UNITED THERAPEUTICS CORP

FORM 10-K
(Annual Report)

Filed 02/22/17 for the Period Ending 12/31/16

Address	1040 SPRING ST
	SILVER SPRING, MD 20910
Telephone	3016089292
CIK	0001082554
Symbol	UTHR
SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Medical Research
Sector	Healthcare
Fiscal Year	12/31

QuickLinks -- Click here to rapidly navigate through this document

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, 2016

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	**52-1984749**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
1040 Spring Street, Silver Spring, MD	**20910**
(Address of Principal Executive Offices)	(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	**Name of each exchange on which registered**
Common Stock, par value $.01 per share and associated preferred stock purchase rights	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 and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

Large accelerated filer ☒	Accelerated filer ☐	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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, 2016, as reported by the NASDAQ Global Select Market was approximately $4,094,026,937.

The number of shares outstanding of the issuer's common stock, par value $0.01 per share, as of February 10, 2017, was 44,961,616.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for the registrant's 2017 annual meeting of shareholders scheduled to be held on June 28, 2017, are incorporated by reference in Part III of this Form 10-K.

TABLE OF CONTENTS

PART I

ITEM 1. BUSINESS

Overview

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. We market and sell four commercial therapies in the United States to treat pulmonary arterial hypertension (PAH): Remodulin ® (treprostinil) Injection; Tyvaso ® (treprostinil) Inhalation Solution (Tyvaso); Orenitram ® (treprostinil) Extended-Release Tablets (Orenitram); and Adcirca ® (tadalafil) Tablets (Adcirca). We also market and sell an oncology product in the United States, Unituxin ® (dinutuximab) Injection (Unituxin), which is approved for treatment of high-risk neuroblastoma. Outside the United States, our only significant revenues are derived from the sale of Remodulin, which is approved in Europe and various other countries. We are also engaged in research and development of new indications and delivery devices for our existing products, as well as new products to treat PAH and other conditions. Finally, we are engaged in early-stage research and development of a number of organ transplantation-related technologies.

We generate revenues from sales of our five commercially approved products noted above. Remodulin was approved by the U.S. Food and Drug Administration (FDA) for subcutaneous and intravenous administration in 2002 and 2004, respectively, and has been sold commercially in the United States since 2002. Tyvaso and Adcirca were both approved by the FDA and launched commercially in the United States in 2009. Orenitram was approved by the FDA in 2013 and Unituxin was approved by the FDA in 2015. We commenced sales of Orenitram and Unituxin during the second quarter of 2014 and third quarter of 2015, respectively. We expect sales of our current commercial products will continue to be our primary sources of revenues for the next several years. Our sales and marketing staff supports the availability of our commercial products in the United States, and these efforts are supplemented by our contract distributors. Outside the United States, our contract distributors are primarily responsible for sales and marketing efforts.

United Therapeutics was incorporated in Delaware in June 1996. 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
Remodulin	Continuous subcutaneous	PAH	Commercial in the U.S., most of Europe*, Argentina, Brazil, Canada, Chile, China, Israel, Japan, Mexico, Peru, Saudi Arabia, South Korea, Taiwan and Venezuela	Worldwide
Remodulin	Continuous intravenous	PAH	Commercial in the U.S., most of Europe*, Argentina, Canada, China, Israel, Japan, Mexico, Peru, Saudi Arabia, South Korea and Switzerland	Worldwide
Tyvaso	Inhaled	PAH	Commercial in the U.S. and Israel	Worldwide
Adcirca	Oral	PAH	Commercial in the U.S.	United States
Orenitram	Oral	PAH	Commercial in the U.S.	Worldwide
Unituxin	Intravenous	High-risk neuroblastoma	Commercial in the U.S.	Worldwide

* We have obtained approval for subcutaneous and intravenous Remodulin in 24 member countries of the European Economic Area (EEA), as well as other non-EEA countries in Europe, and have received pricing approval in most of these countries.

Products to Treat Cardiopulmonary Diseases

Pulmonary Arterial Hypertension

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 FDA-approved therapies for PAH focus on three distinct molecular pathways: the prostacyclin pathway, the nitric oxide (NO) pathway, and the endothelin (ET) 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 substance that relaxes the pulmonary

blood vessels, prevents platelet aggregation and inhibits the proliferation of smooth muscle cells in the pulmonary vessels. Therefore, drugs that mimic the action of prostacyclin, known as prostacyclin analogues, are established PAH treatments. Another class of therapy, called IP prostacyclin receptor agonists, has recently been developed to address PAH through the prostacyclin pathway. As compared with prostacyclin analogues, which broadly mimic the effect of prostacyclin, IP prostacyclin receptor agonists bind selectively to the IP receptor, one of several prostacyclin receptors.

- *Phosphodiesterase Type 5 (PDE-5) Inhibitors and Guanylate Cyclase (sGC) Stimulators.* Patients with PAH have also been shown to have reduced levels of the enzyme responsible for producing NO, a naturally occurring substance in the body that causes relaxation of the pulmonary blood vessels. NO 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 NO. When NO 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 substance 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 (ETRAs).

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. Remodulin, Tyvaso and Orenitram are prostacyclin analogues, and Adcirca is a PDE-5 inhibitor.

The clinical severity of PAH is classified according to a system originally developed for heart failure by the New York Heart Association and then modified by the World Health Organization (WHO) for patients with PAH, 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.

PAH is a subset of the condition more broadly known as pulmonary hypertension. The WHO has classified pulmonary hypertension into five groups, with PAH being designated WHO Group 1, which includes multiple etiologies such as idiopathic (meaning the cause is unknown) and heritable PAH, as well as PAH associated with connective tissue diseases. While our PAH therapies' labeling is limited to the treatment of WHO Group 1 PAH, we are engaged in research and development efforts to expand the use of Orenitram to treat pulmonary hypertension in certain categories of WHO Groups 2 and 5, and Tyvaso to treat pulmonary hypertension in certain categories of WHO Group 3. For further details, see *Research and Development* below.

