.

Many states also have statutes or regulations similar to the AKS and the FCA, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs; file periodic reports with the state, including reports on gifts and payments to individual health care providers; make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities; and/or register their sales representatives. Some states prohibit certain sales and marketing practices, including the provision of gifts, meals, or other items to health care providers, and still others prohibit offering co-pay support to patients for certain prescription drugs.

The federal Physician Payments Sunshine Act, implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers are also required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives.

We are also subject to numerous other anti-bribery and anti-fraud laws, including the U.S. Foreign Corrupt Practices Act, the UK Bribery Act, and the federal Civil Monetary Penalties Law.

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act (**PDMA**) imposes requirements and limitations upon the distribution of drugs and drug samples, and prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage and handling, as well as record keeping requirements for information regarding sample requests and distribution. The PDMA sets forth civil and criminal penalties for violations. In addition, PDMA requires manufacturers and distributors to submit similar drug sample information to the FDA.

Sanctions under these federal and state laws may include treble damages, civil penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines, and imprisonment.

Outside the U.S., interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct, and physicians' codes of professional conduct. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products, which is prohibited in the EU, is governed by the national anti-bribery laws of the EU member states. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states, or industry codes of conduct, require that payments made to physicians be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her competent professional organization, and/or the competent authorities of the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

21st Century Cures Act

The Cures Act, which was signed into law in 2016, contains a wide range of provisions designed to promote clinical research and streamline and expedite the FDA review and approval process. For example, the law clarifies the FDA's authority regarding drugs that target rare diseases, and broadens the type of data and information that may be used to support a drug or biologic application for a genetically targeted drug or variant protein targeted drug. The law requires the FDA to facilitate development programs for, and provides expedited review of, regenerative advanced therapies. The law further requires the FDA to establish a program to evaluate the use of real-world evidence, i.e., evidence from sources other than randomized clinical trials, to support the approval of certain drug and biological product applications and to satisfy post-approval requirements; in 2018, the FDA published a framework for evaluating real-world evidence. In 2019, the FDA announced numerous initiatives and guidance documents intended to improve and streamline the drug approval process. For example, the FDA's "Safety and Performance Based Pathway" final guidance described an optional premarket process for certain well-understood medical devices. Other key provisions related to orphan drugs, combination products, and medical devices, are discussed separately above.

State Pharmaceutical and Medical Device Marketing Laws

Several jurisdictions require pharmaceutical companies to report expenses related to the marketing and promotion of pharmaceutical products and to report gifts and payments to healthcare practitioners in those jurisdictions, or to obtain licenses for sales representatives and require them to satisfy educational and other requirements. Some of these jurisdictions also prohibit various marketing related activities. Still other states require the disclosure of information related to drug pricing and clinical studies and their outcomes. In addition, certain states require pharmaceutical companies to implement compliance programs or marketing codes and several other states are considering similar proposals. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties or other civil enforcement action.

Privacy Laws

We must comply with numerous federal, state, and non-U.S. laws that govern the privacy and security of health and other personal information. In the U.S., numerous federal and state laws and regulations govern the collection, use, disclosure, and protection of health related and other personal information. Many of these laws differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Compliance with these laws is difficult, constantly evolving, and time consuming. Federal regulators, state attorneys general, and plaintiffs' attorneys, including class action attorneys, have been and will likely continue to be active in this space.

The Health Insurance Portability and Accountability Act of 1996 (**HIPAA**) imposes privacy, security, and breach reporting obligations, including mandatory contractual terms, with respect to safeguarding the privacy and security of individually-identifiable health information upon covered entities subject to the rule. Although we are not directly subject to HIPAA—other than with respect to providing certain employee benefits—we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually-identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA. We also may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA.

In addition, we are required to comply with the California Consumer Privacy Act (**CCPA**). The CCPA became effective in 2020 and establishes certain requirements for data use and sharing transparency, and provides California residents certain rights concerning the use, disclosure, and retention of their personal data. The CCPA and its implementing regulations have already been amended multiple times since their enactment. Similarly, there are a number of legislative proposals in the United States, at both the federal and state level, that could impose new obligations or limitations in areas affecting our business. These laws and regulations are evolving and subject to interpretation, and may impose limitations on our activities or otherwise adversely affect our business. The obligations to comply with the CCPA and evolving legislation require us, among other things, to update our notices and develop new processes internally and with our partners. We may be subject to fines, penalties, or private actions in the event of non-compliance with these laws.

Outside the U.S., the legislative and regulatory landscape for privacy and data security continues to evolve. There has been increased attention to privacy and data security issues that could potentially affect our business, including the EU General Data Protection Regulation (**GDPR**), which became effective in 2018 and imposes potential penalties up to the greater of €20 million or four percent of annual global revenue for failure to comply with its requirements. In addition, the CCPA and laws and regulations enacted in the United States, Europe, Asia, and Latin America, increase potential enforcement and litigation activity.

In the event we enroll subjects in our ongoing or future clinical trials in the EU, we may be subject to additional privacy restrictions, including restrictions relating to the collection, use, storage, transfer, and other processing of personal data, including personal health data, regarding individuals in the European Economic Area (**EEA**) as governed by the GDPR. The GDPR imposes several requirements on companies that process personal data, strict rules on the transfer of personal data out of the EEA, including to the U.S., and fines and penalties for failure to comply with the requirements of the GDPR and the related national data protection laws of the EU member states. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. The obligations under the GDPR may be onerous and adversely affect our business, financial condition, results of operations, and prospects. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities. Further, the United Kingdom's exiting of the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

Because of the remote work policies we implemented due to the COVID-19 pandemic, information that is normally protected, including company confidential information, may be less secure. Cybersecurity and data security threats continue to evolve and raise the risk of an incident that could affect our operations or compromise our business information or sensitive personal information, including health data.

We may also need to collect more extensive health-related information from our employees to manage our workforce. If we or our third-party partners fail to comply or are alleged to have failed to comply with applicable data protection and privacy laws and regulations, and related employment rules, or if we were to experience a data breach involving personal information, we could be subject to government enforcement actions or private lawsuits.

In addition, our business could be adversely impacted if our ability to transfer personal data outside of the EEA or Switzerland is restricted, which could adversely impact our operating results.

Other Laws and Regulations

Numerous other statutory and regulatory regimes affect our business and operations. For example, our research and development efforts may be subject to laws, regulations, and recommendations related to safe working conditions, laboratory practices, use of animals in research and development activities, and the purchase, storage, movement, import, export, and use and disposal of hazardous or potentially hazardous substances. Antitrust and competition laws may restrict our ability to enter into certain agreements involving exclusive license rights. Future legislation and administrative action will continue to affect our business, the extent and degree of which we cannot accurately predict.

Environmental Matters

We are subject to a number of laws and regulations that require compliance with federal, state, and local regulations for the protection of the environment. We believe that our operations comply in all material respects with such applicable laws and regulations. Our compliance with these requirements did not change during the past year, and is not expected to have a material effect upon our capital expenditures, cash flows, earnings, or competitive position.

Human Capital

We are united by our commitment to developing innovative therapies for unmet needs and our dedication to be responsible citizens that have a positive impact on patients, the environment, and society. Our employees, whom we call “**Unitherians**,” are mission critical to these commitments because they share the same passion and dedication to meeting our purpose. As of December 31, 2022, we had approximately 985 employees working across our 10 facilities worldwide. None of our employees are covered by a collective bargaining agreement and we believe our overall relations with our employees are good.

Our people mission focuses on five key commitments, providing Unitherians with:

- Challenging, innovative work
- Opportunities for career advancement
- Autonomy to do their best work
- Inspiring work environment allowing for work/life integration
- Competitive pay and benefits

In 2022, we achieved approximately \$2.0 million in revenue per employee, which ranks near the top of our industry peer group. We feel strongly that such industry-leading productivity cannot be maintained without a core focus on our family of Unitherians, and a dedication to encouraging engagement, motivation, and focus on our goals and objectives. The Compensation Committee of our Board of Directors (**Board**) oversees our human capital management priorities, which are driven by the five key commitments noted above.

The “Unitherian” Culture. We are intentional in our effort to maintain our entrepreneurial culture. We believe this instills a greater sense of ownership, meaning, and commitment in Unitherians, motivating them to go above and beyond to achieve our ambitious goals. Moreover, we are confident that our culture provides us with a competitive advantage by enabling us to attract the best talent to drive innovation and excellence in pursuit of our key strategic objectives. United Therapeutics is proud to be an equal opportunity employer, and does not discriminate based on race, religion, national origin, gender, age, marital status, disability, pregnancy, sexual orientation, gender identity or expression, military and veteran status, or any other basis protected by applicable law. We have a policy that prohibits all forms of unlawful harassment and retaliation and provide training to all Unitherians on their responsibilities and protections under this policy.

PBC Conversion. In 2021, we converted United Therapeutics into a public benefit corporation, becoming the first company in our industry to do so. As a public benefit corporation, our Board is now obligated to balance the interests of its patient-focused public benefit purpose, the financial interests of shareholders, and the interests of other stakeholders who are materially impacted by our conduct, such as Unitherians. We believe that this conversion has helped further underscore our commitment to Unitherians, and well as our mission-driven public benefit purpose of creating a brighter future for patients.

Recruitment, Retention, and Talent Development. We strive to hire and retain exceptionally talented people who are passionately committed to our goals and who will thrive in our unique culture. We provide Unitherians with a variety of personal and professional development opportunities for them to grow and thrive. We believe that our recruitment, talent management, and talent development efforts are key factors in our low turnover compared to our industry peer group, which historically has trended well below the industry average. In 2022, we continued that trend with our voluntary turnover at 8.8 percent, well below industry average of 16.1 percent (based on June 1, 2021 through June 1, 2022 data from Aon/Radford's *Turnover Study for the Life Sciences/Biotech/Pharma Sector*, published December 2022).

Diversity, Equity, and Inclusion (DEI). We are proud of our diverse workforce, and we firmly believe that being a great place to work means being diverse and inclusive. Women represent 51 percent of all Unitherians and 36 percent of our workforce identify as members of a racial or ethnic minority. We foster diversity and inclusion in many different ways, including through support of Unitherian resource groups and through our Inclusion Advisory Group, which is chaired by our Chief People Officer and provides ongoing input to our DEI Executive Council on DEI strategies and initiatives. In 2022, we refreshed our core values, adding "Inclusive" as a core Unitherian value. We work to identify diverse and representative candidates for our open positions, and have enhanced our efforts by posting all open positions on targeted diversity recruitment sites. As part of our multi-year, company-wide training initiative to promote and enrich awareness of important DEI topics, we offered a number of focused training and development activities to Unitherians worldwide. In our annual DEI survey we saw year-over-year improvement in employee perception of the impact our DEI efforts have had on our culture and workplaces.

Employee Development and Engagement. We believe in the value of refresher training and continuous learning. Required training on our Code of Conduct and other content areas across our organization, support our commitment to quality and integrity. We also offer professional and leadership development training programs to help employees grow their careers. Our Education Assistance Program enables full-time employees to attend external courses that support business goals, add value to the organization, and correspond with the employees' own career development plans. In addition, we encourage Unitherians to provide input on our programs and speak up when they identify concerns, and we take action in response when appropriate. Our regular town hall meetings, which feature executive updates and patient-focused sessions, provide an avenue for Unitherians to connect with company management and the patient experience. Through Workplace by Facebook, we created an internal social environment to connect Unitherians across functions. We regularly conduct broad surveys to solicit the views of Unitherians, which give us insights that help us evolve our programming, monitor the quality of our initiatives, and measure engagement. The impacts of our efforts are evident in the results of a recent external engagement survey conducted by Great Place to Work, which showed that approximately 93 percent of respondents consider United Therapeutics "a great place to work."

Health and Safety. We are committed to providing and maintaining a safe, healthy, and secure workplace for all Unitherians. We have an environmental health and safety program. We routinely provide training on workplace safety and security to all Unitherians.

A Holistic Approach to Total Rewards and Employee Wellness. We require an exceptionally talented workforce. Because Unitherians are key to driving our strategic goals, we provide robust people programs that demonstrate the high value we place on the financial, mental, and physical wellness of Unitherians. Our comprehensive total rewards package includes a competitive base salary, short-term cash incentive compensation, stock awards, and an employee stock purchase plan, which encourages all of our full-time Unitherians to participate in our financial success. For example, all full-time domestic Unitherians are eligible to receive minimum annual compensation of \$75,000, including salary and bonus. We offer market-leading benefit programs, including a 401(k) savings plan with a company match, as well as health and welfare benefits such as flexible spending accounts, generous paid time off, parental bonding leave, employee assistance programs, flexible work arrangements, tuition assistance, and more. We offer competitive medical, dental, vision, and prescription coverage that is available to both part-time and full-time Unitherians. Our inspiring work environments include several employee-focused amenities, such as on-site cafeterias, childcare centers, and state-of-the-art fitness centers.

Board Oversight. Our Board, through its Compensation Committee, oversees our human capital management strategies, including our focus on DEI; workplace environment and culture; and talent development and retention. These topics are generally reviewed and discussed at meetings of both the Compensation Committee and of the full Board.

Corporate Website

Our Internet website address is <http://www.unither.com>. Our filings on Form 10-K, Form 10-Q, Form 3, Form 4, Form 5, Form 8-K, and any and all amendments thereto are available free of charge through this Internet website as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission (SEC). They are also available through the SEC at <http://www.sec.gov/edgar/searchedgar/companysearch.html>.

INFORMATION ABOUT OUR EXECUTIVE OFFICERS

The following is a list, as of February 22, 2023, setting forth certain information regarding our executive officers. Each executive officer holds office until the first meeting of the Board of Directors after the annual meeting of shareholders, and until his or her successor is elected and qualified or until his or her earlier resignation or removal. Each executive officer's employment will end pursuant to the terms of his or her employment contract.

Name	Age	Position
Martine Rothblatt, Ph.D., J.D., M.B.A.	68	Chairperson and Chief Executive Officer
Michael Benkowitz	51	President and Chief Operating Officer
James C. Edgemond	55	Chief Financial Officer and Treasurer
Paul A. Mahon, J.D.	59	Executive Vice President, General Counsel, and Corporate Secretary

Martine Rothblatt, Ph.D., J.D., M.B.A., founded United Therapeutics in 1996 and has served as Chairperson and Chief Executive Officer since its inception. Previously, she created the satellite radio company SiriusXM. She is an inventor or co-inventor on nine U.S. patents, with additional patents pending. Her pioneering book, *Your Life or Mine: How Geoethics Can Resolve the Conflict Between Private and Public Interests in Xenotransplantation*, anticipated the need for both global virus bio-surveillance and a greatly expanded supply of transplantable organs. Dr. Rothblatt has a Ph.D. in medical ethics from the University of London.

Michael Benkowitz joined United Therapeutics in 2011 as our Executive Vice President, Organizational Development, and was promoted to President and Chief Operating Officer in 2016. He is responsible for all of our commercial, medical affairs, and corporate compliance activities, most company-wide administrative functions, including human resources and information technology, many of our business development efforts, and several of our key business alliances and partnerships.

James C. Edgemond joined United Therapeutics in January 2013 as Treasurer and Vice President, Strategic Financial Planning. Mr. Edgemond was promoted to Chief Financial Officer and Treasurer in March 2015. Prior to joining United Therapeutics, he was Vice President, Corporate Controller, and Treasurer of Clark Construction Group from 2008 through January 2013. He also served in a variety of roles at The Corporate Executive Board Company from 1998 to 2008, serving as Executive Director, Finance from 2005 to 2008. He began his career as a public accountant at KPMG Peat Marwick LLP, from 1990 through 1998, where he served in a variety of roles, including as a Senior Manager prior to his departure.

Paul A. Mahon, J.D., has served as General Counsel and Corporate Secretary of United Therapeutics since its inception in 1996. In 2001, Mr. Mahon joined United Therapeutics full-time as Senior Vice President, General Counsel, and Corporate Secretary. In 2003, Mr. Mahon was promoted to Executive Vice President, General Counsel, and Corporate Secretary. Prior to 2001, he served United Therapeutics, beginning with its formation in 1996, in his capacity as principal and managing partner of a law firm specializing in technology and media law.

Item 1A. Risk Factors

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, 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. 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) 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 ineffective, or physicians and/or patients believe that the drug is ineffective, or that other therapies are more effective or convenient; (3) patients do not enroll in or complete clinical trials at the rate we expect; (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 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 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 if successful would compete with our treprostinil-based products.

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 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.

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 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, 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 Addicra revenues and which may materially impact our Remodulin revenues. 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 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 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 Remodulin and Tyvaso. We 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-party sole manufacturers for certain elements of our 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. 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 FDA's current good manufacturing practices regulations, 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 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.
- 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 FDA and other 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.

- 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 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 be sold.
- Our business partners who manufacture the devices to deliver our products are subject to the FDA's medical device requirements. 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, 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 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 product 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 in Ukraine. Although we do not directly source any raw materials or consumables from Ukraine, Russia, or Belarus, our European-based suppliers and service providers could be impacted by an extended conflict or an escalation of the conflict into neighboring countries.

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.

We rely in part on third parties to perform activities that are critical to our business.

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 drug safety, reporting adverse events, and handling product complaints; (5) obtaining medical device clearances and approvals for the devices used to deliver 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 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 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 discontinued manufacturing the MS-3 system used to deliver subcutaneous Remodulin, and specialty pharmacy distributors have informed us that supplies of MS-3 pumps are nearly exhausted. Smiths Medical has also announced plans to discontinue the CADD Legacy system used to deliver intravenous Remodulin. Historically, these are the pumps primarily used to deliver Remodulin to patients in the United States. In 2021, we launched the Remunity Pump to deliver subcutaneous Remodulin, and Smiths Medical plans to make an alternative pump, the CADD Solis, available for intravenous Remodulin. We are also engaged in further efforts to develop alternative pumps to deliver 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

Adcirca. We rely entirely on Minnetronix Inc. as the sole manufacturer of the Tyvaso Inhalation System. As Tyvaso is a drug-device combination, we cannot sell Tyvaso without the Tyvaso Inhalation System.

We rely entirely on MannKind to manufacture Tyvaso DPI for us. If MannKind is unable to manufacture Tyvaso DPI for us for any reason, our commercial sales of Tyvaso DPI would 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. 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 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. Development of new products, and 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. 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

manufacture, distribution, advertising, and marketing of our products are subject to extensive regulation, including 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 approval 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 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. Failure to follow FDA rules and guidelines related to promotion and advertising can result in the FDA's refusal to approve a product, suspension or withdrawal of an approved product from the market, product recalls, enforcement action, 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 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.

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.

Government healthcare reform and other reforms could adversely affect our revenue, costs, and results of 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,

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.

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. For that and other reasons, it is currently unclear how the IRA will be effectuated, and 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. We anticipate paying increased rebates for Part D 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 a 20 percent rebate 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 will have an industry-wide impact on the cost of Part D drugs, including Tyvaso DPI and Orenitram. This could be offset, to some degree or to a large degree, by an expansion in the number of patients able to afford these medicines, but these impacts are inherently uncertain and difficult to predict.

In addition, Congress has recently enacted other statutes that could adversely affect our ability to successfully commercialize our products. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate program rebates that manufacturers pay to state Medicaid programs will be eliminated, which 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. 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 regarding 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.

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. Additionally, we could be held liable for errors 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 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. 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.

Similar political, economic, and regulatory developments are occurring in other countries, including within the EU, and may affect the ability of pharmaceutical companies to profitably commercialize their products. In particular in the EU, and in addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase operating costs. The delivery of 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 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 June 23, 2021 in the U.S. District Court for the District of Columbia. On 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 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 been fully briefed, and we are awaiting the court's decision. If HRSA prevails on appeal or develops a new theory of liability, we may face enforcement action or penalties as well as adverse publicity. We expect the compliance of policies like ours will continue to be litigated.

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.

Patient assistance programs for pharmaceutical products have come under increasing scrutiny by governments, legislative bodies, and enforcement agencies. 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.

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 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 treatment of particular diseases); and

- 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. We entered into settlement agreements with a number of generic drug companies permitting certain companies to launch generic versions of Remodulin in the United States and other companies to launch generic versions of Orenitram and Tyvaso in the United States. A U.S. patent for Adcirca for 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*.

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.

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 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 technological advances that we do not publicly disclose. Our confidentiality agreements with our Unitherians 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 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 breaches and other disruptions could compromise our 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 of this information is critical to our operations and business strategy. We are

subject to laws and regulations in the United States and abroad, such as HIPAA and EU regulations related to data privacy, which require us to protect the privacy and security of certain types of information. Our information technology and infrastructure may be vulnerable to attacks by hackers, 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 such information to 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 operations, and damage to our reputation, any of which could adversely affect our business, financial condition, or results of operations. Costs we may incur as a result of any of the foregoing, could adversely affect our business, financial condition, or results of operations.

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. Currently, our outstanding principal balance is \$800.0 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, 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.

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:

- 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 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, 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 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.

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 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.

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.

Our bylaws provide that, to the fullest extent permitted by law, unless we agree in writing to an alternative forum, (a) 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, or stockholder in such capacity, or as to which the Delaware General Corporation Law confers jurisdiction upon the Court of Chancery, and (b) 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, 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.

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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Maryland—We own a 415,000 square foot combination laboratory and office building complex in Silver Spring, Maryland that serves as our co-headquarters, is used to manufacture our products, and houses one of our *ex vivo* lung perfusion centers. These manufacturing activities include the synthesis of treprostinil, the active ingredient in Tyvaso, Tyvaso DPI, and Remodulin, and treprostinil diolamine, the active ingredient in Orenitram, as well as dinutuximab, the active ingredient in Unituxin. We also manufacture Tyvaso, Remodulin, and Unituxin drug product in our Silver Spring complex. In 2019, we completed construction of a new cell culture and purification facility. In early 2021, we decided to repurpose this facility to produce manufactured lungs for clinical studies.

North Carolina—We own a 380,000 square foot combination manufacturing facility and office building in Research Triangle Park, North Carolina (**RTP facility**), which serves as our co-headquarters and is occupied by our clinical research and development, commercialization, and our logistics and manufacturing personnel. We manufacture Orenitram drug product and we package, warehouse, and distribute Tyvaso, Remodulin, Orenitram, and Unituxin at this location. We also own a 170-acre site containing approximately 217,000 square feet of building space adjacent to our RTP facility, which we use for our research, development, and manufacturing facilities related to our lung regeneration program, office space, and for future expansion.

We believe that these facilities, along with various other owned and leased facilities, are adequate for our current operations and that additional land and facilities for future expansion are reasonably available.

Item 3. Legal Proceedings

Currently, and from time to time, we are subject to claims in legal proceedings arising in the normal course of business. While we presently believe that the ultimate outcome of these proceedings, individually and in the aggregate, will not materially harm our financial position, cash flows or results of operations, legal proceedings are inherently uncertain, and unfavorable rulings could, individually or in aggregate, have a material adverse effect on our business, financial condition, or operating results. Please refer to Note 14—*Litigation*, to our consolidated financial statements, which is incorporated herein by reference.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock trades on the Nasdaq Global Select Market under the symbol “UTHR”.

Number of Holders

As of February 15, 2023, there were 32 holders of record of our common stock.