Remodulin

One of our lead products for treating PAH is Remodulin, the active pharmaceutical ingredient of which is a prostacyclin analogue known as treprostinil. We sell Remodulin to specialty pharmaceutical distributors in the United States and to pharmaceutical distributors internationally. We recognized approximately $602.3 million, $572.8 million and $553.7 million in Remodulin net product sales, representing 38 percent, 39 percent and 43 percent of our total revenues for the years ended December 31, 2016, 2015 and 2014, respectively. The FDA approved Remodulin as a continuous subcutaneous infusion therapy in 2002, and as a continuous intravenous infusion therapy in 2004. 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 approved for the treatment of PAH in 39 countries by continuous subcutaneous administration and in 35 countries by continuous intravenous administration, and is sold commercially in most of these countries. Applications for approval of both subcutaneous and intravenous Remodulin are under review in other countries.

We believe 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 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 intravenously or 72 hours subcutaneously before refilling the external infusion pump, and is packaged as an aqueous solution so patients do not have to reconstitute the drug before refilling their pumps. This profile contrasts favorably with the other continuously infused prostacyclins in 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.

We have settled patent litigation with three generic drug companies that filed abbreviated new drug applications (ANDAs) with the FDA to market generic versions of Remodulin in the United States. The first such settlement permits Sandoz Inc. (Sandoz) to launch its generic version of Remodulin in the United States in June 2018 (or earlier in certain circumstances). The second and third settlements permit Teva Pharmaceuticals USA, Inc. (Teva) and Par Sterile Products, LLC (Par) to launch their generic versions of Remodulin in the United States in December 2018 (or earlier in certain circumstances). For further detail, see the section below entitled *Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity—Generic Competition*.

There are serious adverse events 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 blood stream 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.

Tyvaso

We commenced commercial sales of Tyvaso, our inhaled treprostinil product, in the United States in 2009. We sell Tyvaso to the same specialty pharmaceutical distributors in the United States that distribute Remodulin. For the years ended December 31, 2016, 2015 and 2014, we recognized approximately $404.6 million, $470.1 million and $463.1 million in Tyvaso net product sales, representing 25 percent, 32 percent and 36 percent, respectively, of our total revenues.

Tyvaso is administered four times a day by inhaling up to nine 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 ultra-sonic nebulizer that provides a dose of Tyvaso on a breath-by-breath basis. 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.

Ventavis ® (iloprost) is the only other FDA-approved inhaled prostacyclin analogue. 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.

In 2009, the FDA approved Tyvaso for the treatment of PAH patients to improve exercise capacity using the Tyvaso Inhalation System. Studies establishing effectiveness included predominately patients with functional class III symptoms (may not have symptoms at rest but activities are greatly limited by shortness of breath, fatigue, or near fainting). Tyvaso was generally well tolerated in our trials. The most common adverse events were transient cough, headache, nausea, dizziness and flushing. Tyvaso is also approved in Israel, where we commenced commercial sales during the second quarter of 2015.

We filed a Marketing Authorization Application (MAA) in December 2008 for Tyvaso with the European Medicines Agency (EMA) using the centralized filing process, but withdrew our MAA from consideration by the EMA due to the EMA's major objection related to findings of non-compliance with good clinical practices at two clinical sites. We are evaluating the resubmission of Tyvaso for EMA approval based on experience with the drug since it was approved by the FDA.

Orenitram

Orenitram is an extended-release, oral tablet form of treprostinil, which we launched commercially in the United States during the second quarter of 2014. 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 Remodulin and Tyvaso. For the years ended December 31, 2016, 2015 and 2014, we recognized approximately $157.2 million, $118.4 million and $41.2 million in Orenitram net product sales, representing ten percent, eight percent and three percent, respectively, of our total revenues. Orenitram was approved by the FDA in December 2013 for treatment of PAH patients to improve exercise capacity. The primary study that established efficacy included predominately patients with functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%). The most common side effects observed in our clinical studies were headache, nausea and diarrhea. We have not submitted Orenitram for approval in major markets outside the United States.

Adcirca

We began selling Adcirca in 2009. 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 the treatment of erectile dysfunction. We acquired the commercial rights to Adcirca for the 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. For the years ended December 31, 2016, 2015 and 2014, we recognized approximately $372.2 million, $278.8 million and $221.5 million in Adcirca net product sales, representing 23 percent, 19 percent and 17 percent, respectively, of our total revenues.

In 2009, the FDA approved Adcirca with a recommended dose of 40 mg, making it the only once-daily PDE-5 inhibitor for the 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.

Prior to the approval of Adcirca, Revatio ®, which is marketed by Pfizer Inc. (Pfizer), was the only PDE-5 inhibitor approved for the treatment of PAH. Sildenafil citrate, the active ingredient in Revatio, is also the active ingredient in Viagra ®, which is marketed by Pfizer for the treatment of erectile dysfunction. In 2012, several companies launched generic formulations of sildenafil citrate. Revatio and generic sildenafil citrate are dosed three times daily.

In September 2014, Gilead Sciences, Inc. (Gilead) announced the results of a study of ambrisentan (an ETRA) and tadalafil in PAH patients as a first-line combination treatment, compared to treating PAH patients with only ambrisentan or tadalafil. In the study, first-line treatment with both therapies reduced the risk of clinical failure (a composite endpoint that incorporates clinical worsening events—death, hospitalization and disease worsening—and a component of unsatisfactory long-term clinical response) compared to a monotherapy treatment by 50 percent. Based on these results, in October 2015, the FDA approved an update to the NDA for Letairis ® (ambrisentan), permitting the use of Letairis in combination with tadalafil for PAH to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.

Products 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 (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the 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, composed of a combination of mouse and human DNA, monoclonal antibody 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.

We commenced U.S. sales of Unituxin in the third quarter of 2015. For the years ended December 31, 2016 and 2015, we recognized approximately $62.5 million and $20.5 million in Unituxin net product sales, representing four percent and one percent, respectively, of our total revenues.

Research and Development

We focus most of our research and development efforts on the following pipeline programs:

Product	Mode of Delivery	Indication	Current Status STUDY NAME CAPS	Target FDA Approval Date	Our Territory	Target U.S. Patient Population Size
RemoSynch™ (Implantable System for Remodulin)	Continuous intravenous via implantable pump	PAH	Medtronic PMA pending (FDA action anticipated April 2017). UT NDA pending (FDA action anticipated June 2017).	2017	United States, United Kingdom, Canada, France, Germany, Italy and Japan	6,000
RemUnity™ (treprostinil)	Continuous subcutaneous via pre-filled, semi-disposable pump	PAH	Pre-NDA	2018	Worldwide	6,000
Dinutuximab	Injection or infusion	Multiple GD2 expressing cancers	Phase II/III	2019-2023 for accelerated approval and other regulatory pathways	Worldwide	12,000
OreniPlus™ (Orenitram in combination with approved background therapy)	Oral	PAH (decrease morbidity and mortality)	Phase IV *FREEDOM-EV*	2019	Worldwide	15,000
Tysuberprost™ (esuberaprost in combination with Tyvaso)	Oral (esuberaprost) Inhaled (Tyvaso)	PAH (decrease morbidity and mortality)	Phase III *BEAT*	2019	North America, Europe, Mexico, South America, Egypt, India, South Africa and Australia	10,000
Tyvaso-ILD™ (treprostinil)	Inhaled	Pulmonary hypertension associated with idiopathic pulmonary fibrosis (WHO Group 3)	Phase III *INCREASE*	2020	Worldwide	27,500
Aurora-GT™ (eNOS gene therapy)	Intravenous injection	PAH	Phase II/III *SAPPHIRE*	2020*	United States**	10,000
OreniLeft™ (treprostinil)	Oral	Pulmonary hypertension associated with left ventricular diastolic dysfunction (WHO Group 2)	Phase III *SOUTHPAW*	2021	Worldwide	50,000
OreniCell™ (treprostinil)	Oral	Reduce morbidity and mortality in patients with pulmonary hypertension associated with sickle cell disease (WHO Group 5)	Phase II/III *IRONS*	2022	Worldwide	25,000
Manufactured Organs	Transplant	End-stage organ failure	Pre-clinical	2023	Worldwide	> 30,000

* Reflects anticipated Canadian approval date. FDA filing and approval will follow Canadian approval.

** Canadian rights are held by an affiliated Canadian entity, of which we hold a majority financial stake.

RemoSynch (Implantable System for Remodulin)

We are working with Medtronic, Inc. (Medtronic) on a program to develop Medtronic's proprietary intravascular infusion catheter to be used with its SynchroMed ® II implantable infusion pump and related infusion system components (together referred to as the Implantable System for Remodulin, or RemoSynch) in order to deliver Remodulin for the treatment of PAH. The SynchroMed

II device is already approved for delivery of medication to treat neuropathic pain. With our funding, Medtronic completed the DelIVery clinical trial, which studied the safety of the Implantable System for Remodulin. The primary objective was to demonstrate a rate of catheter-related complications below 2.5 per 1,000 patient-days while using the Implantable System for Remodulin. In September 2013, Medtronic informed us that this primary objective was met. If the Implantable System for Remodulin is approved, the technology has the potential to reduce many of the patient burdens and other complications associated with the use of external pumps to administer prostacyclin analogues. In order to launch RemoSynch in the United States, Medtronic and we are pursuing parallel regulatory filings relating to the device and the drug, respectively. Medtronic's PMA relating to the device is pending review, with FDA action anticipated in April 2017. We have resubmitted our NDA requesting FDA approval to allow the use of Remodulin with the Implantable System for Remodulin, and anticipate FDA action in June 2017.

Medtronic is entirely responsible for regulatory approvals and all manufacturing and quality systems related to its infusion pump and related components. Medtronic has received a consent decree citing violations of the quality system regulation for medical devices and requiring it to stop manufacturing, designing and distributing SynchroMed II implantable infusion pump systems, except in limited circumstances, until the FDA determines that Medtronic has met all the provisions listed in the consent decree. It is unclear how this consent decree will impact our ability to obtain FDA approval for RemoSynch, or its commercial prospects if approved.

RemUnity

In December 2014, we entered into an exclusive agreement with DEKA Research & Development Corp. (DEKA) to develop a pre-filled, semi-disposable pump system for subcutaneous delivery of treprostinil, which we call the RemUnity system. Under the terms of the agreement, we are funding the development costs related to the RemUnity system and will pay product fees and a single-digit royalty to DEKA based on commercial sales of the system and the treprostinil drug product sold for use with the system. Currently, we are engaged in engineering, design and development efforts to optimize the RemUnity pump to deliver treprostinil in pre-filled reservoirs, and intend to complete human factor studies in healthy volunteers and functionality testing in patients before submitting an application to the FDA to approve the pre-filled RemUnity pump.

Tyvaso and Tyvaso-ILD

We are developing further enhancements intended to make the Tyvaso Inhalation System easier to use and have submitted a supplement for the new device, with FDA action anticipated in late 2017. In addition, we have commenced a phase III registration study called INCREASE, which is a study of Tyvaso in patients with WHO Group 3 pulmonary hypertension associated with interstitial lung disease (specifically associated with idiopathic pulmonary fibrosis or emphysema), which we refer to as Tyvaso-ILD. There are presently no FDA approved therapies indicated for treatment of WHO Group 3 pulmonary hypertension.

Orenitram, OreniPlus, OreniLeft and OreniCell

In December 2013, the FDA approved Orenitram for the treatment of PAH in WHO Group 1 patients to improve exercise capacity. The primary study that supported efficacy of Orenitram was a 12-week monotherapy study (FREEDOM-M) in which PAH patients were not on any approved background PAH therapy.

We believe that in order for Orenitram to reach its full commercial potential, we need to complete further studies to support an amendment to Orenitram's label to indicate that Orenitram delays morbidity and mortality (also known as "time to clinical worsening") in PAH patients who are on an approved oral background therapy. We refer to this program to improve Orenitram's label as OreniPlus. As such, we are conducting a phase IV registration study called FREEDOM-EV, which is intended to support such a label amendment if successful.

We are also planning studies of Orenitram in patients with WHO Group 2 pulmonary hypertension (specifically associated with left ventricular diastolic dysfunction), which we refer to as OreniLeft, and WHO Group 5 pulmonary hypertension (specifically associated with sickle cell disease), which we refer to as OreniCell. There are presently no FDA approved therapies indicated for treatment of WHO Group 2 or 5 pulmonary hypertension.

Tysuberprost

In July 2012, we completed a phase I safety trial of esuberaprost, a single-isomer orally bioavailable prostacyclin analogue, and the data suggested that dosing esuberaprost four times a day was safe. We believe that esuberaprost and treprostinil have differing prostacyclin receptor-binding profiles and thus could provide benefits to certain groups of patients with differing sets of safety and efficacy profiles. We also believe that inhaled treprostinil and oral esuberaprost have complimentary pharmacokinetic and pharmacodynamic profiles, which indicate that they should provide greater efficacy in combination. As a result, we are conducting a phase III registration study called BEAT (***BE*** raprost 314d ***A*** dd-on to ***T*** yvaso) to evaluate the clinical benefit and safety of esuberaprost in combination with Tyvaso for patients with PAH who show signs of deterioration on inhaled treprostinil or have a less than optimal response to inhaled treprostinil treatment. We refer to the resulting combination of esuberaprost and Tyvaso therapies as Tysuberprost.