Dividend Policy

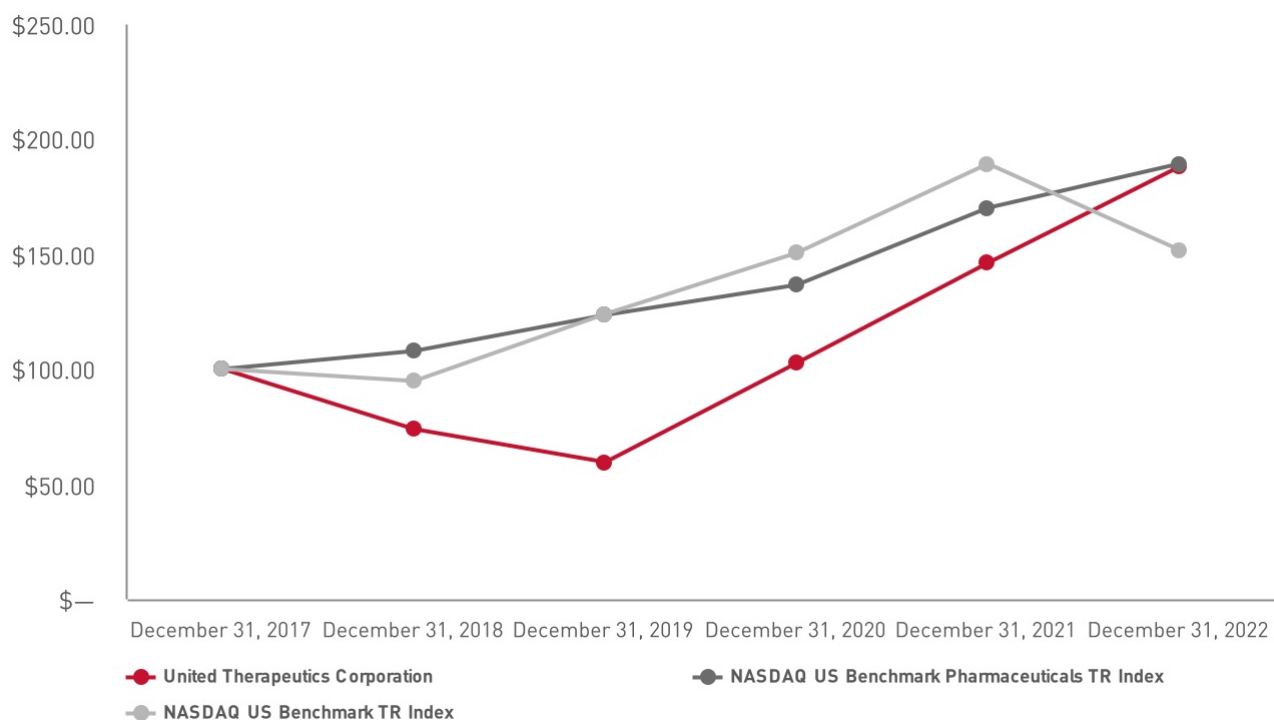
We have never paid and have no present intention to pay cash dividends on our common stock in the foreseeable future, and our 2022 Credit Agreement contains covenants that may restrict us from doing so. We intend to retain any earnings for use in our business operations.

Issuer Purchases of Equity Securities

We did not repurchase any of our outstanding equity securities during the year ended December 31, 2022.

Comparison of Five-Year Total Cumulative Shareholder Return

The following chart shows the performance from December 31, 2017 through December 31, 2022 of our common stock, compared with an investment in the stocks represented in each of the Nasdaq U.S. Benchmark TR Index and the Nasdaq U.S. Benchmark Pharmaceuticals TR Index, assuming the investment of \$100 at the beginning of the period and the reinvestment of dividends, if any.



Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion should be read in conjunction with our consolidated financial statements and related notes to our consolidated financial statements. All statements in this filing are made as of the date this Report is filed with the U.S. Securities and Exchange Commission (**SEC**). We undertake no obligation to publicly update or revise these statements, whether as a result of new information, future events or otherwise.

The following Management's Discussion and Analysis of Financial Condition and Results of Operations and other sections of this Report contain forward-looking statements made pursuant to the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These statements, which are based on our beliefs and expectations about future outcomes and on information available to us through the date this Report on Form 10-K is filed with the SEC, include, among others, statements related to the following:

- Expectations of revenues, expenses, profitability, cash flows, and growth in the number of patients being treated with our products, including anticipated growth in the number of Tyvaso patients as a result of the expansion of its label to include pulmonary hypertension associated with interstitial lung disease (**PH-ILD**) and anticipated growth in revenues following the recent commercial launch of Tyvaso DPI;
- The sufficiency of our cash on hand to support operations;
- Our ability to obtain financing on terms favorable to us or at all;
- Our ability to obtain and maintain domestic and international regulatory approvals;
- Our ability to maintain attractive pricing and reimbursement levels for our products, in light of increasing competition, including from generic products, pressure from government and other payers to decrease the costs associated with healthcare, including the potential impact of the Inflation Reduction Act of 2022 (**IRA**) on our business;
- The expected volume and timing of sales of our commercial products, as well as potential future commercial products, including the anticipated effect of various research and development efforts on sales of these products;
- The timing and outcome of clinical studies, other research and development efforts, and related regulatory filings and approvals;
- The outcome of pending and potential future legal and regulatory actions by the U.S. Food and Drug Administration (**FDA**) and other regulatory and government enforcement agencies, and the anticipated duration of regulatory exclusivity for our products;
- The timing and outcome of ongoing litigation, including the lawsuit filed against us by Sandoz, Inc. and Liquidia PAH, LLC (formerly known as RareGen, LLC); our patent and trade secret litigation with Liquidia Technologies, Inc. (**Liquidia**) related to its new drug application (**NDA**) for Yutrepia; our litigation with Humana Inc., United Healthcare Services, Inc., MSP Recovery Claims, Series LLC, and related entities; and our litigation with the U.S. Department of Health and Human Services and the U.S. Health Resource Services Administration related to the Public Health Service's 340B drug pricing program;
- The impact of competing therapies on sales of our commercial products, including the impact of generic versions of Adcirca and Remodulin; established therapies such as Uptravi; and newly-developed therapies such as Merck's sotatercept and Liquidia's Yutrepia;
- The expectation that we will be able to manufacture sufficient quantities and maintain adequate inventories of our commercial products, through both our in-house manufacturing capabilities and third-party manufacturing sites, and our ability to obtain and maintain related approvals by the FDA and other regulatory agencies;
- The adequacy of our intellectual property protection and the validity and expiration dates of the patents we own or license, as well as the regulatory exclusivity periods for our products;
- The effect of our recent conversion to a Delaware public benefit corporation;
- Any statements that include the words "believe," "seek," "expect," "anticipate," "forecast," "project," "intend," "estimate," "should," "could," "may," "will," "plan," or similar expressions; and
- Other statements contained or incorporated by reference in this Report that are not historical facts.

We caution you that these statements are not guarantees of future performance and are subject to numerous evolving risks and uncertainties that we may not be able to accurately predict or assess, and that may cause our actual results to differ materially from anticipated results, including the risks and uncertainties we describe in *Part I, Item 1A—Risk Factors* of this Report and factors described in other cautionary statements, cautionary language, and risk factors set forth in our other filings with the SEC.

Overview of Marketed Products

We market and sell the following commercial products:

- **Tyvaso and Tyvaso DPI.** Tyvaso is an inhaled formulation of the prostacyclin analogue treprostinil, approved by the FDA and regulatory authorities in Argentina, Israel, and Japan to improve exercise ability in patients with pulmonary arterial hypertension (**PAH**). Tyvaso was also approved by the FDA in March 2021 and by regulators in Israel in December 2022 to improve exercise ability in patients with PH-ILD. In May 2022, we also obtained FDA approval of Tyvaso DPI to treat PAH and PH-ILD, and we initiated commercial shipments of Tyvaso DPI to our distributors in June 2022.
- **Remodulin**, a continuously-infused formulation of treprostinil, approved by the FDA for subcutaneous and intravenous administration to diminish symptoms associated with exercise in patients with PAH. Remodulin has also been approved in various countries outside of the United States. In February 2021, we launched U.S. sales of the Remunity Pump, a new subcutaneous delivery system for Remodulin.
- **Orenitram**, a tablet dosage form of treprostinil, approved by the FDA to delay disease progression and improve exercise capacity in PAH patients.
- **Unituxin**, a monoclonal antibody approved in the United States, Canada, and Japan for treatment of high-risk neuroblastoma.
- **Adcirca**, an oral PDE-5 inhibitor approved by the FDA to improve exercise ability in PAH patients.

For additional detail regarding our commercial products, see *Part I, Item 1—Business—Our Commercial Products*.

Research and Development

We are engaged in research and development of new indications and delivery devices for our existing products. We recently developed a new pump for Remodulin, called the Remunity Pump, and are currently developing a new version of the Remunity Pump. We are also working with a medical device manufacturer to develop new delivery systems for Remodulin. We are studying Tyvaso in patients with idiopathic pulmonary fibrosis (the *TETON* studies).

In addition, we are developing new products to treat PAH (RemoPro and ralinepag). We are also heavily engaged in early-stage research and development of a number of organ transplantation-related technologies including regenerative medicine, 3-D organ bioprinting, xenotransplantation, and *ex vivo* lung perfusion. For additional detail regarding our research and development programs, see *Part I, Item 1—Business—Research and Development*.

Revenues

Our total revenues consist primarily of sales of the commercial products noted above, together with associated sales of delivery devices (in the case of Remodulin, Tyvaso, and Tyvaso DPI). We have entered into separate, non-exclusive distribution agreements with Accredo Health Group, Inc. and its affiliates and Caremark, L.L.C. to distribute Tyvaso, Tyvaso DPI, Remodulin, the Remunity Pump, and Orenitram in the United States, and we have entered into an exclusive distribution agreement with ASD Specialty Healthcare, Inc., an affiliate of AmerisourceBergen Corporation, to distribute Unituxin in the United States. We also sell Tyvaso, Remodulin, and Unituxin to distributors internationally. We sell Adcirca through the pharmaceutical wholesale network of Eli Lilly and Company (**Lilly**). To the extent we have increased the price of any of these products, increases have typically been in the single-digit percentages per year, except for Adcirca, the price of which is set solely by Lilly.

We require our specialty pharmaceutical distributors to maintain reasonable levels of inventory reserves for our treprostinil-based therapies because the interruption of these therapies can be life threatening. Our specialty pharmaceutical distributors typically place monthly or semi-monthly orders based on current utilization trends and contractual minimum and maximum inventory requirements. As a result, sales of our treprostinil-based therapies can vary depending on the timing and magnitude of these orders and do not precisely reflect changes in patient demand.

Operating Expenses

We devote substantial resources to our various clinical trials and other research and development efforts, which are conducted both internally and through third parties. From time to time, we also license or acquire additional technologies and compounds to be incorporated into our development pipeline. Our operating expenses include the costs described below.

Cost of Sales

Our cost of sales primarily includes costs to manufacture our products, royalty and sales-based milestone payments under license agreements granting us rights to sell related products, direct and indirect distribution costs incurred in the sale of our products, and the costs of inventory reserves for current and projected obsolescence. These costs also include share-based

compensation and salary-related expenses for direct manufacturing and indirect support personnel, quality review and release for commercial distribution, direct materials and supplies, depreciation, facilities-related expenses, and other overhead costs.

Research and Development

Our research and development expenses primarily include costs associated with the research and development of products and post-marketing research commitments. These costs also include share-based compensation and salary-related expenses for research and development functions, professional fees for preclinical and clinical studies, costs associated with clinical manufacturing, facilities-related expenses, regulatory costs, and costs associated with payments to third-party contract manufacturers before FDA approval of the relevant product. Expenses also include costs for third-party arrangements, including upfront fees and milestone payments required under license arrangements for therapies under development. We do not track fully-burdened research and development expenses by individual product candidate.

Selling, General, and Administrative

Our selling, general, and administrative expenses primarily include costs associated with the commercialization of approved products and general and administrative costs to support our operations. Selling expenses also include share-based compensation, salary-related expenses, product marketing and sales operations costs, and other costs incurred to support our sales efforts. General and administrative expenses also include our core corporate support functions such as human resources, finance and legal, and external costs to support our core business such as insurance premiums, legal fees, and other professional service fees.

Share-Based Compensation

Historically, we granted stock options under our Amended and Restated Equity Incentive Plan and awards under our Share Tracking Awards Plan (the **STAP**). Issuance of awards under both of these plans was discontinued in 2015. Currently, we grant stock options and restricted stock units under the United Therapeutics Corporation Amended and Restated 2015 Stock Incentive Plan (as amended to date, the **2015 Plan**), which provides for the issuance of up to 11,500,000 shares of our common stock, including the 500,000 shares added pursuant to an amendment and restatement of the 2015 Plan approved by our shareholders in June 2022. In February 2019, our Board of Directors approved the 2019 Inducement Stock Incentive Plan (the **2019 Inducement Plan**), which provides for the issuance of up to 99,000 shares of our common stock pursuant to awards granted to newly-hired Unitherians. Currently, we grant equity-based awards to Unitherians and members of our Board of Directors in the form of stock options and restricted stock units under the 2015 Plan, and we may grant restricted stock units to newly-hired Unitherians under the 2019 Inducement Plan. The grant date fair values of stock options and restricted stock units are recognized as share-based compensation expense ratably over their vesting periods.

The fair value of STAP awards and stock options is measured using inputs and assumptions under the Black-Scholes-Merton model. The fair value of restricted stock units is measured using our stock price on the date of grant. Although we no longer grant STAP awards, we had approximately 0.6 million STAP awards outstanding as of December 31, 2022. We account for STAP awards as liabilities because they are settled in cash. As such, we must re-measure the fair value of STAP awards at the end of each financial reporting period until the awards are no longer outstanding. Changes in our liability associated with outstanding STAP awards as a result of such re-measurements are recorded as adjustments to share-based compensation expense (benefit) and can create substantial volatility within our operating expenses from period to period. The following factors, among others, have a significant impact on the amount of share-based compensation expense (benefit) recognized in connection with STAP awards from period to period: (1) volatility in the price of our common stock (specifically, increases in the price of our common stock will generally result in an increase in our liability and related compensation expense, while decreases in our stock price will generally result in a reduction in our liability and related compensation expense); and (2) decreases in the number of outstanding awards.

Future Prospects

We anticipate that overall revenue growth over the near-term will be driven primarily by: (1) growth in sales of Tyvaso as a result of the expansion of its label to include PH-ILD; (2) growth in sales of the newly-launched Tyvaso DPI; (3) continued growth in the number of patients prescribed Orenitram following our expansion of the Orenitram label to reflect the results of the *FREEDOM-EV* study; and (4) modest price increases for some of our products; partially offset by further generic erosion of Adcirca sales. We believe that additional revenue growth in the medium- and longer-term will be driven by new products and new indications for existing products being developed in our pipeline, as described above under *Part I, Item 1—Business—Research and Development*.

Our ability to achieve our objectives, grow our business, and maintain profitability will depend on many factors, including among others: (1) the timing and outcome of preclinical research, clinical trials, and regulatory approval applications for products we develop; (2) the timing and degree of our success in commercially launching new products; (3) the demand for our products; (4) the price of our products and the reimbursement of our products by public and private health insurance organizations, including the impact on such prices and reimbursement amounts as a result of the IRA; (5) the competition we face within our industry,

including competition from generic companies and new PAH therapies; (6) our ability to effectively manage our business in an increasingly complex legal and regulatory environment; (7) our ability to defend against challenges to our patents; and (8) the risks identified in *Part I, Item 1A—Risk Factors*, included in this Report.

We operate in a highly competitive market in which a small number of large pharmaceutical companies control a majority of available PAH therapies. These pharmaceutical companies are well established in the market and possess greater financial, technical, and marketing resources than we do. In addition, there are a number of investigational products in late-stage development that, if approved, may erode the market share of our existing commercial therapies and make market acceptance more difficult to achieve for any therapies we attempt to market in the future.

Results of Operations

This section of this Report generally discusses 2022, 2021, and 2020 items and year-to-year comparisons between 2022 and 2021. Discussions of year-to-year comparisons between 2021 and 2020 that are not included in this Report can be found in *Part II, Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations* of our Form 10-K filed on February 24, 2022 (our **2021 Annual Report**).

Revenues

The table below presents the components of total revenues (dollars in millions):

	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
Net product sales:							
Tyvaso ⁽¹⁾	\$ 873.0	\$ 607.5	\$ 483.3	\$ 265.5	\$ 124.2	44 %	26 %
Remodulin ⁽²⁾	500.2	513.7	516.7	(13.5)	(3.0)	(3)%	(1)%
Orenitram	325.1	306.1	293.1	19.0	13.0	6 %	4 %
Unituxin	182.9	202.3	122.9	(19.4)	79.4	(10)%	65 %
Adcirca	41.3	55.9	67.3	(14.6)	(11.4)	(26)%	(17)%
Other	13.8	—	—	13.8	—	NM ⁽³⁾	NM ⁽³⁾
Total revenues	\$ 1,936.3	\$ 1,685.5	\$ 1,483.3	\$ 250.8	\$ 202.2	15 %	14 %

(1) Net product sales include both the drug product and the respective inhalation devices for both Tyvaso and Tyvaso DPI.

(2) Net product sales include sales of infusion devices, such as the Remunity Pump.

(3) Calculation is not meaningful.

Net product sales from our treprostinil-based products (Tyvaso, Remodulin, and Orenitram) grew by \$271.0 million in 2022, as compared to 2021.

Tyvaso net product sales increased in 2022, as compared to 2021, primarily due to an increase in quantities sold and, to a lesser extent, the impact of a price increase and lower gross-to-net deductions. The increase in quantities sold was driven by the commercial launch of Tyvaso DPI in June 2022 and continued growth in the number of patients following the PH-ILD label expansion in March 2021.

Remodulin net product sales decreased in 2022, as compared to 2021, due to a \$15.9 million decrease in U.S. Remodulin net product sales, partially offset by a \$2.4 million increase in international Remodulin net product sales. The decrease in U.S. Remodulin net product sales was driven by a decrease in quantities sold, partially offset by lower gross-to-net deductions.

Orenitram net product sales increased in 2022, as compared to 2021, primarily due to a price increase and lower gross-to-net deductions.

Unituxin net product sales decreased in 2022, as compared to 2021, primarily due to a decrease in quantities sold, partially offset by a price increase.

Adcirca net product sales decreased in 2022, as compared to 2021, due to a decline in quantities sold as a result of generic competition for Adcirca and higher gross-to-net deductions.

Gross-to-Net Deductions

We recognize revenues net of: (1) rebates and chargebacks; (2) prompt pay discounts; (3) allowance for sales returns; and (4) distributor fees. These are referred to as gross-to-net deductions and are primarily based on estimates reflecting historical experiences as well as contractual and statutory requirements. We currently estimate our allowance for sales returns using reports from our distributors and available industry data, including our estimate of inventory remaining in the distribution channel. The tables below include a reconciliation of the liability accounts associated with these deductions (in millions):

	Year Ended December 31, 2022					Total
	Rebates & Chargebacks	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees		
Balance, January 1, 2022	\$ 67.8	\$ 3.8	\$ 6.3	\$ 7.9	\$	85.8
Provisions attributed to sales in:						
Current period	202.8	43.2	2.3	34.5		282.8
Prior periods	(4.3)	(0.5)	(3.1)	0.5		(7.4)
Payments or credits attributed to sales in:						
Current period	(121.1)	(38.9)	(0.7)	(23.6)		(184.3)
Prior periods	(63.9)	(3.2)	(1.5)	(8.4)		(77.0)
Balance, December 31, 2022	\$ 81.3	\$ 4.4	\$ 3.3	\$ 10.9	\$	99.9

	Year Ended December 31, 2021					Total
	Rebates & Chargebacks	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees		
Balance, January 1, 2021	\$ 65.3	\$ 3.0	\$ 12.5	\$ 3.7	\$	84.5
Provisions attributed to sales in:						
Current period	217.0	38.5	—	31.3		286.8
Prior periods	1.6	—	(3.9)	0.2		(2.1)
Payments or credits attributed to sales in:						
Current period	(151.8)	(34.7)	—	(22.4)		(208.9)
Prior periods	(64.3)	(3.0)	(2.3)	(4.9)		(74.5)
Balance, December 31, 2021	\$ 67.8	\$ 3.8	\$ 6.3	\$ 7.9	\$	85.8

	Year Ended December 31, 2020					Total
	Rebates & Chargebacks	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees		
Balance, January 1, 2020	\$ 51.7	\$ 2.6	\$ 14.2	\$ 4.1	\$	72.6
Provisions attributed to sales in:						
Current period	196.1	32.5	—	20.6		249.2
Prior periods	(0.2)	—	—	(0.3)		(0.5)
Payments or credits attributed to sales in:						
Current period	(139.7)	(29.6)	—	(16.9)		(186.2)
Prior periods	(42.6)	(2.5)	(1.7)	(3.8)		(50.6)
Balance, December 31, 2020	\$ 65.3	\$ 3.0	\$ 12.5	\$ 3.7	\$	84.5

Cost of Sales

The table below summarizes cost of sales by major category (dollars in millions):

Category:	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
Cost of sales	\$ 146.7	\$ 116.7	\$ 101.0	\$ 30.0	\$ 15.7	26 %	16 %
Share-based compensation expense ⁽¹⁾	4.9	5.8	7.1	(0.9)	(1.3)	(16)%	(18)%
Total cost of sales	\$ 151.6	\$ 122.5	\$ 108.1	\$ 29.1	\$ 14.4	24 %	13 %

(1) Refer to *Share-Based Compensation* section below for discussion.

Cost of sales, excluding share-based compensation. The increase in cost of sales for the year ended December 31, 2022, as compared to the same period in 2021, was primarily due to an increase in royalty expense and product costs for Tyvaso DPI following the commercial launch of the product in June 2022.

Research and Development

The table below summarizes the nature of research and development expense by major expense category (dollars in millions):

Category:	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
External research and development ⁽¹⁾	\$ 168.8	\$ 156.7	\$ 177.4	\$ 12.1	\$ (20.7)	8 %	(12)%
Internal research and development ⁽²⁾	131.4	117.2	111.3	14.2	5.9	12 %	5 %
Share-based compensation expense ⁽³⁾	23.8	24.4	29.5	(0.6)	(5.1)	(2)%	(17)%
Impairments ⁽⁴⁾	—	130.0	0.5	(130.0)	129.5	(100)%	NM ⁽⁶⁾
Other ⁽⁵⁾	(1.1)	111.8	39.0	(112.9)	72.8	(101)%	187 %
Total research and development expense	\$ 322.9	\$ 540.1	\$ 357.7	\$ (217.2)	\$ 182.4	(40)%	51 %

(1) *External research and development* primarily includes fees paid to third parties (such as clinical trial sites, contract research organizations, and contract laboratories) for preclinical and clinical studies and payments to third-party contract manufacturers before FDA approval of the relevant product.

(2) *Internal research and development* primarily includes salary-related expenses for research and development functions, internal costs to manufacture product candidates before FDA approval, and internal facilities-related expenses, including depreciation, related to research and development activities.

(3) Refer to *Share-Based Compensation* section below for discussion.

(4) *Impairments* primarily includes impairment charges to write-down the carrying value of in-process research and development (**IPR&D**) and of certain property, plant, and equipment as a result of research and development activities.

(5) *Other* primarily includes upfront fees and milestone payments to third parties under license agreements related to development-stage products, adjustments to the fair value of our contingent consideration obligations, and a one-time expense associated with the redemption of a pediatric disease priority review voucher in 2021.

(6) Calculation is not meaningful.

Research and development, excluding share-based compensation. The decrease in research and development expense for the year ended December 31, 2022, as compared to the same period in 2021, was due to: (1) a \$107.3 million IPR&D impairment charge related to our March 2021 decision to discontinue the U.S. development of Trevyent; (2) a \$105.0 million purchase of a pediatric disease priority review voucher in January 2021, which we redeemed upon submission of our NDA for Tyvaso DPI; and (3) impairment charges related to property, plant, and equipment during 2021.

Selling, General, and Administrative

The table below summarizes selling, general, and administrative expense by major category (dollars in millions):

	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
Category:							
General and administrative	\$ 333.2	\$ 294.3	\$ 241.8	\$ 38.9	\$ 52.5	13 %	22 %
Sales and marketing	70.8	64.4	54.9	6.4	9.5	10 %	17 %
Share-based compensation expense ⁽¹⁾	78.1	108.3	127.2	(30.2)	(18.9)	(28)%	(15)%
Total selling, general, and administrative expense	\$ 482.1	\$ 467.0	\$ 423.9	\$ 15.1	\$ 43.1	3 %	10 %

(1) Refer to *Share-Based Compensation* section below for discussion.