Unituxin

Under our BLA approval for Unituxin, the FDA has imposed certain post-marketing requirements and post-marketing commitments on us. We are conducting additional clinical and non-clinical studies to satisfy these requirements and commitments. While we believe we will be able to complete these studies, any failure to satisfy these requirements or commitments could result in penalties, including fines or withdrawal of Unituxin from the market, unless we are able to demonstrate good cause for the failure.

In addition, we are planning studies of Unituxin in adult patients with other forms of GD2-expressing cancers. These research and development efforts into new indications for Unituxin have been substantially outsourced to a contract research organization called Precision Oncology, LLC.

Finally, we are working on the development of a fully humanized (non-chimeric) version of dinutuximab, the active ingredient in Unituxin. We intend this new version to reduce some of the side effects associated with Unituxin, which is a chimeric form of the drug composed of a combination of mouse and human DNA.

Aurora-GT

We are planning a phase II/III study 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 NO-synthase (eNOS), expanded ex-vivo and then delivered to the same patient. This product is intended to rebuild the blood vessels in the lungs that are destroyed by PAH.

Organ Transplantation

We are engaged in research and development of a variety of technologies designed to increase the supply of transplantable organs and tissues and improve outcomes for transplant recipients. These programs include preclinical research and development of alternative tissue sources through tissue and organ xenotransplantation, as well as regenerative medicine to create engineered organs and organ tissues. Although our primary focus is on engineered lungs, we are also developing technology for other engineered organs, such as kidneys and hearts. Through our wholly-owned subsidiary, Lung

Biotechnology PBC, we are also developing technologies to improve outcomes for lung transplant recipients and to increase the supply of donor lungs through ex-vivo lung perfusion.

Research and Development Expenditures

We have incurred substantial expenses for our research and development activities and expect to continue to do so in connection with the programs described above. For details regarding our research and development expenses, see *Part II—Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations—Overview—Research and Development.*

Sales and Marketing

Our marketing strategy for our commercial products is to use our sales and marketing teams to reach out to the prescriber community to: (1) increase PAH awareness; (2) increase understanding of the progressive nature of PAH; and (3) increase awareness of our commercial products and how they fit into the various stages of disease progression and treatment. Our sales and marketing teams consisted of approximately 130 employees as of December 31, 2016. During the second half of 2016, we consolidated and restructured our domestic sales force into a unified team that sells all of our PAH products, in order to better educate physicians about how our products can be used to create a "continuum of care" for treating patients across all stages of the disease. Previously, our sales and marketing personnel were divided into two teams that sold different PAH products.

Distribution of Commercial Products

United States Distribution of Remodulin, Tyvaso, Orenitram, and Unituxin

We distribute Remodulin, Tyvaso and Orenitram throughout the United States through two contracted specialty pharmaceutical distributors: Accredo Health Group, Inc. (Accredo) and CVS Caremark (Caremark). 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 Caremark 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 Remodulin, Tyvaso or Orenitram 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 Caremark assist us with the administration of these programs.

In the second quarter of 2015, we entered into an exclusive distribution agreement with ASD Specialty Healthcare, Inc. (ASD), an affiliate of AmerisourceBergen Corporation, to distribute Unituxin in the United States. 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 in the single-digit percentages per year.

United States Distribution of Adcirca

Under our manufacturing and supply agreement with Lilly (see *Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity* below for more details), Lilly manufactures Adcirca and

distributes on our behalf through Lilly's wholesaler network, which includes Accredo and Caremark, 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. When customers take delivery of Adcirca, 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 expiration or termination of the license agreement. 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. Since receiving FDA approval of Adcirca, Lilly has generally increased the net wholesale price of Adcirca two or three times each year by approximately nine to ten percent each time. 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 Remodulin

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, Israel and the Middle East, Asia and South and Central America. We also distribute Remodulin in Canada through a specialty pharmaceutical wholesaler. In some of the European markets where we are not licensed to market Remodulin, such as Spain and the United Kingdom, we sell (but do not market) Remodulin 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.

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, 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.

Remodulin, Tyvaso and Orenitram Proprietary Rights

We have a number of issued patents and pending patent applications covering the stable prostacyclin analogue known as treprostinil, which is the active pharmaceutical ingredient in Remodulin, Tyvaso and Orenitram.

In January 1997, we acquired patents covering the use of treprostinil for PAH from GlaxoSmithKline PLC (formerly Glaxo Wellcome, Inc.) (Glaxo) in exchange for certain payments including a royalty on sales of any product containing treprostinil. All of these patents expired in October 2014, as did our royalty payment obligation to Glaxo.

In October 1997, we filed patent applications for a new synthesis method for treprostinil in the United States, Europe and various other countries. These applications resulted in the grant of three patents in the United States, all of which expire in October 2017, as well as patents granted in a number of other countries which expire in October 2018.

We continue to conduct research into new methods to synthesize treprostinil and have filed a number of additional patent applications relating to manufacturing treprostinil, several of which have already been granted in the United States. One such patent was granted, expiring in 2028, and is listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book (see *Orange Book* below), for Remodulin, Tyvaso and Orenitram.

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

- *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. All four of these patents are listed in the Orange Book.

- *Tyvaso.* We have been granted two U.S. patents, as well as patents in other countries, for Tyvaso that cover methods of treating PAH by inhaled delivery. These patents will expire in the United States in 2018 and in various countries throughout the world in 2020. We recently were granted two additional patents directed to a method of treating pulmonary hypertension and a kit for treating pulmonary hypertension. These two new patents expire in 2028 and are listed in the Orange Book. Counterparts to these patents are issued in several other countries.

- *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 relating to Remodulin, Tyvaso 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 six unexpired Orange Book-listed patents with expiration dates ranging from 2017 to 2029. Tyvaso currently has six unexpired Orange Book listed patents with expiration dates ranging from 2017 to 2028. Orenitram currently has twelve unexpired Orange Book

listed patents with expiration dates ranging from 2017 to 2031. Additional patent applications are pending, and if granted, may be eligible for listing in the Orange Book.

Regulatory Exclusivity

Remodulin's regulatory exclusivity in the U.S. and Europe has expired. In June 2010, the FDA granted orphan drug designation for Tyvaso, which resulted in an orphan exclusivity period that expired in July 2016. In April 2004, the EMA designated Tyvaso an orphan medicinal product for the 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. As a result of FDA approval of our NDA for Orenitram as a new dosage form, Orenitram had three years of market exclusivity for PAH, which expired in December 2016. A request for orphan drug designation for Orenitram was denied by the FDA.

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. This royalty will be paid for approximately twelve years commencing with the first product sale, which occurred in the second quarter of 2014.

Generic Competition

We settled litigation with Sandoz, Teva and Par relating to their ANDAs seeking FDA approval to market generic versions of Remodulin before the expiration of certain of our U.S. patents. Under the terms of our settlement agreements, Sandoz will be permitted to market its generic version of Remodulin in the United States beginning in June 2018, and both Teva and Par will be permitted to market their generic versions of Remodulin in the United States in December 2018, although each of these companies may be permitted to enter the market earlier under certain circumstances.

We are engaged in litigation with Watson Laboratories, Inc. (Watson), based on its ANDA to market a generic version of Tyvaso before the expiration of certain of our U.S. patents at various dates from November 2018 through December 2028. We also are engaged in litigation with Actavis Laboratories FL, Inc. (Actavis), contesting its ANDA to market a generic version of the 0.25 mg, 1.0 mg and 2.5 mg strengths of Orenitram before the expiration of certain of our U.S. patents at various dates from 2024 through 2031.

Finally, SteadyMed Ltd. (SteadyMed) has filed a petition for *inter partes* review seeking to invalidate the claims of one of our patents that expires in December 2028 and relates to treprostinil (U.S. Patent No. 8,497,393, which we refer to as the '393 Patent), which is the active ingredient in Remodulin, Tyvaso and Orenitram. In April 2016, the Patent Trial and Appeal Board (PTAB) of the U.S. Patent and Trademark Office instituted an *inter partes* review of the '393 Patent on the basis of SteadyMed's petition. The PTAB preliminarily agreed with SteadyMed's arguments concerning invalidity, and initially found that there is a reasonable likelihood that SteadyMed would prevail in challenging the '393 patent. Oral argument was held before the PTAB in November 2016. We are currently awaiting the PTAB's final decision, which we expect in or before April 2017. SteadyMed announced that it is developing a product called Trevyent ®, which is a single-use, pre-filled pump intended to deliver a two-day supply of treprostinil subcutaneously using SteadyMed's PatchPump ® technology. In January 2016, SteadyMed announced that Trevyent had been granted orphan drug

designation by the FDA for the treatment of PAH. SteadyMed has announced plans to file an NDA for Trevyent during the second quarter of 2017, and launch the product in 2018.

For further details regarding the Watson, Actavis and SteadyMed matters, please see Note 19— *Litigation* , to our consolidated financial statements.

As a result of our settlements with Sandoz, Teva and Par, we expect to see generic competition for Remodulin from these companies in the United States beginning in June 2018 (Sandoz) and December 2018 (Teva and Par) (or earlier under certain circumstances). This increased competition could reduce our net product sales and profits. In addition, while we intend to vigorously enforce our intellectual property rights relating to our products, there can be no assurance that we will prevail in defending our patent rights, or that additional challenges from other ANDA filers or other challengers will not surface with respect to our products. Our patents could be invalidated, found unenforceable or found not to cover one or more generic forms of Remodulin, Tyvaso or Orenitram. If any ANDA filer were to receive approval to sell a generic version of Remodulin, Tyvaso or Orenitram and/or prevail in any patent litigation, the affected product(s) would become subject to increased competition, which could reduce our net product sales and profits.

Certain patents for Revatio, a PDE-5 inhibitor marketed by Pfizer for treatment of PAH, expired in 2012, leading several manufacturers to launch generic formulations of sildenafil citrate, the active ingredient in Revatio. Generic sildenafil's lower price relative to Adcirca could lead to pressure from payers to use generic products within the same class of therapy initially, which could erode Adcirca's market share and limit its potential sales. Although we believe Adcirca's once-daily dosing regimen provides a significant competitive advantage over generic sildenafil's multiple dosing regimen, government payers and private insurance companies may favor the use of less expensive generic sildenafil over Adcirca. Thus far, we have not observed any measurable impact of generic sildenafil on sales of Adcirca; however, circumstances could change over time and our revenues could be adversely impacted. The U.S. patent for Adcirca for the treatment of pulmonary hypertension will expire in November 2017, after which time we expect to see generic competition for Adcirca that could have a material adverse impact on our Adcirca revenues.

Patent expiration and generic competition for any of our commercial PAH products could have a significant, adverse impact on our revenues and profits, and is 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 profit* s, contained in *Item 1A — Risk Factors* included in this Report.

Lilly Agreements Related to Adcirca

In 2008, we entered into several agreements with Lilly regarding Adcirca, including a license agreement and a manufacturing and supply agreement.

License Agreement

Under the terms of the license agreement, Lilly granted us an exclusive license for the right to develop, market, promote and commercialize Adcirca for the treatment of pulmonary hypertension in the United States. We agreed to pay Lilly royalties equal to five percent of our net product sales of Adcirca, as a pass through of Lilly's third-party royalty obligations, for so long as Lilly is required to make such payments.

Lilly retained the exclusive rights to develop, manufacture and commercialize pharmaceutical products containing tadalafil, the active pharmaceutical ingredient in Adcirca, for the treatment of pulmonary hypertension outside of the United States and for the 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.

The license agreement will continue in effect until the later of: (1) expiration, lapse, cancellation, abandonment or invalidation of the last claim to expire within a Lilly patent covering the commercialization of Adcirca for the treatment of pulmonary hypertension in the United States; or (2) expiration of any government-conferred exclusivity rights to use Adcirca for the treatment of pulmonary hypertension in the United States. The U.S. patent for Adcirca for the treatment of pulmonary hypertension will expire in November 2017. Lilly has two additional patents expiring in 2020 covering Adcirca and claiming pharmaceutical compositions and free drug particulate forms. The PTAB issued a final decision finding these patents invalid as the result of an *inter partes* review proceeding initiated by Actelion Pharmaceuticals Ltd (Actelion). Lilly's appeal of the PTAB's decision is pending before the United States Court of Appeals for the Federal Circuit. As a result, it is unclear whether our license agreement will expire in November 2017. In any event, we are likely to face generic competition following the expiration of the November 2017 patent, as the FDA has already tentatively approved ANDAs filed by several generic companies to market generic versions of Adcirca following the expiration of the November 2017 patent.