General and administrative, excluding share-based compensation. The increase in general and administrative expense for the year ended December 31, 2022, as compared to the same period in 2021, was primarily due to: (1) an increase in branded prescription drug fee expense associated with sales of Tyvaso; and (2) impairment charges related to property, plant, and equipment. The branded prescription drug fee is a required fee imposed under the Patient Protection and Affordable Care Act of 2010, which became applicable to Tyvaso in 2021, and is now applicable to Tyvaso DPI, as a result of their approval for treatment of PH-ILD, an indication that currently does not have orphan designation from the FDA.

Share-Based Compensation

The table below summarizes share-based compensation expense by major category (dollars in millions):

	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
Category:							
Stock options	\$ 22.6	\$ 25.4	\$ 44.0	\$ (2.8)	\$ (18.6)	(11)%	(42)%
Restricted stock units	35.7	24.7	20.5	11.0	4.2	45 %	20 %
STAP awards	46.7	86.6	97.8	(39.9)	(11.2)	(46)%	(11)%
Employee stock purchase plan	1.8	1.8	1.5	—	0.3	— %	20 %
Total share-based compensation expense	\$ 106.8	\$ 138.5	\$ 163.8	\$ (31.7)	\$ (25.3)	(23)%	(15)%

The table below summarizes share-based compensation expense by line item in our consolidated statements of operations (dollars in millions):

	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
Cost of sales	\$ 4.9	\$ 5.8	\$ 7.1	\$ (0.9)	\$ (1.3)	(16)%	(18)%
Research and development	23.8	24.4	29.5	(0.6)	(5.1)	(2)%	(17)%
Selling, general, and administrative	78.1	108.3	127.2	(30.2)	(18.9)	(28)%	(15)%
Total share-based compensation expense	\$ 106.8	\$ 138.5	\$ 163.8	\$ (31.7)	\$ (25.3)	(23)%	(15)%

The decrease in share-based compensation expense for the year ended December 31, 2022, as compared to the same period in 2021, was primarily due to: (1) a decrease in STAP expense driven by a 29 percent increase in our stock price during 2022, as compared to a 42 percent increase in our stock price during 2021; and (2) a decrease in stock option expense due to fewer awards granted and remaining outstanding in 2022, as compared to the same period in 2021, partially offset by an increase in restricted stock unit expense. Refer to Note 8—*Share-Based Compensation*, to our consolidated financial statements for more information.

Other (Expense) Income, Net

The change in *other (expense) income, net* for the year ended December 31, 2022, as compared to the same period in 2021, was primarily due to net unrealized and realized gains and losses on equity securities. Refer to Note 4—*Investments* and Note 5—*Fair Value Measurements*, to our consolidated financial statements for more information.

Income Tax Expense

Income tax expense was \$223.3 million for the year ended December 31, 2022, as compared to \$118.1 million for the same period in 2021. For the years ended December 31, 2022 and 2021, our effective income tax rates (**ETR**) were approximately 23 percent and 20 percent, respectively. Our ETR for the year ended December 31, 2022 increased, as compared to our ETR for the year ended December 31, 2021, primarily due to an increase in valuation allowance in the current year compared to a decrease in the prior year, and an increase in the reserve for uncertain tax positions, partially offset by an increase in excess tax benefits from share-based compensation. For additional details, refer to Note 10—*Income Taxes* to our consolidated financial statements.

Financial Condition, Liquidity, and Capital Resources

We have funded our operations principally through sales of our commercial products and, from time-to-time, third-party financing arrangements. We believe that our current sources of liquidity are sufficient to fund ongoing operations and future business plans as we expect aggregate growth in revenues from our commercial products. Furthermore, our customer base remains stable and we believe that it presents minimal credit risk. However, any projections of future cash flows are inherently subject to uncertainty and we may seek other forms of financing. In March 2022, we entered into a credit agreement (the **2022 Credit Agreement**), which provides for unsecured revolving credit facilities of up to \$2.0 billion in the aggregate. Our aggregate outstanding balance under the 2022 Credit Agreement, which matures in 2027, was \$800.0 million and classified as a non-current liability in our consolidated balance sheets as of December 31, 2022. See *Unsecured Revolving Credit Facilities* below for further details.

For information regarding the fluctuation explanations between 2021 and 2020, refer to our 2021 Annual Report.

Cash and Cash Equivalents and Marketable Investments

Cash and cash equivalents and marketable investments comprise the following (dollars in millions):

	Year Ended December 31,		Dollar Change		Percentage Change
	2022	2021	2022 v. 2021	2022 v. 2021	2022 v. 2021
Cash and cash equivalents	\$ 961.2	\$ 894.8	\$ 66.4		7 %
Marketable investments—current	1,877.5	1,035.9	841.6		81 %
Marketable investments—non-current	1,316.2	1,649.9	(333.7)		(20)%
Total cash and cash equivalents and marketable investments	\$ 4,154.9	\$ 3,580.6	\$ 574.3		16 %

Cash Flows

Cash flows comprise the following (dollars in millions):

	Year Ended December 31,			Dollar Change		Percentage Change	
	2022	2021	2020	2022 v. 2021	2021 v. 2020	2022 v. 2021	2021 v. 2020
Net cash provided by operating activities	\$ 802.5	\$ 598.2	\$ 755.7	\$ 204.3	\$ (157.5)	34 %	(21)%
Net cash used in investing activities	\$ (811.5)	\$ (486.9)	\$ (738.5)	\$ (324.6)	\$ 251.6	(67)%	34 %
Net cash provided by (used in) financing activities	\$ 75.4	\$ 44.8	\$ (16.9)	\$ 30.6	\$ 61.7	68 %	365 %

Operating Activities

Our operating assets and liabilities consist primarily of accounts receivable, inventories, accounts payable, accrued expenses, liabilities for our STAP awards, and tax-related payables and receivables.

The increase of \$204.3 million in net cash provided by operating activities for the year ended December 31, 2022, as compared to the year ended December 31, 2021, was primarily due to: (1) a \$105.0 million purchase of a pediatric disease priority review voucher during the year ended December 31, 2021; and (2) a \$12.9 million decrease in cash paid to settle STAP awards. The remainder of the increase in cash provided by operating activities was due to other changes in assets and liabilities.

Investing Activities

The increase of \$324.6 million in net cash used in investing activities for the year ended December 31, 2022, as compared to the year ended December 31, 2021, was primarily due to: (1) a \$317.2 million increase in cash used for total purchases, sales, and maturities of marketable investments; and (2) a \$18.0 million increase in cash paid to purchase property, plant, and equipment.

Financing Activities

The increase of \$30.6 million in net cash provided by financing activities for the year ended December 31, 2022, as compared to the year ended December 31, 2021, was primarily due to a \$38.4 million increase in proceeds from the exercise of stock options, partially offset by a \$7.5 million increase in payments of debt issuance costs related to the 2022 Credit Agreement.

Unsecured Revolving Credit Facilities

In March 2022, we entered into the 2022 Credit Agreement, which provides for unsecured revolving credit facilities of up to \$2.0 billion in the aggregate. On March 31, 2022, we borrowed \$800.0 million under the facilities and used the funds to repay outstanding indebtedness under our then-existing credit agreement (the **2018 Credit Agreement**). The aggregate balance of \$800.0 million under our 2022 Credit Agreement remained outstanding as of both December 31, 2022 and February 22, 2023. Refer to Note 7—*Debt*, to our consolidated financial statements.

Contractual Obligations

As of December 31, 2022, we had the following contractual obligations (in millions):

	Payments Due by Period				
	Total	Less than 1 year	2-3 Years	4-5 Years	More than 5 Years
Operating lease obligations	\$ 31.7	\$ 3.9	\$ 7.0	\$ 7.1	\$ 13.7
Long-term debt obligations ⁽¹⁾	1,014.2	50.4	100.8	863.0	—
Obligations under the STAP ⁽²⁾	76.4	76.4	—	—	—
Obligations under the SERP ⁽³⁾	67.7	19.5	18.1	—	30.1
Purchase obligations ⁽⁴⁾	654.4	464.4	150.5	25.3	14.2
Total ^{(5) (6)}	\$ 1,844.4	\$ 614.6	\$ 276.4	\$ 895.4	\$ 58.0

- (1) Long-term debt obligations include future principal and interest payments on our adjusted variable rate obligations under the 2022 Credit Agreement, assuming contractual maturity of the 2022 Credit Agreement. The 2022 Credit Agreement will mature in March 2027. As of December 31, 2022, we have classified the entire \$800.0 million outstanding balance as a non-current liability because we do not intend to repay any portion of this amount within one year. Refer to Note 7—*Debt* to our consolidated financial statements for further details.
- (2) Estimated based on the intrinsic value of exercisable outstanding STAP awards as of December 31, 2022. Refer to Note 8—*Share-Based Compensation—STAP Awards* to our consolidated financial statements for further details.
- (3) Consists of actuarially derived, undiscounted, estimated future payouts of benefits. Refer to Note 11—*Employee Benefit Plans—Supplemental Executive Retirement Plan* to our consolidated financial statements for further details.
- (4) Purchase obligations primarily include: (1) commitments related to research and development (including clinical trials) for new and existing products; (2) open purchase orders for capital expenditures primarily related to our continued investment in construction of additional facilities to support the development and commercialization of our products and technologies; and (3) open purchase orders for the acquisition of goods and services in the ordinary course of business. The timing and amount of our obligations may differ based on certain future events.
- (5) In addition to amounts in the table above, we are contractually obligated to make payments upon the achievement of various development, regulatory, and commercial milestones for agreements we have entered into with third parties. These payments are contingent upon the occurrence of various future events, some of which have a high degree of uncertainty of occurring. These contingent payments have not been included in the table above, and, except with respect to the fair value of the contingent consideration obligations, are not recorded in our consolidated balance sheets. Refer to Note 12—*Commitments and Contingencies* to our consolidated financial statements for further details.
- (6) As of December 31, 2022, our other non-current liabilities in our consolidated balance sheets includes a liability of \$15.9 million for unrecognized tax benefits, including related interest and penalties. Due to the high degree of uncertainty on the timing of future events that could extinguish these unrecognized tax benefits, we are unable to estimate the period of settlement and therefore we have excluded these unrecognized tax benefits from the table above. Refer to Note 10—*Income Taxes* to our consolidated financial statements for further details.

Obligations Under License Agreements

We pay Lilly a royalty equal to ten percent of our net product sales of Adcirca, as well as milestone payments of \$325,000 for each \$1,000,000 in Adcirca net product sales. We pay a single-digit percentage royalty based on net product sales of Orenitram under our license agreement with Supernus. We also pay The Scripps Research Institute a one percent royalty on sales of Unituxin. We have entered into other license agreements under which we are required to make milestone payments upon the achievement of certain developmental and commercialization objectives and royalty payments upon the commercialization of products covered by the license agreements. Refer to Note 12—*Commitments and Contingencies* to our consolidated financial statements for further details.

Off-Balance Sheet Arrangements

We hold an interest in an unconsolidated variable interest entity (**VIE**). We determined that we are not the primary beneficiary of this entity. As a result, we do not consolidate this VIE. Refer to Note 4—*Investments—Variable Interest Entities*. We do not have any other off-balance sheet arrangements within the meaning of Item 303(a)(4) of Regulation S-K.

Summary of Critical Accounting Policies and Estimates

We prepare our consolidated financial statements in conformity with generally accepted accounting principles in the United States (**GAAP**). GAAP requires that we make estimates and assumptions that affect the amounts and timing reported in our consolidated financial statements. As we become aware of updated information or new developments, these estimates and assumptions may change and materially impact reported amounts. We consider the following accounting policies to be critical to our consolidated financial statements because they require the use of our judgment and estimates (including those that are forward-looking) in their application.

Revenue Recognition

We generate revenues from the sale of our commercial products: Tyvaso, Tyvaso DPI, Remodulin, Orenitram, Unituxin, and Adcirca. Revenue is recognized when we transfer control of our products to our distributors, as our contracts have a single performance obligation (delivery of our product). These revenues are subject to various product sales allowances, referred to as gross-to-net deductions, which are deducted from revenues to determine net product sales. For a description of our related accounting policies, refer to Note 2—*Summary of Significant Accounting Policies—Revenue Recognition* to our consolidated financial statements.

The following category of gross-to-net deductions involves the use of significant estimates and judgments and information obtained from external sources.

Rebates and Chargebacks

Our most significant rebates relate to our participation in state Medicaid programs, contractual rebates to certain of our domestic distributors, and contractual rebates offered to managed care organizations covering Medicare Part D and commercial plans. Chargebacks relate to our participation in programs with the U.S. Department of Veterans Affairs and 340B covered entities. Although we accrue for our allowance for rebates and chargebacks in the same period that we recognize revenue, the actual rebate or chargeback on the sale of our product to a distributor is not invoiced to us until a future period, generally within six months from the date of sale. Due to this time lag, we must estimate the amount of rebates and chargebacks to accrue. As of December 31, 2022 and 2021, we had a liability of \$81.3 million and \$67.8 million, respectively, related to rebates and chargebacks.

Estimates associated with our participation in state Medicaid programs are particularly susceptible to adjustment given the extensive time lag that may occur between our recording of an accrual and its ultimate invoicing by individual state Medicaid programs, which can occur up to several years after the sale of our product. Because of the time lag for Medicaid and other rebates, in any particular quarter, our adjustments may incorporate revisions of accruals for prior quarters. Historically, adjustments to our estimates to reflect actual results or updated expectations have not been material to our overall financial results. Provisions attributed to sales in prior periods have been less than one percent of our total revenues for each of the years ended December 31, 2022, 2021, and 2020.

For a roll-forward of the liability accounts associated with our gross-to-net deductions, see the section above entitled *Results of Operations—Gross-to-Net Deductions*.

Share-Based Compensation

Our share-based awards are classified as either liabilities (STAP awards) or as equity (stock options, restricted stock units, and rights to purchase stock under our employee stock purchase plan). We recognize related share-based compensation expense based on (1) the fair value of outstanding STAP awards on the grant date and at the end of each reporting period; (2) the grant date fair value of stock options and restricted stock units; and (3) the purchase date fair value of stock under our employee stock purchase plan. With the exception of restricted stock units, we estimate the fair value of all share-based awards using the Black-Scholes-Merton valuation model. We measure the fair value of restricted stock units using the stock price on the grant date. Valuation models, like the Black-Scholes-Merton model, require the use of subjective assumptions that could materially impact the estimation of fair value and related compensation expense to be recognized. These assumptions include the expected volatility of our stock price and the expected term of awards. Developing these assumptions requires the use of judgment. For additional information on the assumptions used in the Black-Scholes-Merton valuation model, see Note 8—*Share-Based Compensation*, to our consolidated financial statements.

Recently Issued Accounting Standards

See Note 3—*Recently Issued Accounting Standards*, to our consolidated financial statements for information on our anticipated adoption of recently issued accounting standards.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Investment Risk

As of December 31, 2022, we have invested \$3.2 billion in corporate debt securities and U.S. government and agency securities. The market value of these investments varies inversely with changes in prevailing market interest rates. In general, as interest rates increase, the market value of a debt investment would be expected to decrease. Conversely, as interest rates decrease, the market value of a debt investment would be expected to increase. During 2022, we experienced significant volatility in the value of these investments as a direct result of the current interest rate environment. To address market risk, we invest in debt securities with terms no longer than three years and typically hold these investments to maturity so that they can be redeemed at their stated or face value. Many of our investments may be called by their respective issuers prior to maturity. The following table summarizes the expected maturities and weighted average interest rates as of December 31, 2022 (dollars in millions):

	Expected Maturity		
	2023	2024	2025
Available-for-sale investments	\$ 1,862.4	\$ 1,159.5	\$ 156.7
Weighted average interest rate	1.1 %	1.7 %	3.2 %

During sustained periods of instability and uncertainty in the financial markets, we may be subjected to additional investment-related risks that could materially affect the value and liquidity of our investments. In light of these risks, we actively monitor market conditions and developments specific to the securities and security classes in which we invest. In addition, we believe that we maintain a conservative investment approach in that we invest exclusively in unstructured, highly-rated securities with relatively short maturities that we believe reduce our exposure to undue risks. While we believe that we take prudent measures to mitigate investment related risks, such risks cannot be fully eliminated, as circumstances can occur that are beyond our control.

Interest Rate Risk

As of December 31, 2022 and 2021, we had \$800.0 million aggregate principal amounts outstanding under our 2022 Credit Agreement and 2018 Credit Agreement, respectively, which bears interest at a variable rate. As a result, we are subject to interest rate risk with respect to such floating-rate debt. A 100 basis point increase in the variable interest rate component of our borrowings would increase our annual interest expense by approximately \$8.0 million or 25 percent, and \$8.0 million or 43 percent, for the years ended December 31, 2022 and 2021, respectively. Refer to Note 7—*Debt*, to our consolidated financial statements.

Stock Price Risk

As of both December 31, 2022 and 2021, we had 0.6 million and 1.1 million awards outstanding under our Share Tracking Awards Plan, respectively. These awards are referred to as **STAP awards**. STAP awards convey the right to receive in cash an amount equal to the appreciation of our common stock, which is measured as the increase in the closing price of our common stock between the dates of grant and exercise. As of December 31, 2022 and 2021, the aggregate STAP awards liability balance was \$80.8 million and \$102.4 million, respectively. Estimating the fair value of STAP awards requires the use of certain inputs that can materially impact the determination of fair value and the amount of share-based compensation expense (benefit) we recognize. Inputs used in estimating fair value include the price of our common stock, the expected volatility of the price of our common stock, the risk-free interest rate, the expected term of STAP awards, and the expected dividend yield. As of December 31, 2022 and 2021, a one dollar change in our stock price would, holding other factors constant, increase or decrease the fair value of our STAP awards liability by approximately \$0.5 million and \$1.0 million, respectively.

As of December 31, 2022 and 2021, we held investments in equity securities with readily determinable fair values of \$30.7 million and \$70.4 million, respectively, which are included in *current marketable investments* in our consolidated balance sheets. Our investments in these publicly-traded equity securities are recorded at fair value and are subject to market price volatility. Changes in the fair value of these investments are recorded in our consolidated statements of operations within *other (expense) income, net*. As of December 31, 2022 and 2021, a price change of 10 percent would increase or decrease the fair value of these investments by \$3.1 million and \$7.0 million, respectively.

Item 8. Financial Statements and Supplementary Data

United Therapeutics Corporation Index to Consolidated Financial Statements

<u>Report of Independent Registered Public Accounting Firm</u> (PCAOB ID: 42)	<u>F-2</u>
<u>Consolidated Balance Sheets as of December 31, 2022 and 2021</u>	<u>F-5</u>
<u>Consolidated Statements of Operations for the years ended December 31, 2022, 2021, and 2020</u>	<u>F-6</u>
<u>Consolidated Statements of Comprehensive Income for the years ended December 31, 2022, 2021, and 2020</u>	<u>F-7</u>
<u>Consolidated Statements of Stockholders' Equity for the years ended December 31, 2022, 2021, and 2020</u>	<u>F-8</u>
<u>Consolidated Statements of Cash Flows for the years ended December 31, 2022, 2021, and 2020</u>	<u>F-9</u>
<u>Notes to Consolidated Financial Statements</u>	<u>F-10</u>

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of United Therapeutics Corporation:

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of United Therapeutics Corporation (the **Company**) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive income, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2022, and the related notes and financial statement schedule listed in the Index at Item 15(a)(2) (collectively referred to as the **consolidated financial statements**). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (**PCAOB**), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (**2013 framework**) and our report dated February 22, 2023, expressed an unqualified opinion thereon.

Basis for Opinion

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

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

Critical Audit Matter

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

Revenue Reductions — Accounting for Rebates

Description of the Matter

As of December 31, 2022, accrued rebates and chargebacks were \$81.3 million, a portion of which related to rebates, and the Company recognized \$198.5 million in revenue reductions associated with rebates and chargebacks during the year-ended December 31, 2022. As discussed in Note 2 to the consolidated financial statements, the Company recognizes revenues net of rebates, commonly referred to as “revenue reductions” or “gross-to-net deductions.” Allowances for rebates include mandated discounts due to the Company’s participation in various government health care programs. The Company estimates accrued rebates on a product-by-product basis, considering actual revenue, contractual discount rates, expected utilization under each contract, historical payment experience, and changes in product pricing and information regarding changes in program regulations and guidelines. The Company accrues for rebates in the same period the product is sold; however, third-party reporting and payment of the rebate amount occur on a time lag.

Auditing rebates is complex due to the time lag associated with third-party reporting of rebate amounts, calculations of government pricing used to determine the rebate price, and the judgmental nature of the time lag assumptions. The complexities associated with government pricing calculations required the involvement of specialists.

How We Addressed the Matter in Our Audit

We tested controls that address the risks of material misstatement relating to the measurement and valuation of rebates. For example, we tested controls over management’s review of the accrued rebate, including the significant assumptions and data inputs provided by third parties.

To test rebates, our audit procedures included, among others, evaluating the methodologies and assumptions used and the underlying data used by the Company. We evaluated the assumptions used by management against historical trends, evaluated the change in estimated accruals from the prior periods, and assessed the historical accuracy of the Company’s estimates against actual results. We performed substantive analytics disaggregated by product. We utilized government pricing specialists in evaluating the Company’s government pricing methodology and calculations of government prices used to estimate rebates for a sample of the Company’s products.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 2003.
Tysons, Virginia
February 22, 2023

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of United Therapeutics Corporation:

Opinion on Internal Control Over Financial Reporting

We have audited United Therapeutics Corporation's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the **COSO criteria**). In our opinion, United Therapeutics Corporation (the **Company**) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (**PCAOB**), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive income, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2022 and the related notes and financial statement schedule of the Company listed in the Index at Item 15(a)(2) and our report dated February 22, 2023, expressed an unqualified opinion thereon.

Basis for Opinion

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

Tysons, Virginia
February 22, 2023

Consolidated Balance Sheets

(In millions, except share and per share data)

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 961.2	\$ 894.8
Marketable investments	1,877.5	1,035.9
Accounts receivable, no allowance for 2022 and 2021	220.4	198.7
Inventories, net	102.0	93.8
Other current assets	219.2	100.4
Total current assets	3,380.3	2,323.6
Marketable investments	1,316.2	1,649.9
Goodwill and other intangible assets, net	44.5	44.6
Property, plant, and equipment, net	861.5	780.9
Deferred tax assets, net	327.7	261.9
Other non-current assets	114.3	108.2
Total assets	\$ 6,044.5	\$ 5,169.1
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued expenses	\$ 229.9	\$ 174.6
Share tracking awards plan	80.8	102.4
Other current liabilities	32.5	28.4
Total current liabilities	343.2	305.4
Line of credit	800.0	800.0
Other non-current liabilities	104.6	104.8
Total liabilities	1,247.8	1,210.2
Commitments and contingencies—Note 12		
Stockholders' equity:		
Preferred stock, par value \$.01, 10,000,000 shares authorized, no shares issued	—	—
Common stock, par value \$.01, 245,000,000 shares authorized, 72,651,280 and 71,727,021 shares issued, and 46,032,064 and 45,107,805 shares outstanding as of December 31, 2022 and 2021, respectively	0.7	0.7
Additional paid-in capital	2,388.4	2,245.4
Accumulated other comprehensive loss	(55.5)	(23.0)
Treasury stock, 26,619,216 shares as of December 31, 2022 and 2021	(2,579.2)	(2,579.2)
Retained earnings	5,042.3	4,315.0
Total stockholders' equity	4,796.7	3,958.9
Total liabilities and stockholders' equity	\$ 6,044.5	\$ 5,169.1

See accompanying notes to consolidated financial statements.

Consolidated Statements of Operations

(In millions, except per share data)

	Year Ended December 31,		
	2022	2021	2020
Total revenues	\$ 1,936.3	\$ 1,685.5	\$ 1,483.3
Operating expenses:			
Cost of sales	151.6	122.5	108.1
Research and development	322.9	540.1	357.7
Selling, general, and administrative	482.1	467.0	423.9
Total operating expenses	956.6	1,129.6	889.7
Operating income	979.7	555.9	593.6
Interest income	45.2	16.7	28.6
Interest expense	(32.4)	(18.6)	(23.5)
Other (expense) income, net	(40.2)	42.2	49.3
Impairments of investments in privately-held companies	(1.7)	(2.3)	(9.1)
Total other (expense) income, net	(29.1)	38.0	45.3
Income before income taxes	950.6	593.9	638.9
Income tax expense	(223.3)	(118.1)	(124.1)
Net income	\$ 727.3	\$ 475.8	\$ 514.8
Net income per common share:			
Basic	\$ 15.98	\$ 10.60	\$ 11.65
Diluted	\$ 15.00	\$ 10.06	\$ 11.54
Weighted average number of common shares outstanding:			
Basic	45.5	44.9	44.2
Diluted	48.5	47.3	44.6

See accompanying notes to consolidated financial statements.