We have the right to terminate the license agreement upon six months written notice to Lilly. Lilly has the right to terminate in the event of a change of control of our company. Either party may terminate upon a material breach by the other party of the license agreement or the manufacturing and supply agreement, described above.

Manufacturing and Supply Agreement

Under the terms of the manufacturing and supply agreement, Lilly agreed to manufacture Adcirca and distribute it on our behalf via its pharmaceutical 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 its manufacture by Lilly. Adcirca is shipped to customers, generally pharmaceutical wholesalers, in accordance with customers' purchase orders received by Lilly. Lilly invoices and collects amounts due from the customer subject to customary discounts and rebates, if any, and remits the collections to us. Although Lilly is providing these services on our behalf, we maintain the risk of loss as it pertains to inventory, product returns and nonpayment of sales invoices. The manufacturing and supply agreement will continue in effect until expiration or termination of the license agreement.

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

In 2010, we entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) of the United States National Institutes for Health (NIH) to collaborate on the late-stage development and regulatory approval process for Unituxin for children with high-risk neuroblastoma and patients with other forms of cancer. In lieu of a royalty payment to the NCI, we are obligated to provide the NCI with Unituxin for certain of its studies free of charge. We previously received orphan drug designation for Unituxin from the FDA. Orphan designation, coupled with FDA approval of our BLA in March 2015, confers an exclusivity period through March 2022, during which the FDA may not approve any application to market the same drug for the same indication, except in limited circumstances. In addition, approval of our BLA conferred a 12-year exclusivity period through March 2027, during which the FDA may not approve a biosimilar for Unituxin. Under a non-exclusive license agreement with The Scripps Research Institute, we pay a royalty of one percent of net Unituxin sales.

Medtronic Agreement

We are collaborating with Medtronic under an exclusive agreement to develop and commercialize Medtronic's proprietary intravascular infusion catheter for use with Medtronic's SynchroMed II implantable infusion pump and related infusion system components (together referred to as the Implantable System for Remodulin, or RemoSynch) to deliver Remodulin for the treatment of PAH in the United States, United Kingdom, Canada, France, Germany, Italy and Japan. Under our agreement, we have been working together at our expense to develop RemoSynch, conduct a clinical trial (which was completed in 2013) and obtain regulatory approval. If this development program is successful, our agreement provides that, upon commercialization, we will purchase infusion pumps and supplies from Medtronic and will also pay a ten percent royalty to Medtronic based on net product sales of Remodulin for use in the Implantable System for Remodulin within the exclusive territories, subject to certain adjustments specified in the agreement. The Implantable System for Remodulin will be exclusive to Remodulin so long as we purchase a minimum percentage of our annual requirement for implantable pump systems from Medtronic. We will be solely responsible for all marketing and promotion of RemoSynch for the treatment of PAH in the exclusive territories.

Tysuberprost and the Toray Amended License Agreement

In 2000, we licensed from Toray Industries, Inc. (Toray) the exclusive right to develop and market beraprost for cardiovascular indications. Beraprost is a chemically stable oral prostacyclin analogue in a sustained release formulation, which is approved to treat PAH in Japan and certain other countries. This license gives us exclusive rights to develop beraprost and its variants (including esuberaprost) throughout North America, Europe, and certain other territories. We are currently developing esuberaprost under this license agreement in combination with Tyvaso, which we refer to collectively as Tysuberprost.

Pursuant to a March 2007 amendment to our license agreement with Toray, we issued 200,000 shares of our common stock to Toray. Toray has the right to request that we repurchase these shares (which have since split into 400,000 shares) upon 30 days prior written notice at the price of $27.21 per share. The 2007 amendment also provided for certain milestone payments during the development period and upon receipt of regulatory approval for beraprost in the United States or the EU.

In 2011, we amended our license agreement with Toray to reduce the royalty rates in exchange for a total of $50.0 million in equal, non-refundable payments to Toray over the five-year period ending in 2015. As of December 31, 2015, this obligation was fully satisfied. Toray has the right to terminate the license agreement in the event of a change of control of our company under certain circumstances.

In 2011, the FDA granted orphan designation for esuberaprost for treatment of pulmonary arterial hypertension. Thus, the FDA should grant orphan drug exclusivity if Tysuberprost is approved; such exclusivity will extend for seven years from approval.

DEKA Agreement

In December 2014, we entered into an exclusive agreement with DEKA to develop a pre-filled, semi-disposable pump system for subcutaneous delivery of Remodulin. Under the terms of the agreement, we are funding the development costs related to the semi-disposable pump system and will pay product fees and a single-digit royalty to DEKA based on commercial sales of the system and the Remodulin sold for use with the system. Our goal is to be in a position to receive FDA approval for this delivery system by the end of 2018.

Other

We are party to various other license agreements relating 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 manufacture our primary supply of Remodulin, Tyvaso, Orenitram and Unituxin at our own facilities. In particular, we synthesize treprostinil, the active ingredient in Remodulin and Tyvaso, and treprostinil diolamine, the active ingredient in Orenitram, at our facility in Silver Spring, Maryland. We also produce dinutuximab, the active ingredient in Unituxin, at our Silver Spring facility. We also manufacture finished Tyvaso, Remodulin, and Unituxin at our Silver Spring facility. We manufacture Orenitram and we package, warehouse and distribute Remodulin, Tyvaso, Orenitram and Unituxin at our facility in Research Triangle Park, North Carolina.

We maintain a two-year inventory of Remodulin, Tyvaso and Orenitram based on expected demand, and we also contract with third-party contract manufacturers to supplement our capacity, in order to mitigate the risk that we might not be able to manufacture 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. In the case of Tyvaso, we rely on Catalent Pharma Solutions, Inc. to serve as an additional manufacturer of Tyvaso, and we rely entirely on Minnetronix Inc. to manufacture the nebulizer used in our Tyvaso Inhalation System. We are working to obtain FDA approval of a third party contract manufacturer to serve as an additional manufacturer of Orenitram, and we are constructing an additional facility to increase our manufacturing capacity for Unituxin.