Consolidated Statements of Comprehensive Income

(In millions)

	Year Ended December 31,		
	2022	2021	2020
Net income	\$ 727.3	\$ 475.8	\$ 514.8
Other comprehensive (loss) income:			
Defined benefit pension plan:			
Actuarial gain (loss) arising during period, net of tax	18.7	5.6	(8.0)
Amortization of prior service cost included in net periodic pension cost, net of tax	0.6	0.6	1.3
Total defined benefit pension plan, net of tax	19.3	6.2	(6.7)
Unrealized (loss) gain on available-for-sale securities, net of tax	(51.8)	(15.0)	6.7
Other comprehensive (loss) income, net of tax	(32.5)	(8.8)	—
Comprehensive income	\$ 694.8	\$ 467.0	\$ 514.8

See accompanying notes to consolidated financial statements.

Consolidated Statements of Stockholders' Equity (In millions)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Treasury Stock	Retained Earnings	Stockholders' Equity
	Shares	Amount					
Balance, December 31, 2019	70.5	\$ 0.7	\$ 2,047.9	\$ (14.2)	\$ (2,579.2)	\$ 3,325.2	\$ 2,780.4
Net income	—	—	—	—	—	514.8	514.8
Unrealized gains on available-for-sale securities	—	—	—	6.7	—	—	6.7
Defined benefit pension plan	—	—	—	(6.7)	—	—	(6.7)
Shares issued under employee stock purchase plan (ESPP)	0.1	—	4.7	—	—	—	4.7
Common stock issued for restricted stock units (RSUs) vested	0.1	—	—	—	—	—	—
RSUs withheld for taxes	—	—	(3.7)	—	—	—	(3.7)
Exercise of stock options	0.4	—	33.8	—	—	—	33.8
Share-based compensation	—	—	66.0	—	—	—	66.0
Cumulative effect of accounting change	—	—	—	—	—	(0.8)	(0.8)
Balance, December 31, 2020	71.1	\$ 0.7	\$ 2,148.7	\$ (14.2)	\$ (2,579.2)	\$ 3,839.2	\$ 3,395.2
Net income	—	—	—	—	—	475.8	475.8
Unrealized losses on available-for-sale securities	—	—	—	(15.0)	—	—	(15.0)
Defined benefit pension plan	—	—	—	6.2	—	—	6.2
Shares issued under ESPP	0.1	—	5.6	—	—	—	5.6
Common stock issued for RSUs vested	0.1	—	—	—	—	—	—
RSUs withheld for taxes	—	—	(10.8)	—	—	—	(10.8)
Exercise of stock options	0.4	—	50.0	—	—	—	50.0
Share-based compensation	—	—	51.9	—	—	—	51.9
Balance, December 31, 2021	71.7	\$ 0.7	\$ 2,245.4	\$ (23.0)	\$ (2,579.2)	\$ 4,315.0	\$ 3,958.9
Net income	—	—	—	—	—	727.3	727.3
Unrealized losses on available-for-sale securities	—	—	—	(51.8)	—	—	(51.8)
Defined benefit pension plan	—	—	—	19.3	—	—	19.3
Shares issued under ESPP	0.1	—	5.9	—	—	—	5.9
Common stock issued for RSUs vested	0.1	—	—	—	—	—	—
RSUs withheld for taxes	—	—	(11.4)	—	—	—	(11.4)
Exercise of stock options	0.8	—	88.4	—	—	—	88.4
Share-based compensation	—	—	60.1	—	—	—	60.1
Balance, December 31, 2022	72.7	\$ 0.7	\$ 2,388.4	\$ (55.5)	\$ (2,579.2)	\$ 5,042.3	\$ 4,796.7

See accompanying notes to consolidated financial statements.

Consolidated Statements of Cash Flows

(In millions)

	Year Ended December 31,		
	2022	2021	2020
Cash flows from operating activities:			
Net income	\$ 727.3	\$ 475.8	\$ 514.8
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation and amortization	51.3	49.9	49.9
Share-based compensation expense	106.8	138.5	163.8
Impairments of investments in privately-held companies	1.7	2.3	9.1
Impairments of property, plant, and equipment	11.2	19.2	5.4
Intangible asset impairment charges	—	113.4	—
Realized gain on sale of investment in privately-held company	(6.2)	—	—
Realized gain on sale of equity securities	(0.9)	(92.6)	(3.4)
Other	52.5	65.9	(47.0)
Changes in operating assets and liabilities:			
Accounts receivable	(21.7)	(41.3)	(6.0)
Inventories	(13.4)	(7.5)	10.3
Accounts payable and accrued expenses	44.5	(12.5)	38.6
Other assets and liabilities	(150.6)	(112.9)	20.2
Net cash provided by operating activities	802.5	598.2	755.7
Cash flows from investing activities:			
Purchases of property, plant, and equipment	(138.8)	(120.8)	(59.3)
Proceeds from sale of property, plant, and equipment	—	—	2.4
Purchases of available-for-sale debt securities	(1,708.6)	(1,895.3)	(2,308.8)
Maturities of available-for-sale debt securities	1,021.5	1,370.1	1,523.4
Sales of available-for-sale debt securities	—	47.6	76.5
Sales of investments in equity securities	3.8	111.5	27.3
Sale of investment in privately-held company	8.6	—	—
Proceeds from note receivable	3.5	—	—
Purchase of investment in privately-held company	(1.5)	—	—
Net cash used in investing activities	(811.5)	(486.9)	(738.5)
Cash flows from financing activities:			
Proceeds from line of credit	800.0	—	—
Repayment of line of credit	(800.0)	—	(50.0)
Payments of debt issuance costs	(7.5)	—	(1.7)
Proceeds from the exercise of stock options	88.4	50.0	33.8
Proceeds from the issuance of stock under ESPP	5.9	5.6	4.7
RSUs withheld for taxes	(11.4)	(10.8)	(3.7)
Net cash provided by (used in) financing activities	75.4	44.8	(16.9)
Net increase in cash and cash equivalents	\$ 66.4	\$ 156.1	\$ 0.3
Cash and cash equivalents, beginning of year	894.8	738.7	738.4
Cash and cash equivalents, end of year	\$ 961.2	\$ 894.8	\$ 738.7
Supplemental cash flow information:			
Cash paid for interest	\$ 29.1	\$ 16.2	\$ 20.7
Cash paid for income taxes	\$ 275.7	\$ 153.3	\$ 92.8
Non-cash investing and financing activities:			
Non-cash additions to property, plant, and equipment	\$ 14.5	\$ 3.7	\$ 3.5
Receivable from maturity of available-for-sale debt securities	\$ 70.0	\$ —	\$ —

See accompanying notes to consolidated financial statements.

Notes to Consolidated Financial Statements

1. Organization and Business Description

United Therapeutics Corporation is a biotechnology company focused on the development and commercialization of innovative products to address the unmet medical needs of patients with chronic and life-threatening conditions. On September 30, 2021, we converted to a Delaware public benefit corporation (**PBC**), with the express public benefit purpose *to provide a brighter future for patients through (a) the development of novel pharmaceutical therapies; and (b) technologies that expand the availability of transplantable organs.*

We have approval from the U.S. Food and Drug Administration (**FDA**) to market the following therapies: Tyvaso® (treprostinil) Inhalation Solution (**Tyvaso**), Tyvaso DPI® (treprostinil) Inhalation Powder (**Tyvaso DPI**), Remodulin® (treprostinil) Injection (**Remodulin**), Orenitram® (treprostinil) Extended-Release Tablets (**Orenitram**), Unituxin® (dinutuximab) Injection (**Unituxin**), and Adcirca® (tadalafil) Tablets (**Adcirca**). We also derive revenues outside the United States from sales of Tyvaso, Remodulin, and Unituxin.

As used in these notes to our consolidated financial statements, unless the context otherwise requires, the terms “**we**”, “**us**”, “**our**”, and similar terms refer to United Therapeutics Corporation and its consolidated subsidiaries.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements of United Therapeutics Corporation and its consolidated subsidiaries have been prepared in accordance with accounting principles generally accepted in the United States (**GAAP**). All intercompany balances and transactions have been eliminated in consolidation. Certain prior year amounts have been reclassified to conform to the current year presentation. In Note 10—*Income Taxes*, we reclassified certain prior period amounts between the various components of the reconciliation of income tax expense to conform with the current period presentation.

Use of Estimates

The preparation of our consolidated financial statements in accordance with GAAP requires our management to make estimates and assumptions that affect reported amounts of assets and liabilities at the date of our consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. We base our estimates on assumptions regarding historical experience, currently available information, and anticipated developments that we believe are reasonable and appropriate. However, because the use of estimates involves an inherent degree of uncertainty, actual results could differ from those estimates. Estimates are used for, but not limited to, revenue recognition, share-based compensation, determining the fair value of assets acquired and liabilities assumed in business combinations, marketable investments, fair value measurements (including those related to contingent consideration), inventory reserves, investments in privately-held companies, income taxes, goodwill and other intangible assets, and obligations related to our Supplemental Executive Retirement Plan.

Fair Value Measurements

Fair value is a market-based measurement, not an entity-specific measurement. The objective of a fair value measurement is to estimate the price to sell an asset or transfer a liability in an orderly transaction between market participants at the measurement date under current market conditions. Such transactions to sell an asset or transfer a liability are assumed to occur in the principal market for that asset or liability, or in the absence of the principal market, the most advantageous market for the asset or liability.

Assets and liabilities subject to fair value measurement disclosures are required to be classified according to a three-level fair value hierarchy with respect to the inputs (or assumptions) used to determine fair value. The level in which an asset or liability is disclosed within the fair value hierarchy is based on the lowest level input that is significant to the related fair value measurement in its entirety. The guidance under the fair value measurement framework applies to other existing accounting guidance in the Financial Accounting Standards Board (**FASB**) codification that requires or permits fair value measurements. Refer to related disclosures in Note 5—*Fair Value Measurements*.

Cash Equivalents

Cash equivalents consist of highly liquid investments with maturities of three months or less from the date of acquisition.

Marketable Investments

Our marketable investments are primarily debt securities that we classify as available-for-sale. If we have both the positive intent and the ability to hold the securities until maturity, we have the option to classify the securities as held-to-maturity. We determine the appropriate classification of the securities at the time they are acquired and evaluate the appropriateness of such classifications at each balance sheet date. Available-for-sale debt securities are recorded at fair value, with the portion of the unrealized gains and losses that are not credit-related included as a component of *accumulated other comprehensive income (loss)* in stockholders' equity, until realized. Held-to-maturity debt securities are recorded at amortized cost, adjusted for the amortization of discounts or premiums. Related discounts and premiums are amortized over the term of these securities as an adjustment to the yield using the effective interest method. Marketable investments are classified as either *current* or *non-current assets* in our consolidated balance sheets based on their contractual maturity dates.

We monitor our available-for-sale debt securities for impairment quarterly or more frequently if circumstances warrant. In the event that the carrying value of a debt security exceeds its fair value, we evaluate whether any impairment is a result of credit loss or other factors. For investments in an unrealized loss position, we determine whether a credit loss exists by considering information about the collectibility of the instrument, current market conditions, the investment issuer's financial condition and business outlook, and reasonable and supportable forecasts of economic conditions. An allowance for credit losses would be recorded in our consolidated statements of operations in the event the decline in the investment's fair value was a result of credit loss, and unrealized losses not related to credit losses would be recorded in *other comprehensive income (loss)*.

Our marketable investments also include investments in publicly-traded companies. The equity securities we own in these companies are recorded at fair value. Changes in the fair value of publicly-traded equity securities are recorded in our consolidated statements of operations within *other (expense) income, net*.

Inventories

Inventories are stated at the lower of cost (first-in, first-out method) or net realizable value and consist of the following, net of reserves (in millions):

	As of December 31,	
	2022	2021
Raw materials	\$ 18.0	\$ 17.6
Work-in-progress	33.3	31.9
Finished goods	50.7	44.3
Total inventories	\$ 102.0	\$ 93.8

Goodwill and Other Intangible Assets

The carrying amount of goodwill is not amortized but is subject to annual impairment testing. We conduct our impairment testing of goodwill annually during the fourth quarter, or more frequently if impairment indicators exist. Initially, we evaluate various pertinent qualitative factors to assess whether it is more likely than not that the fair value of a reporting unit to which goodwill has been assigned is less than its carrying value. Such qualitative factors can include, among others: (1) industry and market conditions; (2) present and anticipated sales and cost factors; and (3) overall financial performance. If we conclude based on our qualitative assessment that it is more likely than not that the fair value of a reporting unit is less than its carrying value, we then measure the fair value of the reporting unit and compare its fair value to its carrying value (Step 1 of the goodwill impairment test). Following adoption of ASU 2017-04 on January 1, 2020, we are no longer required to perform Step 2 of the goodwill impairment test. The impairment charge is limited to the amount of goodwill allocated to the reporting unit, thus, the new standard eliminates the requirement to calculate a goodwill impairment charge using Step 2. We performed a qualitative assessment for our goodwill impairment testing for 2022, 2021, and 2020. During the years ended December 31, 2022, 2021, and 2020 our evaluation of goodwill did not result in any impairment losses.

Indefinite-lived intangible assets are not amortized but are evaluated annually or more frequently for impairment if impairment indicators exist. Our indefinite-lived intangible assets include purchased in-process research and development (**IPR&D**) assets, which were measured at their estimated fair values as of their acquisition dates. There were no impairment losses related to indefinite-lived intangible assets during the year ended December 31, 2022. During the year ended December 31, 2021, we recognized IPR&D impairment charges of \$113.4 million related to our decision to discontinue the U.S. development of Trevynt® and our decision to discontinue our research and development efforts related to biomechanical lungs, described in footnotes 1 and 2, respectively, to the Goodwill table below. There were no impairment losses related to indefinite-lived intangible assets during the year ended December 31, 2020.

Intangible assets subject to amortization are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an intangible asset may not be recoverable. Impairment losses are measured and recognized to the extent the carrying value of such assets exceeds their fair value. We recorded no impairment losses during the years ended December 31, 2022, 2021, and 2020 related to intangible assets subject to amortization.

Goodwill and other intangible assets comprise the following (in millions):

	As of December 31, 2022			As of December 31, 2021		
	Gross	Accumulated Amortization	Net	Gross	Accumulated Amortization	Net
Goodwill	\$ 28.0	\$ —	\$ 28.0	\$ 28.0	\$ —	\$ 28.0
Other intangible assets:						
Technology, patents, and trade names	6.7	(5.7)	1.0	6.7	(5.6)	1.1
In-process research and development ⁽¹⁾⁽²⁾	15.5	—	15.5	15.5	—	15.5
Total	\$ 50.2	\$ (5.7)	\$ 44.5	\$ 50.2	\$ (5.6)	\$ 44.6

(1) In March 2021, we decided to discontinue the U.S. development of Trevyent due to written comments provided by the FDA in February 2021. The FDA provided these written comments following a meeting between us and the FDA to discuss our planned resubmission of our NDA for Trevyent in light of a complete response letter issued by the FDA in April 2020. We determined these FDA comments to be a potential indicator of impairment of our IPR&D asset related to Trevyent and fully impaired the \$107.3 million IPR&D asset during 2021. The impairment charge was recorded within *research and development* in our consolidated statements of operations for the year ended December 31, 2021.

(2) In January 2021, we decided to discontinue our research and development efforts related to biomechanical lungs. As a result of the decision, we fully impaired the IPR&D asset related to these efforts, which had a carrying value of \$6.1 million, during 2021. The impairment charge was recorded within *research and development* in our consolidated statements of operations for the year ended December 31, 2021.

Related amortization expense for the years ended December 31, 2022, 2021, and 2020, was \$0.1 million, \$0.1 million, and \$0.2 million, respectively. As of December 31, 2022, aggregate amortization expense related to definite-lived intangible assets for each of the five succeeding years and thereafter is estimated at less than \$1.0 million per year.

Property, Plant, and Equipment

Property, plant, and equipment (**PP&E**) is recorded at cost and depreciated over its estimated useful life using the straight-line method. The estimated useful lives of PP&E by major category are as follows:

Land improvements	15 Years
Buildings	25-39 Years
Building improvements	10-39 Years
Furniture, equipment, and vehicles	3-25 Years
Leasehold improvements	Remaining lease term, or the estimated useful life of the improvement, whichever is shorter

PP&E consists of the following (in millions):

	As of December 31,	
	2022	2021
Land and land improvements	\$ 142.7	\$ 132.6
Buildings, building improvements, and leasehold improvements	636.7	612.7
Buildings under construction	110.9	55.1
Furniture, equipment, and vehicles	353.9	322.9
Subtotal	1,244.2	1,123.3
Less—accumulated depreciation	(382.7)	(342.4)
PP&E, net	\$ 861.5	\$ 780.9

Depreciation expense for the years ended December 31, 2022, 2021, and 2020, was \$51.2 million, \$49.8 million, and \$49.7 million, respectively.

Buildings under construction consists of direct costs related to our construction projects.

For the year ended December 31, 2022, we recorded \$11.2 million of PP&E impairment charges in the aggregate, which was recorded within *selling, general, and administrative* in our consolidated statements of operations. For the year ended December 31, 2021, we recorded \$19.2 million of PP&E impairment charges in the aggregate, of which \$16.7 million was recorded within *research and development* in our consolidated statements of operations and \$2.5 million was recorded within *selling, general, and administrative* in our consolidated statements of operations. For the year ended December 31, 2020, we recorded a \$5.4 million PP&E impairment charge, which was recorded within *selling, general, and administrative* in our consolidated statements of operations.

In October 2021, we acquired a 141,960 square foot commercial building located in Silver Spring, Maryland for future expansion. The total purchase price was \$50.9 million, inclusive of taxes, closing costs, and other related expenses, the majority of which was capitalized as land and land improvements based on our intended use of the property.

Investments in Privately-Held Companies

We measure our non-controlling equity investments in privately-held companies using the measurement alternative because the fair values of these investments are not readily determinable. Under this alternative, the investments are measured at cost, less any impairment, adjusted for any observable price changes. We monitor these investments individually for any observable price changes or impairment indicators. We adjust the measurement of these investments for observable price changes in orderly transactions for the identical or a similar investment of the same issuer. We consider relevant transactions, including any potential funding opportunities, which occur on or before the balance sheet date in evaluating whether any observable price changes have occurred. When a relevant transaction is identified, a careful review of the attendant rights and obligations, such as voting rights, liquidation preferences, and protective provisions, is necessary to evaluate whether such transaction is deemed to be a similar or identical investment. When a transaction is identified as similar or identical to our investment, we assess the fair value of our investment using various inputs, such as the discount rate, time to a liquidation event, and volatility, in a valuation model or analysis. We include our investments in privately-held companies within *other non-current assets* in our consolidated balance sheets.

These investments are subject to a periodic impairment review and if impaired, the investment is measured and recorded at fair value in accordance with FASB Accounting Standards Codification (ASC) 820, *Fair Value Measurements*. At each reporting date, we review these investments individually for impairment by evaluating whether events or circumstances have occurred that may have a significant adverse effect on the fair value of the investments. If such events or circumstances have occurred, we will estimate the fair value of the investment. In such cases, we determine the estimated fair value of the investment using unobservable inputs including assumptions by the company's management.

Treasury Stock

Repurchased treasury stock is recorded at cost, including commissions and fees. The cost of treasury shares sold or reissued is determined using the first-in, first-out method. Related gains and losses on sales of treasury stock are recognized as adjustments to stockholders' equity.

Revenue Recognition

We determine revenue recognition for our contractual arrangements with customers based on the following five steps: (1) identify each contract with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to our performance obligations in the contract; and (5) recognize revenue when (or as) we satisfy the relevant performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Revenues are generated from the sale of our commercially approved products: Tyvaso, Tyvaso DPI, Remodulin, Orenitram, Unituxin, and Adcirca. We recognize revenue when we transfer control of our product to our distributors, which is generally when the product is shipped or delivered to the distributor. Future revenue from delivery of our products will be based on purchase orders provided to us by our distributors.

See Note 13—*Segment Information*, for information on revenues disaggregated by commercial products and other, geographic area, and customer.

Gross-to-Net Deductions

As is customary in the pharmaceutical industry, our product sales are recorded net of various forms of gross-to-net deductions. These deductions vary the consideration to which we are entitled in exchange for the sale of our products to our distributors, and include reserves for: (1) rebates and chargebacks; (2) prompt payment discounts; (3) allowance for sales returns; and (4) distributor fees and other allowances. We estimate these reserves in the same period that we recognize revenue for product sales to distributors. The net product sales amount recognized represents the amount we believe will not be subject to a significant future reversal of revenue.

Estimating gross-to-net deductions involves the use of significant assumptions and judgments, as well as information obtained from external sources. For our rebate and chargeback liabilities, in particular, the time lag experienced in the payment of the rebate or chargeback may result in revisions of these accruals in future periods. However, based on our significant history and experience estimating these accruals and our development of these accruals based on the expected value method, we do not believe there will be significant changes to our estimates recorded during the period of sale. We recognized aggregate increases in our net product sales of \$7.4 million, \$2.1 million, and \$0.5 million for the years ended December 31, 2022, 2021, and 2020, respectively, related to changes in these estimates of revenue recognized from product sales in prior periods.

Rebates and chargebacks. Allowances for rebates include mandated discounts due to our participation in various government health care programs, contracted rebates to certain domestic distributors, and contracted discounts with commercial payers. We estimate our rebate liability on a product-by-product basis, considering actual revenue, contractual discount rates, expected utilization under each contract, and historical payment experience. We also consider changes in our product pricing and information regarding changes in program regulations and guidelines. Our chargebacks represent contractual discounts payable to distributors for the difference between the invoice price paid to us by the distributor for a particular product and the contracted price that the distributor's customer pays for that product. We estimate our chargeback liability on a product-by-product basis, primarily considering historical payment experience. Although we accrue a liability for rebates and chargebacks in the same period the product is sold, third-party reporting and payment of the rebate or chargeback amount occur on a time lag, with the majority of rebates and chargebacks paid within six months from date of sale. Our liability for rebates and chargebacks is included in accounts payable and accrued expenses in our consolidated balance sheets. As of December 31, 2022 and 2021, our accrued rebates and chargebacks were \$81.3 million and \$67.8 million, respectively. In addition, during the years ended December 31, 2022, 2021, and 2020, we recognized \$198.5 million, \$218.6 million, and \$195.9 million, respectively, in revenue deductions associated with rebates and chargebacks.

Prompt payment discounts. We offer prompt pay discounts to many of our distributors, typically for payments made within 30 days. Prompt pay discounts are estimated in the period of sale based on our experience with sales to eligible distributors. Our domestic distributors have routinely taken advantage of these discounts and we expect them to continue to do so. Prompt pay discounts are recorded as a deduction to the accounts receivable balance presented in our consolidated balance sheets.

Product returns. The sales terms for Adcirca and Unituxin include return rights that extend throughout the distribution channel. For Adcirca, we recognize an allowance for returns as customers have the right to return expired product for up to 12 months after the product's expiration date (generally 18 to 36 months after the initial sale). Returned product is destroyed. Regulatory exclusivity for Adcirca expired in May 2018, and generic versions of Adcirca became available for purchase beginning in the third quarter of 2018. Due to the availability of the generic versions, we experienced a significant decline in Adcirca demand, resulting in inventory held by distributors and other downstream customers expiring unsold. Our allowance for product returns for Adcirca as of December 31, 2022 and 2021 is \$2.4 million and \$6.3 million, respectively. We record our allowance for product returns in *other current* and *non-current liabilities* in our consolidated balance sheets. We developed our returns liability as of December 31, 2022 based on historical return rates accumulated since the expiration of the regulatory exclusivity in 2018. The returns liability as of December 31, 2021 was based on our estimate of the amount of Adcirca inventory that was in the downstream channel and the amount of that inventory that we expected would not be sold by distributors and other downstream customers. The estimates were developed using reports from our distributors and other third-party data, including estimates of Adcirca dispenses and the historical impact of generic entrants on other branded products that we deemed comparable to Adcirca.

For Unituxin, we ship product with expiration dates that are generally nine to 14 months after the initial sale. Unituxin product returns for each of the years ended December 31, 2022 and 2021 were not material. For sales of our other commercial products, we do not offer our customers a general right of return.

Distributor fees. Distributor fees include distribution and other service fees paid to certain distributors. These fees are based on contractual amounts or rates applied to purchases of our product or units of service provided in a given period. Our liability for distributor fees is included in *accounts payable and accrued expenses* in our consolidated balance sheets.

Trade Receivables

We invoice and receive payment from our customers after we recognize revenue, resulting in receivables from our customers that are presented as *accounts receivable* in our consolidated balance sheets. Accounts receivable consist of short-term amounts due from our distributors (generally 30 to 90 days) and are stated at the amount we expect to collect. We establish an allowance for doubtful accounts, if deemed necessary, based on our assessment of the collectability of specific distributor accounts. We did not recognize any impairment losses for accounts receivable for each of the years ended December 31, 2022 and 2021. Changes in accounts receivable are primarily due to the timing and magnitude of orders of our products, the timing of when control of our products is transferred to our distributors, and the timing of cash collections.

Adcirca

Adcirca is manufactured for us by Lilly and distributed through its pharmaceutical wholesaler network on our behalf. Specifically, Lilly handles all of the administrative functions associated with the sale of Adcirca on our behalf, including the receipt and processing of customer purchase orders, shipment to customers, and invoicing and collection of customer payments. We recognize sales of Adcirca on a gross basis (net of reserves for gross-to-net deductions) based on our determination that we are acting as a principal due to our control of the product prior to its transfer to our customers. Our control is evidenced by our substantive ownership of product inventory, the fact that we bear all inventory risks, our primary responsibility for the

acceptability of the product to our customers, and our ability to influence net product sales through our contracting decisions with commercial payers and participation in governmental-funded programs.

Research and Development

Research and development costs are expensed as incurred except for payments made in advance of services to be provided to us. Related expenses consist of internal labor and overhead, costs to acquire pharmaceutical products and product rights for development, materials used in clinical trials, amounts paid to third parties for services, and materials related to drug development and clinical trials.

As part of our business strategy, we may in-license the rights to develop and commercialize product candidates. For each in-license transaction, we evaluate whether we have acquired processes or activities along with inputs that would be sufficient to constitute a “business” as defined under GAAP. As defined under GAAP, a “business” consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When we determine that we have not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as pre-commercial milestone payments, are immediately expensed as acquired IPR&D in the period in which they are incurred. Milestone payments made to third parties subsequent to regulatory approval are capitalized as intangible assets and amortized over the estimated remaining useful life of the related product.

We recognize the following costs, among others, as research and development expense in the period related costs are incurred:

- costs associated with in-house or contracted manufacturing activities prior to receiving FDA approval for such facilities, or for major unproven changes to our manufacturing processes;
- costs incurred in-licensing the rights to technologies in the research and development stage that have no alternative future use; and
- up-front payments made in connection with arrangements to obtain license and distribution rights to pharmaceutical product candidates prior to regulatory approval, absent any alternative future use.

Share-Based Compensation

Generally, the fair value of a stock option grant is measured on its grant date and related compensation expense is recognized ratably over the requisite service period. We issue new shares of our common stock upon the exercise of stock options. Additionally, certain executives sometimes have stock options with performance conditions that have vesting rights tied to achievement of specific targeted criteria. Share-based compensation expense for all awards is recorded ratably over their vesting period, depending on the specific terms of the award and achievement of the specified performance conditions. Forfeitures are recognized as they occur. Refer to Note 8—*Share-Based Compensation*.

We measure the fair value of restricted stock units using the stock price on the date of grant and related compensation expense is recognized ratably over the vesting period. Each restricted stock unit entitles the holder to receive one share of our common stock upon vesting. We issue new shares of our common stock upon the vesting of restricted stock units.

Awards under our share tracking awards plan require cash settlement upon exercise and are classified as a liability. Accordingly, the fair value of related cash-settled awards is re-measured at each reporting date until awards are exercised or are otherwise no longer outstanding. Related changes in the fair value of outstanding cash-settled awards at each financial reporting date are recognized as adjustments to share-based compensation expense.

We measure the fair value of stock to be purchased through our employee stock purchase plan at the beginning of an offering period, or grant date, and recognize related compensation expense ratably over the requisite service period (the offering period). We issue new shares of our common stock upon the end of each offering period, or exercise date.

Income Taxes

We account for income taxes in accordance with the asset and liability method. Under this method, we determine deferred tax assets and liabilities based on the difference between the financial statement carrying amounts and the tax bases of assets and liabilities, using enacted tax rates in effect for years in which the temporary differences are expected to reverse. We apply a valuation allowance against any net deferred tax asset if, based on the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

We recognize the benefit of an uncertain tax position that has been taken or that we expect to take on income tax returns only if such tax position is more likely than not to be sustained. We recognize the benefit in an amount equal to the largest amount that we determine has a greater than 50 percent likelihood of being realized upon settlement. The ultimate resolution of uncertain tax positions could result in amounts different from those recognized in our consolidated financial statements.

We have elected to account for the tax on Global Intangible Low-Taxed Income as a component of tax expense in the period in which the tax is incurred.

Earnings per Share

Basic earnings per share is computed by dividing net income by the weighted average number of shares of common stock outstanding during the period. Diluted earnings per common share is computed by dividing net income by the weighted average number of shares of common stock outstanding during the period, plus the potential dilutive effect of other securities if such securities were converted or exercised. During periods in which we incur net losses, both basic and diluted loss per share are calculated by dividing the net loss by the weighted average shares outstanding. Potentially dilutive securities are excluded from the calculation because their effect would be anti-dilutive.

Concentration of Credit Risk

Financial instruments that are exposed to credit risk consist of cash, money market funds, certificates of deposit, marketable debt securities, and trade receivables. We maintain our cash and money market funds with financial institutions that are federally insured. While balances deposited in these institutions often exceed Federal Deposit Insurance Corporation limits, we have not experienced any losses on related accounts to date. Furthermore, we limit our risk exposure by maintaining funds in financial institutions that we believe are creditworthy and financially sound. Our investments in marketable debt securities have been issued by corporate entities and government-sponsored enterprises with high credit ratings. We mitigate investment risks by investing in highly-rated securities with relatively short maturities that we believe do not subject us to undue investment or credit risk. In addition, our investment policy does not provide for investments in complex or structured financial instruments. At any given time, our trade receivables are concentrated among a small number of principal customers. If any of these financial institutions, issuers, or customers fail to perform their obligations under the terms of these financial instruments, our maximum exposure to potential losses would be equal to amounts reported in our consolidated balance sheets.

3. Recently Issued Accounting Standards

Accounting Standards Adopted

None.

Accounting Standards Not Yet Adopted

None.

4. Investments

Marketable Investments

Available-for-Sale Debt Securities

Available-for-sale debt securities are recorded at fair value, with the portion of the unrealized gains and losses that are not credit-related included as a component of *accumulated other comprehensive loss* in stockholders' equity, until realized. Available-for-sale debt securities consisted of the following (in millions):

As of December 31, 2022	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. government and agency securities	\$ 2,697.8	\$ 0.1	\$ (58.9)	\$ 2,639.0
Corporate debt securities	555.6	—	(16.0)	539.6
Total ⁽¹⁾	\$ 3,253.4	\$ 0.1	\$ (74.9)	\$ 3,178.6

Reported under the following captions in our consolidated balance sheets:

Cash and cash equivalents	\$ 15.6
Current marketable investments	1,846.8
Non-current marketable investments	1,316.2
Total ⁽¹⁾	\$ 3,178.6

As of December 31, 2021	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. government and agency securities	\$ 2,178.9	\$ 2.0	\$ (7.3)	\$ 2,173.6
Corporate debt securities	482.5	0.6	(2.0)	481.1
Total	\$ 2,661.4	\$ 2.6	\$ (9.3)	\$ 2,654.7

Reported under the following captions in our consolidated balance sheets:

Cash and cash equivalents	\$ 39.3
Current marketable investments	965.5
Non-current marketable investments	1,649.9
Total	\$ 2,654.7

(1) Total excludes \$70.0 million related to available-for-sale debt securities that matured on December 31, 2022, however cash receipt did not occur until January 3, 2023. We recorded the \$70.0 million receivable within *other current assets* in our consolidated balance sheets.

The following tables present gross unrealized losses and fair value for those available-for-sale debt securities that were in an unrealized loss position as of December 31, 2022 and December 31, 2021, aggregated by investment category and length of time that the individual securities have been in a continuous loss position (in millions):

	Less than 12 months		12 months or longer		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
As of December 31, 2022						
U.S. government and agency securities	\$ 1,324.6	\$ (24.2)	\$ 1,111.6	\$ (34.7)	\$ 2,436.2	\$ (58.9)
Corporate debt securities	254.2	(6.7)	274.1	(9.3)	528.3	(16.0)
Total	\$ 1,578.8	\$ (30.9)	\$ 1,385.7	\$ (44.0)	\$ 2,964.5	\$ (74.9)

	Less than 12 months		12 months or longer		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
As of December 31, 2021						
U.S. government and agency securities	\$ 1,729.9	\$ (7.3)	\$ —	\$ —	\$ 1,729.9	\$ (7.3)
Corporate debt securities	352.3	(2.0)	—	—	352.3	(2.0)
Total	\$ 2,082.2	\$ (9.3)	\$ —	\$ —	\$ 2,082.2	\$ (9.3)

As of December 31, 2022 and December 31, 2021, we held 411 and 251 available-for-sale debt securities, respectively, that were in an unrealized loss position. In assessing whether the decline in fair value as of December 31, 2022 of any of these securities resulted from a credit loss, we consulted with our investment managers and reviewed the credit ratings for each security. We believe that these unrealized losses are a direct result of the current interest rate environment and do not represent an indication of credit loss. We do not intend to sell the investments in unrealized loss positions prior to their maturity and it is not more likely than not that we will be required to sell these investments before recovery of their amortized cost basis. There were no impairments due to credit loss on our available-for-sale debt securities during the years ended December 31, 2022 and 2021.

The following table summarizes the contractual maturities of available-for-sale debt securities (in millions). Actual maturities may differ from contractual maturities because the issuers of certain of these debt securities have the right to call the securities or prepay their obligations under the securities with or without penalties.

	As of December 31, 2022	
	Amortized Cost	Fair Value
Due within one year	\$ 1,890.7	\$ 1,862.4
Due in one to three years	1,362.7	1,316.2
Total	\$ 3,253.4	\$ 3,178.6

Investments in Equity Securities with Readily Determinable Fair Values

We held investments in equity securities with readily determinable fair values of \$30.7 million and \$70.4 million as of December 31, 2022 and 2021, respectively, which are included in *current marketable investments* in our consolidated balance sheets. One of the privately-held companies in which we invested became publicly traded in 2021. As a result, our investment in the equity securities of this company is now recorded at fair value and included within *current marketable investments* in our consolidated balance sheets rather than measured as described below under *Investments in Privately-Held Companies*. Changes in the fair value of publicly-traded equity securities are recorded in our consolidated statements of operations within *other (expense) income, net*. Refer to Note 5—*Fair Value Measurements*.

During the years ended December 31, 2022, 2021, and 2020, we received \$3.8 million, \$111.5 million, and \$27.3 million, respectively, in cash from the sale of investments in equity securities. During 2022, we sold a portion of our investment in a publicly-traded company and realized a gain of \$0.9 million. During 2021, we sold our investments in two publicly-traded companies and realized a gain of \$92.6 million. During 2020, we sold our investment in one publicly-traded company and realized a gain of \$3.4 million. The gains were recorded within *other (expense) income, net* in our consolidated statements of operations for the years ended December 31, 2022, 2021, and 2020.

Investments in Privately-Held Companies

As of December 31, 2022 and 2021, we maintained non-controlling equity investments in privately-held companies of \$28.5 million and \$31.1 million, respectively, in the aggregate. We made a payment of \$1.5 million for an investment in a privately-held company during the year ended December 31, 2022. No such payments were made during the years ended December 31, 2021 and 2020.

When an observable price transaction occurs that is identified as similar or identical to our investment, we perform a valuation analysis to assess the fair value of our investment using various inputs, such as the discount rate, expected time to a liquidation event, and price volatility of peer company stocks. We adjust the fair value of our investment based on the valuation analysis and recognize the gain or loss in the period in which the observable price change occurred. During the years ended December 31, 2022, 2021, and 2020, we recorded an aggregate increase of zero, zero, and \$25.5 million, respectively, in the value of our investments. These gains were recorded within *other (expense) income, net* in our consolidated statements of operations.

During 2022, a privately-held company in which we held an investment was acquired. We received \$8.6 million in cash as a result of the acquisition and realized a gain of \$6.2 million. The gain was recorded within *other (expense) income, net* in our consolidated statements of operations.

During 2022, we identified an indicator of impairment for one of the private companies in which we hold an investment and recognized an impairment charge of \$1.7 million. During 2021, we identified an indicator of impairment for two of the private companies in which we held investments and recognized aggregate impairment charges of \$2.3 million. During 2020, we recorded \$9.1 million of impairment charges related to our investments in privately-held companies. These impairment charges were recorded within *impairments of investments in privately-held companies* in our consolidated statements of operations.

For non-controlling equity investments in privately-held companies in which we held an investment as of December 31, 2022, cumulative impairments and downward fair value adjustments were \$5.1 million and cumulative upward fair value adjustments were \$1.9 million.

Variable Interest Entities (VIEs)

We evaluate our interests in VIEs and will consolidate any VIE in which we have a controlling financial interest and are deemed to be the primary beneficiary. A controlling financial interest has both of the following characteristics: (1) the power to direct the activities of the VIE that most significantly impact its economic performance; and (2) the obligation to absorb losses of the VIE that could potentially be significant to the VIE or the right to receive benefits from the VIE that could be significant to the VIE. If both of the characteristics are met, we are considered to be the primary beneficiary and therefore will consolidate that VIE into our consolidated financial statements.

Unconsolidated VIE

In November 2019, we entered into a supply agreement with an affiliate of DEKA Research & Development Corporation (**DEKA**) to manufacture and supply the Remunity® Pump to us. Under the terms of the supply agreement, we reimburse all of the affiliate's costs to manufacture and supply the Remunity Pump. We determined that the affiliate is a VIE as we are the primary customer of the affiliate and the affiliate currently relies on our reimbursement of its costs to sustain its operations. We have determined we are not the primary beneficiary of the affiliate as we do not have the power to direct or control its significant activities related to the manufacturing of medical devices. Accordingly, we have not consolidated the affiliate's results of operations and financial position with ours. As of December 31, 2022 and 2021, our consolidated balance sheets included \$9.2 million and \$10.6 million of assets, respectively, related to the supply agreement. As of December 31, 2022 and 2021, our consolidated balance sheets included a \$2.0 million liability for our obligation to reimburse costs related to the supply agreement. While the terms of the supply agreement expose us to various future risks of loss given our responsibility to reimburse all costs incurred by the affiliate to manufacture and supply the Remunity Pump, we believe that our maximum exposure to loss as of December 31, 2022 as a result of our involvement with the affiliate is \$9.2 million, the amount of assets related to the supply agreement noted above.

Consolidation of VIEs

In August 2019 and July 2022, we entered into operating agreements and trust agreements related to the contribution of assets to newly created trusts of which we are the beneficiary. The trusts were created for legal and administrative purposes and are not expected to make future purchases. As the operator of the assets, we are required to incur all future expenses related to the operation and maintenance of the assets. Accordingly, the trusts are deemed VIEs because they rely on our capital to sustain future operating expenses. We are deemed the primary beneficiary of the VIEs because we are the sole provider of financial support and can unilaterally remove the trustee without cause. Accordingly, we consolidate the VIE's balance sheet and results of operations.

As of December 31, 2022, our consolidated balance sheets included \$72.9 million of assets due to the consolidation of these VIEs included within *property, plant, and equipment, net*. Upon consolidating the VIEs, which were not deemed a business as defined in ASC 805, *Business Combinations*, no gain or loss was recognized. These VIEs have no recourse against our assets and general credit, and the VIEs' assets cannot be used to settle the VIEs' liabilities. Our total risk of loss is the \$72.9 million of assets we contributed, as noted above.

5. Fair Value Measurements

Assets and liabilities subject to fair value measurements are required to be disclosed within a fair value hierarchy. The fair value hierarchy ranks the quality and reliability of inputs used to determine fair value. Accordingly, assets and liabilities carried at, or permitted to be carried at, fair value are classified within the fair value hierarchy in one of the following categories based on the lowest level input that is significant in measuring fair value:

Level 1—Fair value is determined by using unadjusted quoted prices that are available in active markets for identical assets and liabilities.

Level 2—Fair value is determined by using inputs other than Level 1 quoted prices that are directly or indirectly observable. Inputs can include quoted prices for similar assets and liabilities in active markets or quoted prices for identical assets and liabilities in inactive markets. Related inputs can also include those used in valuation or other pricing models such as interest rates and yield curves that can be corroborated by observable market data.

Level 3—Fair value is determined by using inputs that are unobservable and not corroborated by market data. Use of these inputs involves significant and subjective judgment.

We account for certain assets and liabilities at fair value and classify these assets and liabilities within the fair value hierarchy. Our *other current assets* and *other current liabilities* have fair values that approximate their carrying values. Assets and liabilities subject to fair value measurements are as follows (in millions):

	As of December 31, 2022			
	Level 1	Level 2	Level 3	Balance
Assets				
Money market funds ⁽¹⁾	\$ 459.6	\$ —	\$ —	\$ 459.6
Time deposits ⁽¹⁾	75.6	—	—	75.6
U.S. government and agency securities ⁽²⁾	—	2,639.0	—	2,639.0
Corporate debt securities ⁽²⁾	—	539.6	—	539.6
Equity securities ⁽³⁾	30.7	—	—	30.7
Contingent consideration ⁽⁴⁾	—	—	0.1	0.1
Total assets	\$ 565.9	\$ 3,178.6	\$ 0.1	\$ 3,744.6
Liabilities				
Contingent consideration ⁽⁵⁾	—	—	19.7	19.7
Total liabilities	\$ —	\$ —	\$ 19.7	\$ 19.7

	As of December 31, 2021			
	Level 1	Level 2	Level 3	Balance
Assets				
Money market funds ⁽¹⁾	\$ 516.7	\$ —	\$ —	\$ 516.7
U.S. government and agency securities ⁽²⁾	—	2,173.6	—	2,173.6
Corporate debt securities ⁽²⁾	—	481.1	—	481.1
Equity securities ⁽³⁾	70.4	—	—	70.4
Contingent consideration ⁽⁴⁾	—	—	1.2	1.2
Total assets	\$ 587.1	\$ 2,654.7	\$ 1.2	\$ 3,243.0
Liabilities				
Contingent consideration ⁽⁵⁾	—	—	20.8	20.8
Total liabilities	\$ —	\$ —	\$ 20.8	\$ 20.8

(1) Included in *cash and cash equivalents* in our consolidated balance sheets.

(2) Included in *cash and cash equivalents* and *current and non-current marketable investments* in our consolidated balance sheets. Refer to Note 4 —*Investments—Marketable Investments—Available-for-Sale Debt Securities* for further information. The fair value of these securities is principally measured or corroborated by trade data for identical securities for which related trading activity is not sufficiently frequent to be considered a Level 1 input or comparable securities that are more actively traded.

(3) Included in *current marketable investments* in our consolidated balance sheets. The fair value of these securities is based on quoted market prices for identical instruments in active markets. During the years ended December 31, 2022 and 2021, we recognized \$35.9 million and \$50.8 million of net unrealized and realized losses in the aggregate and net unrealized and realized gains in the aggregate, respectively, on these securities. We recorded these gains and losses in our consolidated statements of operations within *other (expense) income, net*. Refer to Note 4 —*Investments—Marketable Investments—Investments in Equity Securities with Readily Determinable Fair Values*.

(4) Included in *other current assets* and *other non-current assets* in our consolidated balance sheets. We estimated the fair value of contingent consideration using a Monte Carlo simulation. The Monte Carlo simulation incorporates Level 3 inputs including price volatility of peer company stocks and the probability of completing certain milestones during a specified period of time. The fair value of our contingent consideration assets decreased by \$1.1 million from December 31, 2021 to December 31, 2022. The loss was recorded within *other (expense) income, net* in our consolidated statements of operations.

(5) Included in *other current liabilities* and *other non-current liabilities* in our consolidated balance sheets. The fair value of our contingent consideration obligations has been estimated using probability-weighted discounted cash flow models (**DCF**s). The DCFs incorporate Level 3 inputs, including estimated discount rates, that we believe market participants would consider relevant in pricing and the projected timing and amount of cash flows, which are estimated and developed, in part, based on the requirements specific to each acquisition agreement. The fair value of our contingent consideration liabilities decreased by \$1.1 million from December 31, 2021 to December 31, 2022. The gain was recorded within *research and development* in our consolidated statements of operations.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, accounts receivable, accounts payable, and accrued expenses approximate fair value because of their short maturities. The fair values of our marketable investments and contingent consideration are

reported above within the fair value hierarchy. Refer to Note 4—*Investments*. The carrying value of our debt is a reasonable estimate of the fair value of the outstanding debt based on the variable interest rate of the debt.

6. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following by major categories (in millions):

	As of December 31,	
	2022	2021
Accounts payable	\$ 4.1	\$ 3.8
Accrued expenses:		
Sales-related (royalties, rebates, and fees)	116.5	85.3
Payroll-related	66.5	53.6
Research and development-related	22.7	19.0
Other	20.1	12.9
Total accrued expenses	\$ 225.8	\$ 170.8
Total accounts payable and accrued expenses	\$ 229.9	\$ 174.6

7. Debt

2022 Credit Agreement

In March 2022, we entered into a credit agreement (the **2022 Credit Agreement**) with Wells Fargo Bank, National Association (**Wells Fargo**), as administrative agent and a swingline lender, and various other lender parties, which provides for: (1) an unsecured revolving credit facility of up to \$1.2 billion; and (2) a second unsecured revolving credit facility of up to \$800.0 million (which facilities may, at our request, be increased by up to \$500.0 million in the aggregate subject to obtaining commitments from existing or new lenders for such increase and other conditions). The facilities will mature five years after the closing date of the 2022 Credit Agreement on March 31, 2027, subject to the lenders' ability to extend the maturity date by one year if we request such an extension in accordance with the terms of the 2022 Credit Agreement, up to a maximum of two such extensions.

At our option, amounts borrowed under the 2022 Credit Agreement bear interest at either an adjusted Term Secured Overnight Finance Rate (**Term SOFR**) or a fluctuating base rate, in each case, plus an applicable margin determined on a quarterly basis based on our consolidated ratio of total indebtedness to EBITDA (as calculated in accordance with the 2022 Credit Agreement). To date, we have elected to calculate interest on the outstanding balance at an adjusted Term SOFR plus an applicable margin.

On March 31, 2022, we borrowed \$800.0 million under the 2022 Credit Agreement, and used the funds to repay outstanding indebtedness under the 2018 Credit Agreement as discussed below under *2018 Credit Agreement*.

As of December 31, 2022 and 2021, our outstanding aggregate principal balance under the 2022 Credit Agreement and the 2018 Credit Agreement, respectively, was \$800.0 million, all of which was classified as a non-current liability because we do not intend to repay any portion of this amount within one year.

The 2022 Credit Agreement contains customary events of default and customary affirmative and negative covenants. As of December 31, 2022, we were in compliance with these covenants. Lung Biotechnology PBC is our only subsidiary that guarantees our obligations under the 2022 Credit Agreement though, from time to time, one or more of our other subsidiaries may be required to guarantee our obligations.