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 and development to commercialize products to treat cardiovascular diseases and cancer. For the treatment of PAH, we compete with many approved products in the United States and the rest of the world, including the following:

- *Flolan, Veletri and generic epoprostenol.* Flolan (epoprostenol) is a prostacyclin that is delivered by intravenous infusion. Glaxo began marketing Flolan in the United States in 1996. In 2008, the FDA approved Teva's version of generic epoprostenol for the treatment of PAH. In 2010, Actelion commenced sales of Veletri, which is another version of intravenous epoprostenol;

- *Ventavis and Ilomedin* ® . Approved in 2004 in the United States and in 2003 in Europe, Ventavis (iloprost) is an inhaled prostacyclin analogue. Ventavis is currently marketed by Actelion in the United States and by Bayer Schering Pharma AG (Bayer) in Europe. Iloprost is also marketed by Bayer in certain countries outside the United States in an intravenous form known as Ilomedin;

- *Tracleer* ® . Tracleer (bosentan), an oral ETRA therapy for the treatment of PAH, was approved in 2001 in the United States and in 2002 in Europe. Tracleer is marketed worldwide by Actelion. Generic bosentan is expected to launch in the U.S. during 2017, and is already available in other countries;

- *Letairis.* Approved in 2007 in the United States, Letairis (ambrisentan) is an oral ETRA therapy marketed by Gilead for the treatment of PAH. In 2008, Glaxo received marketing authorization from the EMA for Letairis in Europe, where it is known as Volibris ® ;

- *Revatio and generic sildenafil citrate.* Approved in 2005 in the United States, Revatio (sildenafil citrate) is an oral PDE-5 inhibitor therapy marketed by Pfizer. Revatio contains sildenafil citrate,

the same active ingredient as Viagra. In the fourth quarter of 2012, several companies began marketing generic formulations of sildenafil citrate;

- *Opsumit* ® . Approved in October 2013 in the United States and December 2013 in the EU, Opsumit (macitentan) is an oral ETRA therapy marketed by Actelion for the treatment of PAH;

- *Adempas* ® . Approved in August 2013 in the United States and March 2014 in the EU, Adempas (riociguat) is a sGC stimulator, which targets a similar vasodilatory pathway as PDE-5 inhibitors and is approved for chronic thromboembolic pulmonary hypertension and PAH. Adempas is an oral therapy marketed by Bayer; and

- *Uptravi* ® . Approved in the United States in December 2015 and by the EMA in May 2016, Uptravi (selexipag) is an oral IP prostacyclin receptor agonist marketed by Actelion. Actelion also has applications pending in various other jurisdictions. Nippon Shinyaku Co., Ltd. holds the right to market Uptravi in Japan, where it submitted an NDA in January 2016.

There are also a variety of investigational PAH therapies in the later stages of development, including the following:

- *Ralinepag,* an oral IP prostacyclin receptor agonist being developed by Arena Pharmaceuticals, Inc. (Arena). Arena commenced a phase II clinical trial of ralinepag in 2014, and has announced that results are expected in mid-2017;

- *Trevyent* , a formulation of treprostinil being developed by SteadyMed Ltd. (SteadyMed) for delivery via its pre-filled, disposable PatchPump ® . SteadyMed has announced plans to file an NDA for Trevyent during the second quarter of 2017, and launch the product in 2018; and

- *Bardoxolone* , a product being developed by Reata Pharmaceuticals, Inc. for treatment of PAH associated with connective tissue disease. Reata has announced enrollment of a phase III clinical trial, with results anticipated during the first half of 2018.

Oral non-prostacyclin therapies (such as PDE-5 inhibitors and ETRAs) are commonly prescribed as first-line treatments for the least severely ill PAH patients (functional class II patients). As patients progress in their disease severity (functional classes III and IV), less convenient approved therapies, such as inhaled prostacyclin analogues (such as Tyvaso) or infused prostacyclin analogues (such as Remodulin) are commonly added. Orenitram was the first approved oral prostacyclin-class therapy for PAH in the United States, and offers a less invasive and more convenient alternative therapy to Remodulin and Tyvaso. 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. As a result, many physicians may choose to prescribe Uptravi instead of Orenitram, which is indicated to improve exercise capacity. As noted above, however, Uptravi is an oral IP prostacyclin receptor agonist, a new class of therapy that addresses PAH through the prostacyclin pathway. 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 limits uptitration to a specific maximum dose. Given the progressive nature of PAH, we believe many patients will initiate Orenitram or another one of our PAH therapies after their disease progresses on Uptravi.

We will also face competition from generic pharmaceutical companies in the future. For example, we have settled litigation with three generic drug companies permitting them to launch generic versions of Remodulin in 2018, and we are engaged in litigation with companies seeking to launch generic

versions of Tyvaso and Orenitram. In addition, we expect to see the launch of generic versions of Adcirca following patent expiry in November 2017. 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* .

Unituxin may face competition from dinutuximab beta, a similar antibody product being developed by Apeiron Biologics AG that is already being used in Europe to treat neuroblastoma under an unmarketed, managed access program. A marketing authorization application for dinutuximab beta is also pending review by the EMA. In October 2016, EUSA Pharma (UK) Ltd. announced it had acquired global commercialization rights to dinutuximab beta, and plans to file for FDA approval in 2017.

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. Many 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 by the FDA in the United States, the EMA in the 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 investigational new drug application (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 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 I 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 II 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 III 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 IV studies are often conducted following marketing approval, in order to meet regulatory requirements or to provide additional data relating 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 an MAA 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 relating 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 a NDA, but do not guarantee that a product will receive FDA approval.

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 IV 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. 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). 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 recently enacted 21st Century Cures Act (Cures Act) expands the types of studies that qualify for orphan drug grants. Orphan drug designation also may qualify an applicant for federal tax credits relating 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. 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.

NDA applicants are required to identify each patent whose claims cover the product or FDA-approved method of using the product. 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 certify to the FDA that (1) the required information for the original product was not filed or (2) every patent listed for the approved product in the Orange Book is either (a) expired or will expire on a particular date and approval is sought after patent expiration or (b) invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid is called a Paragraph IV certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. Alternatively, for a 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.

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. Similar patent term extensions are available under European laws.

An ANDA application 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 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, or 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.