In connection with the 2022 Credit Agreement, we capitalized debt issuance costs of \$7.5 million, which are being amortized to *interest expense* over the contractual term of the 2022 Credit Agreement. As of December 31, 2022, \$3.2 million was recorded in *other current assets* and \$10.5 million in *other non-current assets* in our consolidated balance sheets.

The interest expense reported in our consolidated statements of operations for each of the years ended December 31, 2022, 2021, and 2020, related to our borrowings under the 2022 Credit Agreement and 2018 Credit Agreement.

2018 Credit Agreement

In June 2018, we entered into a credit agreement (the **2018 Credit Agreement**) with Wells Fargo, as administrative agent and a swingline lender, and various other lender parties, providing for: (1) an unsecured revolving credit facility of up to \$1.0 billion; and (2) a second unsecured revolving credit facility of up to \$500.0 million.

On March 31, 2022, we terminated the 2018 Credit Agreement and entered into the 2022 Credit Agreement. We repaid in full all our obligations under the 2018 Credit Agreement in connection with the termination of the 2018 Credit Agreement and our entry into the 2022 Credit Agreement. There were no penalties associated with the early termination of the 2018 Credit Agreement.

8. Share-Based Compensation

As of December 31, 2022, we have two shareholder-approved equity incentive plans: the United Therapeutics Corporation Amended and Restated Equity Incentive Plan (the **1999 Plan**) and the United Therapeutics Corporation Amended and Restated 2015 Stock Incentive Plan (as amended to date, the **2015 Plan**). The 2015 Plan provides for the issuance of up to 11,500,000 shares of our common stock pursuant to awards granted under the 2015 Plan, which includes 500,000 shares added pursuant to an amendment and restatement of the 2015 Plan approved by our shareholders in June 2022. No further awards will be granted under the 1999 Plan. We also have one equity incentive plan, the United Therapeutics Corporation 2019 Inducement Stock Incentive Plan (the **2019 Inducement Plan**), that has not been approved by our shareholders, as permitted by the Nasdaq Stock Market rules. The 2019 Inducement Plan was approved by our Board of Directors in February 2019 and provides for the issuance of up to 99,000 shares of our common stock under awards granted to newly-hired employees. Currently, we grant equity-based awards to employees and members of our Board of Directors in the form of stock options and restricted stock units (**RSUs**) under the 2015 Plan, and we may grant RSUs to newly-hired employees under the 2019 Inducement Plan. Refer to the sections entitled *Stock Options* and *RSUs* below.

We previously issued awards under the United Therapeutics Corporation 2011 Share Tracking Awards Plan (the **STAP**). We refer to awards outstanding under the STAP as **STAP awards**. Refer to the section entitled *STAP Awards* below. We discontinued the issuance of STAP awards in June 2015.

In 2012, our shareholders approved the United Therapeutics Corporation Employee Stock Purchase Plan (**ESPP**), which is structured to comply with Section 423 of the Internal Revenue Code. Refer to the section entitled *ESPP* below.

The following table reflects the components of share-based compensation expense recognized in our consolidated statements of operations (in millions):

	Year Ended December 31,		
	2022	2021	2020
Stock options	\$ 22.6	\$ 25.4	\$ 44.0
RSUs	35.7	24.7	20.5
STAP awards	46.7	86.6	97.8
ESPP	1.8	1.8	1.5
Total share-based compensation expense before tax	\$ 106.8	\$ 138.5	\$ 163.8
Share-based compensation capitalized as part of inventory	\$ 1.3	\$ 1.0	\$ 1.0

Stock Options

We estimate the fair value of stock options using the Black-Scholes-Merton valuation model, which requires us to make certain assumptions that can materially impact the estimation of fair value and related compensation expense. The assumptions used to estimate fair value include the price of our common stock, the expected volatility of our common stock, the risk-free interest rate, the expected term of stock option awards, and the expected dividend yield.

A description of the key inputs, requiring estimates, used in determining the fair value of stock options are provided below:

Expected term—The expected term reflects the estimated time period we expect an award to remain outstanding. For the years ended December 31, 2022, 2021, and 2020, we used the simplified approach to develop this input for our stock options as we do not have sufficient historical data related to stock option exercises. Under the simplified approach, the expected term reflects the weighted average midpoint between the vesting date and the expiration date of the awards. For the expected term input related to our STAP awards, refer to the *STAP Awards* section below.

Expected volatility—Volatility is a measure of the amount the price of our common stock has fluctuated (historical volatility) or is expected to fluctuate (expected volatility) during a period. We use historical volatility based on weekly price observations of our common stock during the period immediately preceding an award that is equal to its expected term up to a maximum period of five years. We believe that the volatility in the price of our common stock over the preceding five years generally provides a reliable projection of future long-term volatility.

Risk-free interest rate—The risk-free interest rate is the average interest rate consistent with the yield available on a U.S. Treasury note with a term equal to the expected term of an award.

Expected dividend yield—We do not pay cash dividends on our common stock and do not expect to do so in the future. Therefore, the dividend yield is zero.

The following weighted average assumptions were used in estimating the fair value of stock options granted to employees during the twelve months ended December 31, 2022, 2021, and 2020:

	Year Ended December 31,		
	2022	2021	2020
Expected term of awards (in years)	5.7	5.7	5.6
Expected volatility	32.5 %	32.5 %	33.4 %
Risk-free interest rate	2.7 %	1.0 %	0.5 %
Expected dividend yield	0.0 %	0.0 %	0.0 %

A summary of the activity and status of stock options under our equity incentive plans during the year ended December 31, 2022 is presented below:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in millions)
Outstanding as of January 1, 2022	7,317,978	\$ 126.73		
Granted	40,029	213.18		
Exercised	(747,485)	118.26		
Forfeited	(2,503)	130.50		
Outstanding as of December 31, 2022	6,608,019	\$ 128.21	3.8	\$ 990.4
Exercisable as of December 31, 2022	5,219,385	\$ 126.81	3.6	\$ 789.6
Unvested as of December 31, 2022	1,388,634	\$ 133.45	4.4	\$ 200.8

The weighted average fair value of a stock option granted during each of the years in the three-year period ended December 31, 2022, was \$75.87, \$56.69, and \$34.56, respectively. The total fair value of stock options that vested for each of the years in the three-year period ended December 31, 2022, was \$16.3 million, \$50.4 million, and \$73.5 million, respectively.

Total share-based compensation expense related to stock options is recorded as follows (in millions):

	Year Ended December 31,		
	2022	2021	2020
Cost of sales	\$ —	\$ 0.1	\$ 0.5
Research and development	0.3	0.5	2.0
Selling, general, and administrative	22.3	24.8	41.5
Share-based compensation expense before taxes	22.6	25.4	44.0
Related income tax benefit	(0.6)	(0.8)	(3.1)
Share-based compensation expense, net of taxes	\$ 22.0	\$ 24.6	\$ 40.9

As of December 31, 2022, unrecognized compensation cost relating to stock options was \$6.2 million. Unvested outstanding stock options as of December 31, 2022 had a weighted average remaining vesting period of 0.6 years.

Stock option exercise data is summarized below (dollars in millions):

	Year Ended December 31,		
	2022	2021	2020
Number of options exercised	747,485	405,536	466,731
Cash received from options exercised	\$ 88.4	\$ 50.0	\$ 33.8
Total intrinsic value of options exercised	\$ 97.5	\$ 26.6	\$ 22.9
Tax benefits realized from options exercised ⁽¹⁾	\$ 21.6	\$ 5.3	\$ 5.4

(1) We recognize these tax benefits in our consolidated statements of operations within *income tax expense*.

RSUs

In June 2016, we began issuing RSUs to our non-employee directors. In October 2017, we also began issuing RSUs to our employees. Each RSU entitles the recipient to one share of our common stock upon vesting. We measure the fair value of RSUs using the stock price on the date of grant. Share-based compensation expense for RSUs is recorded ratably over their vesting period.

A summary of the activity with respect to, and status of, RSUs during the year ended December 31, 2022 is presented below:

	Number of RSUs	Weighted Average Grant Date Fair Value
Unvested as of January 1, 2022	390,539	\$ 129.76
Granted	683,280	205.48
Vested	(201,690)	125.03
Forfeited	(30,878)	154.78
Unvested as of December 31, 2022	841,251	\$ 191.48

Total share-based compensation expense related to RSUs is recorded as follows (in millions):

	Year Ended December 31,		
	2022	2021	2020
Cost of sales	\$ 3.1	\$ 2.1	\$ 1.6
Research and development	13.6	8.2	7.0
Selling, general, and administrative	19.0	14.4	11.9
Share-based compensation expense before taxes	35.7	24.7	20.5
Related income tax benefit	(8.6)	(5.9)	(4.8)
Share-based compensation expense, net of taxes	\$ 27.1	\$ 18.8	\$ 15.7

As of December 31, 2022, unrecognized compensation cost related to the grant of RSUs was \$131.5 million. Unvested outstanding RSUs as of December 31, 2022 had a weighted average remaining vesting period of 3.8 years.

STAP Awards

STAP awards convey the right to receive in cash an amount equal to the appreciation of our common stock, which is measured as the increase in the closing price of our common stock between the dates of grant and exercise. STAP awards expire on the tenth anniversary of the grant date, and in most cases, they vest in equal increments on each anniversary of the grant date over a four-year period. We discontinued the issuance of STAP awards in June 2015.

The aggregate liability balance associated with outstanding STAP awards was \$80.8 million and \$102.4 million as of December 31, 2022 and 2021, respectively, all of which was classified as a current liability in our consolidated balance sheets.

Estimating the fair value of STAP awards requires the use of certain inputs that can materially impact the determination of fair value and the amount of compensation expense (benefit) we recognize. Inputs used in estimating fair value include the price of our common stock, the expected volatility of the price of our common stock, the risk-free interest rate, the expected term of STAP awards, and the expected dividend yield. The fair value of the STAP awards is measured at the end of each financial reporting period because the awards are settled in cash. Refer to the descriptions of these key inputs, requiring estimates, used in determining the fair value of the awards in the *Stock Options* section above. A description of the expected term input for STAP awards is provided below:

Expected term—The expected term reflects the estimated time period we expect an award to remain outstanding. We use the weighted average midpoint of the remaining contractual term to calculate the expected term of outstanding STAP awards.

The table below includes the weighted-average assumptions used to measure the fair value of the outstanding STAP awards:

	As of December 31,		
	2022	2021	2020
Expected term of awards (in years)	1.0	1.3	1.7
Expected volatility	33.5 %	30.0 %	34.8 %
Risk-free interest rate	4.7 %	0.4 %	0.1 %
Expected dividend yield	0.0 %	0.0 %	0.0 %

The closing price of our common stock was \$278.09, \$216.08, and \$151.79 on December 31, 2022, 2021, and 2020, respectively.

A summary of the activity and status of STAP awards during the year ended December 31, 2022 is presented below:

	Number of Awards	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in millions)
Outstanding as of January 1, 2022	1,093,560	\$ 123.89		
Granted	—	—		
Exercised	(527,606)	107.69		
Forfeited	(10,354)	55.86		
Outstanding as of December 31, 2022	555,600	\$ 140.54	1.9	\$ 76.4
Exercisable as of December 31, 2022	555,600	\$ 140.54	1.9	\$ 76.4
Unvested as of December 31, 2022	—	\$ —	—	\$ —

Share-based compensation expense recognized in connection with STAP awards is as follows (in millions):

	Year Ended December 31,		
	2022	2021	2020
Cost of sales	\$ 1.9	\$ 3.5	\$ 4.9
Research and development	9.0	15.0	19.9
Selling, general, and administrative	35.8	68.1	73.0
Share-based compensation expense before taxes	46.7	86.6	97.8
Related income tax benefit	(8.6)	(14.7)	(19.3)
Share-based compensation expense, net of taxes	\$ 38.1	\$ 71.9	\$ 78.5

Cash paid to settle STAP awards exercised during the years ended December 31, 2022, 2021, and 2020 was \$68.2 million, \$81.1 million, and \$26.1 million, respectively.

ESPP

In June 2012, our shareholders approved the ESPP, which is structured to comply with Section 423 of the Internal Revenue Code. The ESPP provides eligible employees with the right to purchase shares of our common stock at a discount through elective accumulated payroll deductions at the end of each offering period. Offering periods, which began in 2012, occur in consecutive six-month periods commencing on September 5th and March 5th of each year. Eligible employees may contribute up to 15 percent of their base salary, subject to certain annual limitations as defined in the ESPP. The purchase price of the shares is equal to the lower of 85 percent of the closing price of our common stock on either the first or last trading day of a given offering period. In addition, the ESPP provides that no eligible employee may purchase more than 4,000 shares during any offering period. The ESPP has a 20-year term and limits the aggregate number of shares that can be issued under the ESPP to 3.0 million.

9. Stockholders' Equity

Earnings Per Common Share

Basic earnings per common share is computed by dividing net income by the weighted average number of shares of common stock outstanding during the period. Diluted earnings per common share is computed by dividing net income by the weighted

average number of shares of common stock outstanding during the period, adjusted for the potential dilutive effect of our outstanding stock options, RSUs, and shares issuable under the ESPP, as if they were vested and, in the case of stock options, exercised.

The components of basic and diluted earnings per common share comprised the following (in millions, except per share amounts):

	Year Ended December 31,		
	2022	2021	2020
Numerator:			
Net income	\$ 727.3	\$ 475.8	\$ 514.8
Denominator:			
Weighted average outstanding shares — basic	45.5	44.9	44.2
Effect of dilutive securities ⁽¹⁾ :			
Stock options, RSUs, and ESPP ⁽²⁾	3.0	2.4	0.4
Weighted average shares — diluted ⁽²⁾	48.5	47.3	44.6
Net income per common share:			
Basic	\$ 15.98	\$ 10.60	\$ 11.65
Diluted	\$ 15.00	\$ 10.06	\$ 11.54
Stock options and RSUs excluded from calculation ⁽²⁾	—	0.1	6.6

(1) Calculated using the treasury stock method.

(2) The common shares underlying certain stock options and RSUs have been excluded from the computation of diluted earnings per share because their impact would be anti-dilutive.

Accumulated Other Comprehensive Loss

The following table includes changes in accumulated other comprehensive loss by component, net of tax (in millions):

	Defined Benefit Pension Plan ⁽¹⁾	Foreign Currency Translation Losses	Unrealized Gains and (Losses) on Available-for-Sale Securities	Total
Balance, January 1, 2022	\$ (0.5)	\$ (17.9)	\$ (4.6)	\$ (23.0)
Other comprehensive (loss) income before reclassifications	18.7	—	(51.8)	(33.1)
Amounts reclassified from accumulated other comprehensive loss	0.6	—	—	0.6
Net current-period other comprehensive (loss) income	19.3	—	(51.8)	(32.5)
Balance, December 31, 2022	\$ 18.8	\$ (17.9)	\$ (56.4)	\$ (55.5)

	Defined Benefit Pension Plan ⁽¹⁾	Foreign Currency Translation Losses	Unrealized Gains and (Losses) on Available-for-Sale Securities	Total
Balance, January 1, 2021	\$ (6.7)	\$ (17.9)	\$ 10.4	\$ (14.2)
Other comprehensive (loss) income before reclassifications	5.6	—	(15.0)	(9.4)
Amounts reclassified from accumulated other comprehensive loss	0.6	—	—	0.6
Net current-period other comprehensive (loss) income	6.2	—	(15.0)	(8.8)
Balance, December 31, 2021	\$ (0.5)	\$ (17.9)	\$ (4.6)	\$ (23.0)

(1) Refer to Note 11—*Employee Benefit Plans—Supplemental Executive Retirement Plan*, which identifies the captions within our consolidated statements of operations where reclassification adjustments were recognized and their associated tax impact.

10. Income Taxes

Components of income tax expense consist of the following (in millions):

	Year Ended December 31,		
	2022	2021	2020
Current:			
Federal	\$ 228.3	\$ 112.3	\$ 114.6
State	45.8	24.6	20.0
Total current	274.1	136.9	134.6
Deferred			
Federal	(44.8)	(10.1)	1.6
State	(6.0)	(8.7)	(12.1)
Total deferred	(50.8)	(18.8)	(10.5)
Total income tax expense	\$ 223.3	\$ 118.1	\$ 124.1

Presented below is a reconciliation of income tax expense computed at the statutory federal tax rate of 21 percent in 2022, 2021, and 2020 to income tax expense as reported (in millions):

	Year Ended December 31,		
	2022	2021	2020
Federal taxes at the statutory rate	\$ 199.6	\$ 124.7	\$ 134.2
State taxes, net of federal benefit	28.4	14.6	7.0
General business credits	(18.0)	(11.5)	(24.0)
Excess tax benefits from share-based compensation	(15.1)	(3.6)	(1.4)
Uncertain tax positions	11.8	(1.0)	4.8
Nondeductible compensation	9.2	11.8	11.5
Change in valuation allowance	10.9	(18.7)	(3.1)
Other	(3.5)	1.8	(4.9)
Total income tax expense	\$ 223.3	\$ 118.1	\$ 124.1
Effective tax rate	23 %	20 %	19 %

Components of the net deferred tax assets are as follows (in millions):

	As of December 31,	
	2022	2021
Deferred tax assets:		
Intangible assets	\$ 168.2	\$ 186.1
Capitalized research and development	90.3	—
Share-based compensation	64.2	73.4
Basis differences in investments	25.0	1.4
Reserves and accrued liabilities	20.7	18.3
SERP	9.9	10.9
NOLs	9.5	8.3
Other	3.3	5.0
Total deferred tax assets	391.1	303.4
Less: Valuation allowance	(22.4)	(11.5)
Total net deferred tax assets	368.7	291.9
Deferred tax liabilities:		
Plant and equipment principally due to differences in depreciation	(37.4)	(28.2)
Other	(3.6)	(1.8)
Total deferred tax liabilities	(41.0)	(30.0)
Total deferred tax assets, net	\$ 327.7	\$ 261.9

As of December 31, 2022, we had gross federal, foreign, and state net operating loss carryforwards of zero, \$6.8 million, and \$140.0 million, respectively, which either expire at various dates beginning in 2030 or have no expiration date. As of December 31, 2022, we had state research credit carryforwards of \$1.2 million. We expect that a significant amount of these carryforwards will expire unused, so we have established valuation allowances for the related deferred tax assets.

We are subject to federal and state taxation in the United States and various foreign jurisdictions. We are no longer subject to income tax examinations by the Internal Revenue Service and all other major jurisdictions for tax years prior to 2014.

As of December 31, 2022 and 2021, we had \$15.1 million and \$3.6 million of unrecognized tax benefits, excluding interest and penalties, that would impact our effective tax rate if recognized. The total amount of unrecognized tax benefits relating to our tax positions is subject to change based on future events including, but not limited to, the settlements of ongoing tax audits and assessments and the expiration of applicable statutes of limitations. Given the uncertainty of these future events, it is reasonably possible that the balance of unrecognized tax benefits could change significantly over the next 12 months. However, due to the number of years remaining that are subject to examination, we are unable to estimate the full range of possible adjustments to the balance of gross unrecognized tax benefits.

The following table represents a reconciliation of the total unrecognized tax benefit liability, excluding interest and penalties, for the years ended December 31, 2022, 2021, and 2020 (in millions):

	Year Ended December 31,		
	2022	2021	2020
Unrecognized tax benefits, beginning of the period	\$ 3.6	\$ 4.5	\$ —
Gross decreases related to prior period tax positions	—	(0.1)	—
Gross increases related to prior period tax positions	10.3	—	3.8
Gross increases related to current period tax positions	1.3	0.7	0.7
Gross decreases as a result of settlements during the current period	—	(1.5)	—
Unrecognized tax benefits, end of the period	\$ 15.2	\$ 3.6	\$ 4.5

We record interest and penalties related to uncertain tax positions as a component of income tax expense. As of December 31, 2022 and 2021, our liability for unrecognized tax benefits included approximately \$0.7 million and \$0.3 million, respectively, for the accrual of interest and penalties. As of December 31, 2022, 2021, and 2020, we recorded approximately a \$0.4 million expense, \$0.1 million benefit, and \$0.3 million expense, respectively, for the accrual of interest and penalties in our consolidated statement of operations.

The Tax Cuts and Jobs Act of 2017 eliminated the option to deduct research and development expenditures in the period incurred beginning in 2022 and requires amortization over five or fifteen years. This change increased our cash paid for income taxes for 2022 and our deferred tax assets as of December 31, 2022.

On August 16, 2022, the Inflation Reduction Act (**IRA**) was enacted. Among other things, the IRA established a 15% corporate minimum tax and adjusted certain energy-related tax credits and incentives. We currently do not expect the tax-related provisions of the IRA to have a material impact on our consolidated financial statements, including our effective tax rate.

11. Employee Benefit Plans

Supplemental Executive Retirement Plan

We maintain the United Therapeutics Corporation Supplemental Executive Retirement Plan (**SERP**) to provide retirement benefits to certain senior members of our management team.

Participants who retire at age 60 or older are eligible to receive either monthly payments or a lump sum payment based on an average of their total gross base salary over the last 36 months of active employment, subject to certain adjustments. Related benefit payments commence on the first day of the sixth month after retirement. Participants who elect to receive monthly payments will continue to receive payments through the remainder of their life. Alternatively, participants who elect to receive a lump sum distribution will receive a payment equal to the present value of the estimated monthly payments that would have been received upon retirement. As of December 31, 2022 and 2021, all SERP participants had elected to receive a lump sum distribution. Participants who terminate employment for any reason other than death, disability, or change in control prior to age 60 will not be entitled to receive any benefits under the SERP.

Because we do not fund the SERP, we recognize a liability equal to the projected benefit obligation as measured at the end of each fiscal year.

A reconciliation of the beginning and ending balances of the projected benefit obligation is presented below (in millions):

	Year Ended December 31,	
	2022	2021
Projected benefit obligation at the beginning of the year	\$ 67.1	\$ 68.6
Service cost	3.1	3.4
Interest cost	1.2	0.9
Benefits paid	(0.2)	—
Net actuarial gain	(19.7)	(5.8)
Projected benefit obligation at the end of the year	\$ 51.5	\$ 67.1
Amount included in Other current liabilities ⁽¹⁾	\$ 19.5	\$ 18.2
Amount included in Other non-current liabilities	\$ 32.0	\$ 48.9

(1) This amount represents the benefit obligation due to participants who are eligible to retire and whose benefit payments could commence within one year of the respective balance sheet date.

The following weighted average assumptions were used to measure the SERP obligation:

	Year Ended December 31,	
	2022	2021
Discount rate	4.95 %	2.05 %
Salary increases	4.00 %	4.00 %
Lump-sum interest rate	5.00 %	2.75 %

The increases in the discount rate and lump-sum interest rate for the year ended December 31, 2022, as compared to the same period in 2021, resulted in a decrease in the projected benefit obligation of \$4.4 million and \$13.4 million, respectively, as of December 31, 2022.

The components of net periodic pension cost recognized in our consolidated statements of operations consisted of the following (in millions):

	Year Ended December 31,		
	2022	2021	2020
Service cost	\$ 3.1	\$ 3.4	\$ 2.8
Interest cost	1.2	0.9	1.3
Amortization of prior service cost	0.7	0.7	1.3
Total	\$ 5.0	\$ 5.0	\$ 5.4

The service cost component is reported within *operating expenses* and the other components are reported in *other (expense) income, net* in our consolidated statements of operations.

Amounts related to the SERP that have been recognized in other comprehensive (loss) income are as follows (in millions):

	Year Ended December 31,		
	2022	2021	2020
Net actuarial gain (loss)	\$ 19.7	\$ 5.8	\$ (8.4)
Prior service cost	0.7	0.7	1.3
Total recognized in other comprehensive (loss) income	20.4	6.5	(7.1)
Tax (expense) benefit	(1.1)	(0.3)	0.4
Total, net of tax	\$ 19.3	\$ 6.2	\$ (6.7)

The table below presents amounts related to the SERP included in accumulated other comprehensive loss that have not yet been recognized as a component of net periodic pension cost in our consolidated statements of operations (in millions):

	Year Ended December 31,		
	2022	2021	2020
Net actuarial (gain) loss	\$ (21.7)	\$ (2.0)	\$ 3.8
Prior service cost	0.6	1.3	2.0
Total included in accumulated other comprehensive loss	(21.1)	(0.7)	5.8
Tax expense	2.3	1.2	0.9
Total, net of tax	\$ (18.8)	\$ 0.5	\$ 6.7

The accumulated benefit obligation, a measure that does not consider future increases in participants' salaries, was \$47.0 million and \$59.1 million as of December 31, 2022 and 2021, respectively.

Future estimated benefit payments, based on current assumptions, including election of lump-sum distributions and expected future service, are as follows (in millions):

Year Ended December 31,	
2023	\$ 19.5
2024	12.8
2025	5.3
2026	—
2027	—
Thereafter	30.1
Total	\$ 67.7

Employee Retirement Plan

We maintain a Section 401(k) Salary Reduction Plan which is open to all eligible full-time employees. Under the 401(k) Plan, eligible employees can make pre-tax or after-tax contributions up to statutory limits. Currently, we make discretionary matching contributions to the 401(k) Plan equal to 40 percent of a participant's elected salary deferral. Matching contributions vest immediately for participants who have been employed for three-years; otherwise, matching contributions vest annually, in one-third increments over a three-year period until the three-year employment requirement has been met.

12. Commitments and Contingencies

Leases

We lease facilities and equipment under operating lease arrangements that have terms expiring at various dates through 2032. Certain lease arrangements include renewal options and escalation clauses. In addition, various lease agreements to which we are party require that we comply with certain customary covenants throughout the term of these leases. If we are unable to comply with these covenants and cannot reach a satisfactory resolution in the event of noncompliance, these agreements could terminate.

Future minimum lease payments under non-cancelable operating leases as of December 31, 2022, are as follows (in millions):

Year Ending December 31,	
2023	\$ 3.9
2024	3.5
2025	3.5
2026	3.5
2027	3.6
Thereafter	13.7
Total	\$ 31.7

Total operating lease expense was \$4.8 million, \$3.6 million, and \$3.5 million for the years ended December 31, 2022, 2021, and 2020, respectively. The amounts recorded in operating lease expense include short-term leases, which are immaterial.

In August 2021, we entered into a commercial supply agreement (**Supply Agreement**) with MannKind Corporation (**MannKind**), which was later amended in October 2021. Pursuant to the Supply Agreement, MannKind is responsible for manufacturing and supplying Tyvaso DPI to us on a cost-plus basis. Unless earlier terminated, the initial term of the Supply Agreement continues until December 31, 2031 and will thereafter be renewed automatically for additional, successive two-year terms unless either party provides notice of non-renewal. We determined that the Supply Agreement contains certain lease components and have elected the expedient to combine lease and non-lease components as a single lease component. All payment obligations under the Supply Agreement are variable in nature and we incurred costs of \$51.2 million and \$9.6 million during the years ended December 31, 2022 and 2021, respectively.

In September 2022, we entered into an agreement (**Lease Agreement**) to lease the entirety of a building. The Lease Agreement modified and replaced several of our pre-existing leases of portions of the same building, and has an initial term expiring in July 2027, with five renewal options of five years each, exercisable in our sole discretion. As a result, we remeasured the lease liability at our incremental borrowing rate, using a lease term that assumed we exercise one renewal option, due to our financing of significant leasehold improvements necessary for the research and development activities being performed at this location. Upon remeasurement, we determined that the lease remains an operating lease. As of December 31, 2022, our consolidated balance sheets included a right-of-use asset of \$12.0 million and lease liability for the building of \$12.1 million. Leasehold improvements were not significant as of December 31, 2022.

Milestone Payments and Royalty Obligations

We are party to certain license agreements pursuant to which we have in-licensed or acquired intellectual property rights covering our commercial and/or development-stage products. Generally, these agreements require that we make milestone payments in cash upon the achievement of certain product development and commercialization goals and payments of royalties upon commercial sales. The following table outlines our financial obligations under certain of these agreements:

Counterparty	Relevant Product	Our Financial Obligation
Supernus Pharmaceuticals, Inc.	Orenitram	Single-digit royalty on net product sales of Orenitram, through the fourth quarter of 2026
Lilly	Adcirca	Ten percent royalty on net sales, plus milestone payments of \$325,000 for each \$1,000,000 in net product sales
The Scripps Research Institute	Unituxin	One percent royalty on net product sales of Unituxin
DEKA Research & Development Corp.	Remunity Pump	Product fees and single-digit royalty on net product sales of the Remunity Pump and on net sales of Remodulin for use with the system; reimbursement of DEKA's development and manufacturing costs
MannKind Corporation	Tyvaso DPI	Low double-digit royalty on net product sales of Tyvaso DPI and up to \$50.0 million in developmental milestone payments (all of which have already been paid)
Arena (now owned by Pfizer)	Ralinepag	Low double-digit, tiered royalty on net product sales of ralinepag (any route of administration); a one-time payment of \$250.0 million upon FDA approval of an inhaled formulation of ralinepag to treat PAH; and a one-time payment of \$150.0 million upon approval in certain non-U.S. jurisdictions of an oral version of ralinepag to treat any indication

13. Segment Information

We operate as one operating segment with a focus on the development and commercialization of products to address the unmet needs of patients with chronic and life-threatening conditions. Our Chief Executive Officer, as our chief operating decision maker, manages and allocates resources to the operations of our company on a consolidated basis. This enables our Chief Executive Officer to assess our overall level of available resources and determine how best to deploy these resources across functions, therapeutic areas, and research and development projects in line with our long-term company-wide strategic goals.

Total revenues, cost of sales, and gross profit for each of our commercial products and other were as follows (in millions):

Year Ended December 31, 2022	Tyvaso ⁽¹⁾	Remodulin ⁽²⁾	Orenitram	Unituxin	Adcirca	Other	Total
Total revenues	\$ 873.0	\$ 500.2	\$ 325.1	\$ 182.9	\$ 41.3	\$ 13.8	\$ 1,936.3
Cost of sales	53.5	34.0	22.4	13.1	17.8	10.8	151.6
Gross profit	\$ 819.5	\$ 466.2	\$ 302.7	\$ 169.8	\$ 23.5	\$ 3.0	\$ 1,784.7

Year Ended December 31, 2021

Total revenues	\$ 607.5	\$ 513.7	\$ 306.1	\$ 202.3	\$ 55.9	\$ —	\$ 1,685.5
Cost of sales	26.8	37.9	19.7	14.2	23.9	—	122.5
Gross profit	\$ 580.7	\$ 475.8	\$ 286.4	\$ 188.1	\$ 32.0	\$ —	\$ 1,563.0

Year Ended December 31, 2020

Total revenues	\$ 483.3	\$ 516.7	\$ 293.1	\$ 122.9	\$ 67.3	\$ —	\$ 1,483.3
Cost of sales	24.5	23.2	18.7	12.6	29.1	—	108.1
Gross profit	\$ 458.8	\$ 493.5	\$ 274.4	\$ 110.3	\$ 38.2	\$ —	\$ 1,375.2

(1) Total revenues and cost of sales include both the drug product and the respective inhalation devices for both Tyvaso and Tyvaso DPI.

(2) Total revenues and cost of sales include sales of infusion devices, such as the Remunity Pump.

Geographic revenues are determined based on the country in which our customers (distributors) are located. Total revenues from external customers by geographic area are as follows (in millions):

Year Ended December 31,	2022	2021	2020
United States	\$ 1,814.1	\$ 1,564.2	\$ 1,412.1
Rest-of-World	122.2	121.3	71.2
Total	\$ 1,936.3	\$ 1,685.5	\$ 1,483.3

We recorded revenue from three distributors in the United States that exceeded ten percent of total revenues. Revenue from these three distributors as a percentage of total revenues is as follows:

Year Ended December 31,	2022	2021	2020
Distributor 1	51 %	50 %	55 %
Distributor 2	32 %	29 %	28 %
Distributor 3	9 %	11 %	8 %

Long-lived assets, including PP&E and right-of-use assets, located by geographic area are as follows (in millions):

Year Ended December 31,	2022	2021	2020
United States	\$ 871.1	\$ 768.1	\$ 717.3
Rest-of-World	12.6	12.8	14.3
Total	\$ 883.7	\$ 780.9	\$ 731.6

14. Litigation

Sandoz Antitrust Litigation

On April 16, 2019, Sandoz Inc. (**Sandoz**) and its marketing partner RareGen, LLC (now known as Liquidia PAH, LLC, a subsidiary of Liquidia Corporation) (**RareGen**), filed a complaint in the U.S. District Court for the District of New Jersey against us and Smiths Medical ASD, Inc. (**Smiths Medical**), alleging that we and Smiths Medical engaged in anticompetitive conduct in connection with plaintiffs' efforts to launch their generic version of Remodulin. In particular, the complaint alleged that we and Smiths Medical unlawfully impeded competition by entering into an agreement to produce CADD-MS[®]3 cartridges specifically for the delivery of subcutaneous Remodulin for our patients, without making these cartridges available for the delivery of Sandoz's generic version of Remodulin. On March 30, 2020, the plaintiffs filed an amended complaint to add a count alleging that we breached our earlier patent settlement agreement with Sandoz by refusing to grant Sandoz access to cartridges purchased for our patients.

Smiths Medical was dismissed from the case in November 2020, based on a settlement resolving the disputes between the plaintiffs and Smiths Medical. As part of this settlement, Smiths Medical paid the plaintiffs \$4.25 million, disclosed and made

available to the plaintiffs certain specifications and other information related to the MS-3 cartridges, and granted to the plaintiffs a non-exclusive, royalty-free license in the United States to Smiths Medical's patents and copyrights associated with the MS-3 cartridges and certain other information related to the MS-3 pumps and cartridges.

On March 30, 2022, the court granted our motion for summary judgment with respect to all claims brought by the plaintiffs except the breach of contract claim. As a result, all antitrust claims, all claims under state competition laws, and the common law tortious interference claim have been resolved in our favor. These were the only claims in the case that gave rise to any potential for trebling of damages, punitive damages, and/or the award of attorneys' fees. The court also denied plaintiffs' request for injunctive relief.

The court granted Sandoz's motion for summary judgment with respect to Sandoz's breach of contract claim. The issue of what, if any, damages Sandoz is entitled to based on the contract claim will proceed to trial. RareGen has no claim for breach of contract and, as a result, has no remaining claims in the litigation. The case will now proceed to trial with respect to damages under the breach of contract claim. The court has not yet set a date for trial. The parties will have the right to appeal the summary judgment decisions upon entry of final judgment following the trial.

We intend to continue to vigorously defend this litigation. Among other things, we believe that plaintiffs, who were on notice that Smiths Medical would discontinue the CADD MS-3 delivery system, failed to fulfill their duty to properly mitigate their exposure as a result of such discontinuation, thereby causing the alleged damages for which they are suing us. However, due to the uncertainty inherent in any litigation, we cannot guarantee that an adverse outcome will not result. Any litigation of this nature could involve substantial cost, and an adverse outcome could result in substantial monetary damages. We currently are not able to reasonably estimate a range of potential losses due to the number of variables that may affect the outcome of the damages trial and any potential appeals, including potential damages amounts sought, the strength of our defenses, the variety of potential legal and factual determinations yet to be made by the court, the rulings that may be subject to appeal, and the inherent unpredictability of any outcome associated with these issues.

Litigation with Liquidia Technologies, Inc.

On March 30, 2020, Liquidia Technologies, Inc. (**Liquidia**) filed two petitions for *inter partes* review (**IPR**) with the Patent Trial and Appeal Board (**PTAB**) of the U.S. Patent and Trademark Office (**USPTO**). In its petitions, Liquidia sought to invalidate U.S. Patent Nos. 9,604,901 (the '**901 patent**') and 9,593,066 (the '**066 patent**'), both of which relate to a method of making treprostinil, the active pharmaceutical ingredient in Tyvaso, Tyvaso DPI, Remodulin, and Orenitram. These patents were issued in March 2017 and are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations publication, also known as the Orange Book, for Tyvaso, Tyvaso DPI, Remodulin, and Orenitram. In October 2020, the PTAB declined to institute IPR proceedings on the '066 patent because Liquidia failed to establish a reasonable likelihood of prevailing on any claim relating to the '066 patent. The PTAB instituted IPR proceedings on the '901 patent in October 2020 and issued a final written decision in October 2021. The final written decision found that Liquidia had proven the invalidity of seven of the claims of the '901 patent but failed to prove the invalidity of two other claims. The parties have each appealed portions of the final written decision adverse to them, and those appeals are pending. No cancellation of claims takes effect until resolution of any appeals.

In January 2020, Liquidia submitted an NDA to the FDA for approval of Yutrepia, a dry powder inhalation formulation of treprostinil, to treat PAH. This NDA was submitted under the 505(b)(2) regulatory pathway with Tyvaso as the reference listed drug. In November 2021, the FDA granted tentative approval of Liquidia's NDA.

In April 2020, we received a Paragraph IV Certification Notice Letter (**Notice Letter**) from Liquidia, stating that it intends to market Yutrepia before the expiration of all patents listed in the Orange Book for Tyvaso. The Notice Letter states that Liquidia's NDA for Yutrepia contains a Paragraph IV certification alleging that these patents are not valid, not enforceable, and/or will not be infringed by the commercial manufacture, use, or sale of Yutrepia.

On June 4, 2020, we filed a lawsuit in the U.S. District Court for the District of Delaware against Liquidia for infringement of the '901 patent and the '066 patent, both of which expire in December 2028. We filed our lawsuit within 45 days of receipt of notice from Liquidia of its NDA filing. As a result, under the Hatch-Waxman Act, the FDA was precluded by regulation from approving Liquidia's NDA for up to 30 months or until the resolution of the litigation, whichever occurs first. In July 2020, Liquidia filed an answer to our complaint that included counterclaims alleging, among other things, that the patents at issue in the litigation are not valid and will not be infringed by the commercial manufacture, use, or sale of Yutrepia.

In July 2020, the USPTO issued a new patent to us related to Tyvaso. The new patent, U.S. Patent No. 10,716,793 (the '**793 patent**'), expires in May 2027, and is listed in the Orange Book for Tyvaso and Tyvaso DPI. In July 2020, we filed an amended complaint against Liquidia to include a claim for infringement of the '793 patent. The '793 patent relates to a method of administering treprostinil via inhalation and includes claims covering the dosing regimen used to administer Tyvaso and Tyvaso DPI. In December 2021, we filed a stipulation that the '901 patent would not be infringed by Liquidia based on the court's claim construction ruling.

Trial took place during March 2022, and the court issued its decision on August 31, 2022. The court found that Liquidia's product would infringe the '793 patent and that Liquidia had not proved that any claim of that patent is invalid. The court also determined that Liquidia had proved certain claims of the '066 patent were invalid and that we had not proved Liquidia's infringement of another '066 patent claim. Accordingly, the court issued a final judgment that bars the FDA from approving Liquidia's approved product until expiration of the '793 patent in May 2027. The parties have appealed portions of the decision adverse to each of

them, and those appeals are pending. Meanwhile, Liquidia filed a motion with the district court seeking to stay the portion of the judgment that bars the FDA from finally approving until expiration of the '793 patent, and we opposed that motion. The court has not yet ruled on that motion.

In January 2021, Liquidia filed another petition for IPR with the PTAB. In its petition, Liquidia sought to invalidate the '793 patent. In July 2022, the PTAB issued a final written decision finding all claims of the '793 patent to be unpatentable. We filed a request for rehearing and for precedential opinion panel review. On October 26, 2022, the PTAB denied our precedential opinion panel review, but "determine[d] that the Board's Final Written Decision did not address adequately whether the [references relied upon as the basis for canceling claims] qualify as prior art." Thus, the PTAB directed the original panel "in its consideration on rehearing, to clearly identify whether the ... references qualify as prior art." The original panel issued its decision on our request for rehearing on February 2, 2023. The original panel agreed that it had overlooked our arguments and that its rationale for determining that certain references are prior art was erroneous. Nonetheless, the original panel determined the references qualify as prior art under a new rationale. Thus, the original panel maintained that the claims of this patent are not valid. We have until April 6, 2023 to appeal. All claims of this patent remain valid until any IPR appeals are exhausted.

Liquidia could obtain final FDA approval for its proposed product prior to May 2027 in two circumstances: (1) Liquidia could prevail on appeal, either from the district court judgment or IPRs, such that it is not found to infringe any valid claims of our patents; or (2) the district court or appeals court could stay the order barring FDA approval during the pendency of its appeals.

In June 2021, we filed a motion in the patent case in the U.S. District Court for the District of Delaware to file an amended complaint adding trade secret misappropriation claims against Liquidia and a former Liquidia employee, Dr. Robert Roscigno. The court denied the motion based on a finding that adding the additional claims would impact the case schedule. Thus, we filed those claims as a separate case against Liquidia and Robert Roscigno in North Carolina state court. Discovery is underway in that case.

We plan to vigorously enforce our intellectual property rights related to Tyvaso and Tyvaso DPI.

MSP Recovery Litigation

On July 27, 2020, MSP Recovery Claims, Series LLC; MSPA Claims 1, LLC; and Series PMPI, a designated series of MAO-MSO Recovery II, LLC filed a "Class Action Complaint" against Caring Voices Coalition, Inc. (**CVC**) and us in the U.S. District Court for the District of Massachusetts. The complaint alleged that we violated the federal Racketeer Influenced and Corrupt Organizations (**RICO**) act and various state laws by coordinating with CVC when making donations to a PAH fund so that those donations would go towards copayment obligations for Medicare patients taking drugs manufactured and marketed by us. Plaintiffs claim to have received assignments from various Medicare Advantage health plans and other insurance entities that allow them to bring this lawsuit on behalf of those entities to recover allegedly inflated amounts they paid for our drugs. In April 2021, the court granted our motion to transfer the case to the U.S. District Court for the Southern District of Florida.

In October 2021, we filed a motion for judgment on the pleadings, seeking to dismiss the plaintiffs' claims in this litigation. On that same day, plaintiffs filed an amended complaint that includes state antitrust claims based on alleged facts similar to those raised by Sandoz and RareGen in the matter described above. The amended complaint added MSP Recovery Claims Series 44, LLC as a plaintiff and Smiths Medical and CVC as defendants. As a result of the amended complaint, the court ruled that our motion for judgment on the pleadings was moot. In December 2021, we filed a motion to dismiss all of the plaintiffs' claims in the amended complaint, including the new antitrust claims. Smiths Medical also filed a motion to dismiss the plaintiffs' claims against Smiths Medical. On September 23, 2022, the court dismissed all of the plaintiffs' claims against us and Smiths Medical without prejudice.

On October 21, 2022, the plaintiffs filed a motion seeking clarification or reconsideration of the court's order dismissing the complaint without prejudice and argued that the court should allow the plaintiffs an opportunity to amend. That same day, the plaintiffs filed a motion for leave to amend the complaint and attached a proposed second amended complaint. In addition to the claims previously asserted, the proposed second amended complaint adds federal antitrust claims and consumer protection claims under other states' laws. The second amended complaint also names Accredo Health Group, CVS Health Corporation, Express Scripts, Inc., Express Scripts Holding Company, and the Adira Foundation as additional defendants. On October 27, 2022, the court granted plaintiffs' motion for leave to amend, and denied as moot plaintiffs' motion seeking clarification. On that same day, plaintiffs filed the second amended complaint. We filed a motion to reconsider the court's decision to allow plaintiffs to amend their complaint, and that motion was denied. Our deadline to respond to the second amended complaint is March 3, 2023.

We intend to vigorously defend against this lawsuit.

Litigation with Humana and United Healthcare

Humana Inc. and United Healthcare Services, Inc. filed separate lawsuits against us in the U.S. District Court for the District of Maryland on December 13, 2022 and November 14, 2022, respectively. Each of these lawsuits includes allegations similar to those in the *MSP Recovery* matter discussed above concerning our charitable contributions to CVC. In particular, these lawsuits allege that our donations to a charitable organization that assisted patients with affording PAH treatments violated RICO and various state laws. Our deadline to respond to the lawsuits is March 3, 2023.

We intend to vigorously defend against these lawsuits.

340B Program Litigation

We participate in the Public Health Service's 340B drug pricing program (the **340B program**), through which we sell our products at discounted prices to covered entities, including through pharmacies that have contracts with such covered entities (**340B contract pharmacies**). Increasing use of 340B contract pharmacies, coupled with a lack of oversight and transparency, has resulted in increased risks of 340B statutory violations related to the diversion of 340B-purchased drugs to individuals who are not patients of the 340B covered entity, and to prohibited "duplicate discounts" when 340B-purchased drugs are also billed to Medicaid. In November 2020, we notified the U.S. Health Resources and Services Administration (**HRSA**) that we would begin implementing narrowly-tailored 340B contract pharmacy policies with the goal of stemming abuses of the 340B program without upsetting the status quo or creating hardship for covered entities or their patients. At around the same time, a number of other manufacturers also announced their own policies aimed at stemming 340B program abuses.

In December 2020, the U.S. Department of Health and Human Services (**HHS**) General Counsel issued a non-binding Advisory Opinion (the **Advisory Opinion**) concluding that, among other things, pharmaceutical manufacturers are obligated to sell their drugs at the 340B discounted price to an unlimited number of 340B contract pharmacies. In May 2021, HRSA sent a letter to us stating that our 340B contract pharmacy policies violated the 340B statute. HRSA also sent materially similar letters to five other pharmaceutical manufacturers. We responded to that letter by clarifying our policies and requesting additional information from HRSA. To date, HRSA has not responded.

The federal government's pronouncements regarding the use of 340B contract pharmacies have triggered a variety of litigation. In one of those cases, the court concluded that the Advisory Opinion was "legally flawed," and in response HHS withdrew the Advisory Opinion. Notwithstanding the withdrawal of the Advisory Opinion, HRSA has made clear that it is not withdrawing its May 2021 letter to us and the threat of enforcement action.

In June 2021, we commenced litigation against HRSA and HHS in the U.S. District Court for the District of Columbia seeking to vindicate the lawfulness of our 340B program contract pharmacy policies. Despite the litigation, in September 2021, HRSA sent to us, along with the other manufacturers challenging HRSA's 340B interpretation, letters stating that HRSA is referring "this issue to the HHS Office of the Inspector General (**OIG**)" for potential enforcement action. We have not received any communication from the OIG regarding our 340B contract pharmacy policy. Meanwhile, the parties submitted and fully briefed cross-motions for summary judgment, and the court heard oral argument on those motions, and also similar motions in a related case involving Novartis, in October 2021. In November 2021, the court granted our motion for summary judgment in part, and issued a decision holding that the HRSA letters threatening enforcement action "contain legal reasoning that rests upon an erroneous reading of Section 340B." The court explained that "[t]he statute's plain language, purpose, and structure do not *prohibit* drug manufacturers from attaching any conditions to the sales of covered drugs through contract pharmacies. Nor do they *permit* all conditions. Accordingly, any future enforcement action must rest on a new statutory provision, a new legislative rule, or a well-developed legal theory that Section 340B precludes the specific conditions at issue here."

HRSA and HHS appealed to the U.S. Court of Appeals for the District of Columbia Circuit in December 2021, and the appeal is pending. Oral argument took place on October 24, 2022, and the parties await the court's decision.

Litigation involving other manufacturers is also moving forward in parallel with our case, and some of the decisions issued in those cases have reached different conclusions regarding HRSA's and HHS's interpretation of the 340B statute than our case.

We intend to vigorously defend our 340B program contract pharmacy policies.

15. Priority Review Voucher

In December 2020, we entered into an agreement to acquire a rare pediatric disease priority review voucher for \$105.0 million. In January 2021, we closed the transaction and expensed the \$105.0 million within *research and development* in our consolidated statements of operations for the year ended December 31, 2021. We redeemed the voucher in connection with our submission of the NDA for Tyvaso DPI in April 2021.

Schedule II—Valuation and Qualifying Accounts

Years Ended December 31, 2022, 2021, and 2020

(In millions)

	Valuation Allowance on Deferred Tax Assets				
	Balance at Beginning of Year	Additions Charged to Expense	Other Additions	Deductions	Balance at End of Year
Year Ended December 31, 2022	\$ 11.5	\$ 10.9	\$ —	\$ —	\$ 22.4
Year Ended December 31, 2021 ⁽¹⁾	\$ 35.5	\$ 4.4	\$ —	\$ (28.4)	\$ 11.5
Year Ended December 31, 2020 ⁽²⁾	\$ 36.6	\$ —	\$ 3.0	\$ (4.1)	\$ 35.5

(1) Deductions relate primarily to changes in capital investments.

(2) Other Additions relate to changes in our investment in a foreign entity. Deductions relate primarily to changes in capital investments.

	Inventory Reserves			
	Balance at Beginning of Year	Additions Charged to Expense	Deductions	Balance at End of Year
Year Ended December 31, 2022	\$ 15.7	\$ 11.2	\$ (5.3)	\$ 21.6
Year Ended December 31, 2021	\$ 16.8	\$ 10.0	\$ (11.1)	\$ 15.7
Year Ended December 31, 2020	\$ 20.9	\$ 7.7	\$ (11.8)	\$ 16.8

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with participation of our Chairperson and Chief Executive Officer and Chief Financial Officer and Treasurer, has evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) of the Securities Exchange Act of 1934, as of December 31, 2022. Based on that evaluation, our Chairperson and Chief Executive Officer and Chief Financial Officer and Treasurer concluded that our disclosure controls and procedures were effective as of December 31, 2022.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended). Our internal control over financial reporting was designed to provide reasonable assurance to our management and Board of Directors regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. All internal controls over financial reporting, no matter how well designed, have inherent limitations. As a result of these inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those internal controls determined to be effective can provide only reasonable assurance with respect to the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework (2013)*. Management's assessment included an evaluation of the design of our internal control over financial reporting and testing of the operational effectiveness of our internal control over financial reporting. Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

Ernst & Young LLP, an independent registered public accounting firm, has issued an attestation report on our internal control over financial reporting. The report of Ernst & Young LLP is contained in *Item 8* of this Report.

Attestation of Independent Registered Public Accounting Firm

The attestation report of our independent registered public accounting firm regarding internal control over financial reporting is set forth in *Item 8* of this Report under the caption "Report of Independent Registered Public Accounting Firm" and incorporated herein by reference.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

Information as to the individuals serving on our board of directors is set forth below under the heading *Board of Directors*. Additional information required by Item 10 regarding nominees and directors appearing under *Proposal No. 1: Election of Directors* in our definitive proxy statement for our 2023 annual meeting of shareholders currently scheduled for June 26, 2023 (the **2023 Proxy Statement**) is hereby incorporated herein by reference. Information regarding our executive officers appears in *Item 1* of this Report under the heading *Information about our Executive Officers*. Information regarding our Audit Committee and our Audit Committee's financial expert appearing under the heading *Committees of our Board of Directors—Audit Committee* in our 2023 Proxy Statement is hereby incorporated herein by reference.

Information appearing under the heading *Delinquent Section 16(a) Reports* in our 2023 Proxy Statement is hereby incorporated herein by reference.

We have a written Code of Conduct and Business Ethics that applies to our principal executive officer, principal financial officer and our principal accounting officer and every other director, officer and employee of United Therapeutics. The Code of Conduct and Business Ethics is available on our Internet website at <http://ir.unither.com/corporate-governance>. A copy of the Code of Conduct and Business Ethics will be provided free of charge by making a written request and mailing it to our corporate headquarters offices to the attention of the Investor Relations Department. If any amendment to, or a waiver from, a provision of the Code of Conduct and Business Ethics that applies to the principal executive officer, principal financial officer and principal accounting officer is made, we intend to post such information on our Internet website within four business days at www.unither.com.

Board of Directors

Christopher Causey, M.B.A.

Former Consultant and Healthcare Executive

Raymond Dwek, C.B.E., F.R.S.

Emeritus Director, Oxford Glycobiology Institute, Oxford University

Richard Giltner

Former Portfolio Manager at Lyxor Asset Management, an asset management group at Société Générale, S.A.

Katherine Klein, Ph.D.

Professor of Management, The Wharton School of the University of Pennsylvania

Ray Kurzweil

Principal Researcher and AI Visionary, Google Inc.

Linda Maxwell, M.D., M.B.A.

Head and Neck Surgeon; Founding Executive Director, the Biomedical Zone (Canada)

Nilda Mesa, J.D.

Adjunct Professor, Columbia University; Former Director, NYC Mayor's Office of Sustainability

Judy D. Olian, Ph.D.

President, Quinnipiac University

Christopher Patusky, J.D., M.G.A.

Founding Principal, Patusky Associates, LLC

Martine Rothblatt, Ph.D., J.D., M.B.A.

Chairperson and Chief Executive Officer of United Therapeutics

Louis Sullivan, M.D.

President Emeritus, Morehouse School of Medicine; Former Secretary, U.S. Department of Health and Human Services

Tommy Thompson, J.D.

Former Governor of Wisconsin; Former Secretary, U.S. Department of Health and Human Services

Item 11. Executive Compensation

Information concerning executive compensation required by Item 11 will appear under the headings *Director Compensation*, *Compensation Discussion and Analysis*, and *Executive Compensation Data* in our 2023 Proxy Statement and is incorporated herein by reference.

Information concerning the Compensation Committee required by Item 11 will appear under the heading *Compensation Committee Report* in our 2023 Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information regarding beneficial ownership of our common stock required by Item 12 will appear under *Beneficial Ownership of Common Stock* in our 2023 Proxy Statement and is incorporated herein by reference.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table presents information as of December 31, 2022, regarding our securities authorized for issuance under equity compensation plans:

Plan category	Number of securities to be issued upon exercise of outstanding options and RSUs (a) ⁽³⁾	Weighted average exercise price of outstanding options (b) ⁽⁴⁾	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c) ⁽⁵⁾
Equity compensation plan approved by security holders ⁽¹⁾	7,444,885	\$ 128.21	5,507,423
Equity compensation plan not approved by security holders ⁽²⁾	4,385	—	73,748
Total	7,449,270	\$ 128.21	5,581,171

- (1) All outstanding stock options were issued under our two equity incentive plans approved by security holders in 1999 and 2015. The majority of outstanding RSUs were issued under the 2015 Plan. In addition, our employees have outstanding rights to purchase our common stock at a discount as part of our ESPP, which was approved by security holders in 2011. No further awards will be issued under the 1999 Plan. Information regarding these plans is contained in Note 8—*Share-Based Compensation* to our consolidated financial statements.
- (2) We have one equity incentive plan, the 2019 Inducement Stock Incentive Plan, that has not been approved by our shareholders, as permitted by the Nasdaq Stock Market rules. The 2019 Inducement Plan was approved by our Board of Directors in February 2019 and provides for the issuance of up to 99,000 shares of our common stock in the aggregate under awards granted to newly-hired employees. Information regarding this plan is contained in Note 8—*Share-Based Compensation* to our consolidated financial statements.
- (3) Column (a) includes 6,608,019 shares of our common stock issuable upon the exercise of outstanding stock options issued under the 1999 and 2015 Plan; 836,866 shares issuable upon the vesting of outstanding RSUs issued under the 2015 Plan; and 4,385 shares issuable upon the vesting of outstanding RSUs issued under the 2019 Inducement Plan. The 2015 Plan and 2019 Inducement Plan use a share counting formula for determining the number of shares available for issuance under the plans. In accordance with this formula, each option issued under the 2015 Plan counts as one share, while each RSU issued under the 2015 Plan and the 2019 Inducement Plan counts as 1.35 shares and 2.14 shares, respectively. The number under column (a) represents the actual number of shares issuable under our outstanding awards without giving effect to the share counting formula.
- (4) Column (b) represents the weighted average exercise price of the outstanding stock options only. The outstanding RSUs are not included in this calculation because they do not have an exercise price.
- (5) Column (c) includes 2,540,942, 2,966,481, and 73,748 of shares available for future issuance under the ESPP, the 2015 Plan, and the 2019 Inducement Plan, respectively. Under the ESPP, employees may purchase shares based upon a six-month offering period at an amount equal to the lesser of (1) 85 percent of the closing market price of the Common Stock on the first day of the offering period; or (2) 85 percent of the closing market price of the Common Stock on the last day of the offering period. Refer to Note 8—*Share-Based Compensation—ESPP* for more information. The number under column (c) assumes that all 841,251 outstanding RSUs included in column (a) vest. Each RSU is only counted as one share in column (a) because only one share is issuable upon vesting. However, if any RSU does not vest, the number of shares available for future issuance will increase by 1.35 and 2.14, under the 2015 Plan and 2019 Inducement Plan, respectively, because of the share counting formula described in note (3) above.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Information concerning related party transactions and director independence required by Item 13 will appear under the headings *Other Matters—Certain Relationships and Related Party Transactions*, *Our Corporate Governance—Board of Directors and Nominees—Director Independence*, and *Our Corporate Governance—Board Structure—Committees of Our Board of Directors* in our 2023 Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

Information required by Item 14 concerning the principal accounting fees paid by the Registrant and the Audit Committee's pre-approval policies and procedures, will appear under the heading *Audit Matters* in our 2023 Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

In reviewing the agreements included or incorporated by reference as exhibits to this Report, it is important to note that they are included to provide investors with information regarding their terms, and are not intended to provide any other facts or disclose any other information about United Therapeutics or the other parties to the agreements. The agreements contain representations and warranties made by each of the parties to the applicable agreement. These representations and warranties have been made solely for the benefit of the other parties to the applicable agreement, and: (1) should not be treated as categorical statements of fact, but rather as a way of allocating risk between the parties; (2) have in some cases been qualified by disclosures that were made to the other party in connection with the negotiation of the applicable agreement, which disclosures are not necessarily reflected in the agreement; (3) may apply standards of materiality in a way that is different from what may be material to investors; and (4) were made only as of the date of the applicable agreement or such other date or dates as may be specified in the agreement and are subject to more recent developments.

Accordingly, these representations and warranties may not describe the actual state of affairs as of the date they were made or at any other time. Additional information about United Therapeutics may be found elsewhere in this Report and our other public filings, which are available without charge through the SEC's website at <http://www.sec.gov>.

- (a)(1) Our financial statements filed as part of this report on Form 10-K are set forth in the Index to Consolidated Financial Statements under Part II, Item 8 of this Form 10-K.
- (a)(2) The Schedule II—Valuation and Qualifying Accounts is filed as part of this Form 10-K. All other schedules are omitted because they are not applicable or not required, or because the required information is included in our consolidated statements or notes thereto.
- (a)(3) Exhibits filed as a part of this Form 10-K are listed on the Exhibit Index, which is incorporated by reference herein.

Certain exhibits to this report have been included only with the copies of this report filed with the Securities and Exchange Commission. Copies of individual exhibits will be furnished to shareholders upon written request to United Therapeutics and payment of a reasonable fee (covering the expense of furnishing copies). Shareholders may request exhibit copies by contacting: United Therapeutics Corporation, Attn: Investor Relations, 1040 Spring Street, Silver Spring, Maryland 20910.

Exhibit Index

Exhibit No.	Description
2.1*	Exclusive License Agreement, dated as of November 15, 2018, by and between Arena Pharmaceuticals, Inc. and the Registrant, incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K filed January 25, 2019.
3.1	Restated Certificate of Incorporation of the Registrant, incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K filed October 1, 2021.
3.2	Ninth Amended and Restated Bylaws of the Registrant, incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K filed February 5, 2021.

4.1	Reference is made to Exhibits 3.1 and 3.2 .
4.2	Description of Securities Registered under Section 12 of the Exchange Act, incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2021.
10.1	Form of Indemnification Agreement between the Registrant and each of its Directors and Executive Officers, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed October 1, 2021.
10.2**	Amended and Restated Executive Employment Agreement dated as of January 1, 2009, between the Registrant and Martine Rothblatt, incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2009.
10.3**	Amendment to Amended and Restated Executive Employment Agreement between the Registrant and Martine Rothblatt, Ph.D., dated as of January 1, 2015, incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K filed December 17, 2014.
10.4**	Employment Agreement, dated as of June 26, 2016, between the Registrant and Michael Benkowitz, incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed June 22, 2016.
10.5**	Change in Control Severance Agreement between the Registrant and Michael Benkowitz, dated as of February 14, 2012, incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed April 28, 2016.
10.6**	Employment Agreement, dated as of March 13, 2015, between the Registrant and James Edgemond, incorporated by reference to Exhibit 10.55 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2014.
10.7**	Amendment to Employment Agreement, dated as of October 25, 2016, between the Registrant and James Edgemond, incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016.
10.8**	Change in Control Severance Agreement between the Registrant and James Edgemond, dated as of November 12, 2014, incorporated by reference to Exhibit 10.56 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2014.
10.9**	Employment Agreement dated as of June 16, 2001 between the Registrant and Paul Mahon, incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2002.
10.10**	Amendment dated December 11, 2002 to Employment Agreement between the Registrant and Paul Mahon, incorporated by reference to Exhibit 10.43 of the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2002.
10.11**	Amendment dated December 29, 2004 to Employment Agreement between Paul A. Mahon and the Registrant dated June 16, 2001, as previously amended, incorporated by reference to Exhibit 10.4 of the Registrant's Current Report on Form 8-K filed on December 29, 2004.
10.12**	Amendment, dated as of July 31, 2006, to amended Employment Agreement, dated June 16, 2001, between Paul Mahon and the Registrant, incorporated by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed on August 4, 2006.
10.13**	Form of Amendment to Employment Agreement between the Registrant and Paul Mahon, dated as of January 1, 2009, incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2009.
10.14**	Form of Amendment to Employment Agreement between the Registrant and Paul Mahon, dated as of February 22, 2010, incorporated by reference to Exhibit 10.46 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2009.
10.15**	United Therapeutics Corporation Amended and Restated Equity Incentive Plan, as amended effective as of September 24, 2004, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004.
10.16**	First Amendment to the United Therapeutics Corporation Amended and Restated Equity Incentive Plan, effective as of June 2, 2015, incorporated by reference to Exhibit 10.6 to Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2015.
10.17**	Form of terms and conditions for awards granted to Employees by the Registrant under the Amended and Restated Equity Incentive Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on December 17, 2004.
10.18**	United Therapeutics Corporation Supplemental Executive Retirement Plan, effective as of July 1, 2006, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on May 4, 2006.
10.19	United Therapeutics Corporation Supplemental Executive Retirement Plan Rabbi Trust Document entered into on December 28, 2007, by and between the Registrant and Wilmington Trust Company, as trustee, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on December 28, 2007.

Exhibit No.	Description
10.20**	<u>Form of terms and conditions for awards granted to employees on or after March 15, 2011 under the United Therapeutics Corporation 2011 Share Tracking Awards Plan and the United Therapeutics Corporation 2008 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.2 of Registrant's Registration Statement on Form S-8 (Registration No. 333-173858), filed on May 2, 2011.</u>
10.21	<u>Stipulation of Settlement, dated October 25, 2010, among the parties to a derivative lawsuit against the directors and officers of the Registrant identified therein, incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2010.</u>
10.22**	<u>United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on March 18, 2011.</u>
10.23**	<u>First Amendment to the United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed on February 6, 2012.</u>
10.24**	<u>Second Amendment to the United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2012.</u>
10.25**	<u>Third Amendment to the United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on February 4, 2013.</u>
10.26**	<u>Fourth Amendment to the United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on January 31, 2014.</u>
10.27**	<u>Form of grant letter used by Registrant under the United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.4 of the Registrant's Current Report on Form 8-K filed on March 18, 2011.</u>
10.28**	<u>United Therapeutics Corporation Employee Stock Purchase Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012.</u>
10.29**	<u>United Therapeutics Corporation Amended and Restated 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed June 28, 2022.</u>
10.30**	<u>Form of Grant Notice and Standard Terms and Conditions for Non-Qualified Stock Options Granted to Non-Employee Directors under the United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed June 29, 2015.</u>
10.31**	<u>Form of Grant Notice and Standard Terms and Conditions for Non-Qualified Stock Options Granted to Certain Executives under the United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed June 29, 2015.</u>
10.32**	<u>Form of Grant Notice and Standard Terms and Conditions for Non-Qualified Stock Options Granted to Employees under the United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.4 of the Registrant's Current Report on Form 8-K filed June 29, 2015.</u>
10.33**	<u>Form of Grant Notice and Standard Terms and Conditions for Restricted Stock Units Granted to Non-Employee Directors under the United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2016.</u>
10.34**	<u>Form of Grant Notice and Standard Terms and Conditions for Non-Qualified Stock Options Granted to Employees (Performance Vesting) under the United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.59 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2016.</u>
10.35**	<u>Form of Grant Notice and Standard Terms and Conditions for Restricted Stock Units Granted to Employees under the United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.45 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2017.</u>
10.36**	<u>Form of Grant Notice and Standard Terms and Conditions for Stock Options Granted to Certain Executives under the United Therapeutics Corporation Amended and Restated 2015 Stock Incentive Plan (applicable to 2019-2022 Stock Options), incorporated by reference to Exhibit 10.45 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2018.</u>
10.37**†	<u>Form of Grant Notice and Standard Terms and Conditions for Stock Options Granted to Employees (Performance Vesting) under the United Therapeutics Corporation Amended and Restated 2015 Stock Incentive Plan (applicable to performance-based stock options granted on or after March 15, 2023).</u>
10.38**†	<u>Form of Grant Notice and Standard Terms and Conditions for Restricted Stock Units Granted to Employees (Performance Vesting) under the United Therapeutics Corporation Amended and Restated 2015 Stock Incentive Plan (applicable to performance-based restricted stock units granted on or after March 15, 2023).</u>

Exhibit No.	Description
10.39**	<u>United Therapeutics Corporation 2019 Inducement Stock Incentive Plan, incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed March 1, 2019.</u>
10.40**	<u>Form of Restricted Stock Unit Grant Notice and Terms and Conditions under the 2019 Inducement Stock Incentive Plan, incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed March 1, 2019.</u>
10.41*	<u>Wholesale Product Purchase Agreement, dated January 1, 2018, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.51 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2017.</u>
10.42	<u>First Amendment to Wholesale Product Purchase Agreement, dated November 27, 2018, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.47 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2018.</u>
10.43	<u>Second Amendment to Wholesale Product Purchase Agreement, dated February 1, 2019, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.48 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2018.</u>
10.44*	<u>Third Amendment to Wholesale Product Purchase Agreement, dated as of March 1, 2019, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.49 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2018.</u>
10.45+	<u>Fourth Amendment to Wholesale Product Purchase Agreement, dated as of September 18, 2019, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.52 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2019.</u>
10.46+	<u>Fifth Amendment to Wholesale Product Purchase Agreement, dated as of November 13, 2019, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.59 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2019.</u>
10.47+	<u>Sixth Amendment to Wholesale Product Purchase Agreement, dated as of March 1, 2020, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, for the quarter ended March 31, 2020.</u>
10.48+	<u>Seventh Amendment to Wholesale Product Purchase Agreement, dated as of May 12, 2020, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, for the quarter ended June 30, 2020.</u>
10.49	<u>Eighth Amendment to Wholesale Product Purchase Agreement, dated as of May 13, 2020, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q, for the quarter ended June 30, 2020.</u>
10.50+	<u>Ninth Amendment to Wholesale Product Purchase Agreement, dated as of October 6, 2021, by and between Priority Healthcare Distribution, Inc., doing business as CuraScript SD Specialty Distribution, and the Registrant, incorporated by reference to Exhibit 10.57 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2021.</u>
10.51	<u>Specialty Pharmacy Network Agreement, dated as of January 1, 2018, between the Registrant and Accredo Health Group, Inc., incorporated by reference to Exhibit 10.52 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2017.</u>
10.52	<u>First Amendment to Specialty Pharmacy Network Agreement, dated as of February 16, 2022, between the Registrant and Accredo Health Group, Inc., incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022.</u>
10.53+	<u>Second Amendment to Specialty Pharmacy Network Agreement, dated as of June 13, 2022, between the Registrant and Accredo Health Group, Inc., incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022.</u>
10.54	<u>Credit Agreement, dated as of March 31, 2022, among the Registrant, certain of its subsidiaries party thereto, as guarantors, the lenders referred to therein, and Wells Fargo Bank, National Association, as administrative agent and as a swingline lender, incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on April 1, 2022.</u>
10.55+	<u>License and Collaboration Agreement, dated as of September 3, 2018, by and between the Registrant and MannKind Corporation, incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, for the quarter ended June 30, 2022.</u>

Exhibit No.	Description
10.56	<u>Settlement Agreement, dated December 19, 2017, among the United States of America, acting through the United States Department of Justice and on behalf of the Office of Inspector General of the Department of Health and Human Services, and the Registrant, incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on December 20, 2017.</u>
10.57	<u>Corporate Integrity Agreement, dated December 18, 2017, between the Registrant and the Office of Inspector General of the Department of Health and Human Services, incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on December 20, 2017.</u>
21†	<u>Subsidiaries of the Registrant.</u>
23.1†	<u>Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.</u>
31.1†	<u>Certification of Principal Executive Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.</u>
31.2†	<u>Certification of Principal Financial Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.</u>
32.1†	<u>Certification of Principal Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2†	<u>Certification of Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
101†	The following financial information from our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on February 22, 2023, formatted in Inline Extensible Business Reporting Language (iXBRL): (1) our Consolidated Balance Sheets as of December 31, 2022 and 2021, (2) our Consolidated Statements of Operations for each of three years in the period ended December 31, 2022, (3) our Consolidated Statements of Comprehensive Income for each of the three years in the period ended December 31, 2022, (4) our Consolidated Statements of Stockholders' Equity for each of the three years in the period ended December 31, 2022, (5) our Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2022, and (6) the Notes to our Consolidated Financial Statements.
104†	Cover Page Interactive Data File (embedded within the iXBRL document)

+ Certain identified information has been omitted from this exhibit because it is both (1) not material and (2) would be competitively harmful if publicly disclosed.

* Confidential treatment has been requested with respect to certain portions of this exhibit pursuant to Rule 406 of the Securities Act of 1933, as amended or Rule 24b-2 of the Securities Act of 1934, as amended. The omitted portions of this document have been filed with the Securities and Exchange Commission.

** Designates management contracts and compensation plans.

† Filed herewith.

Note: Except as otherwise noted above, all exhibits incorporated by reference to the Registrant's previously filed reports with the Securities and Exchange Commission are filed under File No. 000-26301.

Item 16. Form 10-K Summary

None.

Signatures

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

UNITED THERAPEUTICS CORPORATION

By: /s/ MARTINE ROTHBLATT
Martine Rothblatt, Ph.D.
Chairperson and Chief Executive Officer

February 22, 2023

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

Signatures	Title	Date
<u>/s/ MARTINE ROTHBLATT</u> Martine Rothblatt	Chairperson, Chief Executive Officer and Director (Principal Executive Officer)	February 22, 2023
<u>/s/ JAMES C. EDGEMOND</u> James C. Edgmond	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	February 22, 2023
<u>/s/ CHRISTOPHER CAUSEY</u> Christopher Causey	Director	February 22, 2023
<u>/s/ RAYMOND DWEK</u> Raymond Dwek	Director	February 22, 2023
<u>/s/ RICHARD GILTNER</u> Richard Giltner	Director	February 22, 2023
<u>/s/ KATHERINE KLEIN</u> Katherine Klein	Director	February 22, 2023
<u>/s/ RAYMOND KURZWEIL</u> Raymond Kurzweil	Director	February 22, 2023
<u>/s/ LINDA MAXWELL</u> Linda Maxwell	Director	February 22, 2023
<u>/s/ NILDA MESA</u> Nilda Mesa	Director	February 22, 2023
<u>/s/ JUDY D. OLIAN</u> Judy D. Olian	Director	February 22, 2023
<u>/s/ CHRISTOPHER PATUSKY</u> Christopher Patusky	Director	February 22, 2023
<u>/s/ LOUIS W. SULLIVAN</u> Louis W. Sullivan	Director	February 22, 2023
<u>/s/ TOMMY G. THOMPSON</u> Tommy Thompson	Director	February 22, 2023