A reference biologic is granted twelve 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.

Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Cell 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). In 2015 and 2016, the FDA published guidance documents relating to topics such as donor screening, adverse reaction reporting, reducing risks of virus transmission from donors, and the applicability of premarket approval and clearance requirements to cell and tissue based products. Following the numerous public comments on these draft guidance documents, the FDA held a public hearing in September 2016. In November 2016, the FDA released revised recommendations on donor eligibility but did not finalize the other draft guidance.

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.

U.S. Regulation of Medical Devices

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 devices already on the market. Class III devices, again with some exceptions, must be approved through a PMA. A PMA generally requires data from clinical trials that establish the safety and effectiveness of the device. A 510(k) application also sometimes requires clinical data. The recently enacted Cures Act requires FDA to establish a program to provide priority review for "breakthrough" devices and for devices that are more effective in addressing life threatening or debilitating conditions than currently available devices.

Clinical trials for medical devices are subject to similar requirements as those conducting clinical trials with 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 of approval of an investigational device exemption (IDE) application and IRB approval before study initiation; clinical trials involving nonsignificant risk devices are not required to submit an IDE for FDA approval but must obtain IRB approval before study initiation.

The FDA has broad regulatory and enforcement powers with respect to medical devices, similar to those for drugs and biologics. The FDA requires medical device manufacturers to comply with detailed requirements regarding the design and manufacturing practices, labeling and promotion, record keeping, and adverse event reporting.

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, a single regulatory approval process has been created, and approval is represented by the CE Mark.

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 FDA will issue a designation letter within 60 calendar days of the filing of the RFD. Depending on the type of combination product, 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 January 2017, FDA released final guidance recommendations relating to the application of cGMP requirements to combination products and draft guidance on pre-requests for designation.

The Cures Act sets forth a number of provisions pertaining to combination products, such as procedures for negotiating disagreements between sponsors and 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, pay for patient use of our commercial products. Medicare is the federal program that provides health care benefits to senior citizens and certain disabled and chronically ill persons. Medicaid is the federal program jointly funded and administered by the states to provide health care benefits to certain indigent persons. Unituxin is administered entirely as an in-patient therapy and would typically be reimbursed under Medicare Part A, which covers inpatient hospital benefits. However, because Unituxin is indicated for treatment of a pediatric cancer, Medicare beneficiaries are unlikely to receive this treatment. The purchase prices for Remodulin and Tyvaso are reimbursed within the Medicare Part B program, which covers physician services and outpatient care. The Medicare Part B contractors who administer the program provide reimbursement for Remodulin and Tyvaso according to statutory guidelines. In return for the inclusion of our commercial products Adcirca and Orenitram in the Medicare Part D program, which provides a voluntary outpatient prescription drug

benefit, we pay rebates to Medicare Part D plan sponsors that reimburse these products. State Medicaid programs also reimburse the cost of our commercial products at rates established by statutory guidelines. Because Remodulin, Tyvaso, Adcirca, Orenitram and Unituxin are reimbursed by state Medicaid programs, we must pay a rebate to those state Medicaid programs. We are required by government contract to sell our commercial products under contracts with the Department of Veterans Affairs, Department of Defense, Public Health Service and numerous other federal agencies as well as certain hospitals that are designated as 340B covered entities (entities designated by federal programs to receive drugs at discounted prices) at prices that are significantly below the price we charge to our specialty distributors. These programs and contracts are highly regulated and impose restrictions on our business. Failure to comply with these regulations and restrictions could result in a loss of our ability to continue receiving reimbursement for our drugs, exclusion of our products from reimbursement under the federal healthcare programs, or debarment, and expose us to liability under federal and state false claims laws. We estimate that between 40-50 percent of Remodulin, Tyvaso, Adcirca and Orenitram sales are reimbursed under the Medicare and Medicaid programs.

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

The federal healthcare program anti-kickback statute 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 on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

The federal False Claims Act prohibits any person from, among other things, presenting, or causing to be presented, a false claim for payment to the federal government, or making, or causing to be made, a false statement material to a false claim. Many pharmaceutical and other healthcare companies have been prosecuted under the False Claims Act for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates; for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product; and on the basis of allegations relating to marketing practices, including off-label promotion. The majority of states also have statutes or regulations similar to the federal anti-kickback statute and False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Sanctions under these federal and state laws may include civil penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines, and imprisonment.

We are also subject to numerous other anti-bribery and anti-fraud laws, including the U.S. Foreign Corrupt Practices Act (FCPA), 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 FDA.

The Patient Protection and Affordable Care Act of 2010 (PPACA)

The PPACA is intended to expand healthcare coverage within the United States. Several provisions of the law, which have varying effective dates, have impacted us and have increased certain of our costs. The PPACA imposes an annual fee on pharmaceutical manufacturers, based on the manufacturer's sale of branded pharmaceuticals and biologics (excluding orphan drugs) to certain U.S. government programs during the preceding year; expands the 340B drug discount program (excluding orphan drugs) including the creation of new penalties for non-compliance; includes a 50 percent discount on brand name drugs for Medicare Part D participants in the coverage gap, or "donut hole"; and revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of the Medicaid drug rebates paid to states.

In addition, the PPACA imposes new annual reporting requirements for pharmaceutical, biological and device manufacturers with regard to payments or other transfers of value made to physicians and teaching hospitals. In addition, pharmaceutical, biological and device manufacturers are required to report annually investment interests held by physicians and their immediate family members during the preceding calendar year. Many of these laws and regulations contain ambiguous requirements that have not yet been clarified. Further, the PPACA amends the intent requirement of the federal anti-kickback and criminal health care fraud statute. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

21st Century Cures Act

The Cures Act, which was signed into law on December 13, 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 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 FDA to facilitate development programs for, and provides expedited review of, regenerative advanced therapies. The law further requires 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 applications and to satisfy post-approval requirements. Other key provisions relating to orphan drugs, combination products, and medical devices, are discussed separately above.

State Pharmaceutical and Medical Device Marketing Laws

If not preempted by the PPACA, several jurisdictions require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to healthcare practitioners in those jurisdictions. Some of these jurisdictions also prohibit various marketing related activities. Still other states require the posting of information relating to 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.

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 relating to data privacy and protection, 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.

Employees

We had approximately 750 employees as of December 31, 2016. The success of our business is highly dependent on attracting and retaining highly talented and qualified personnel.

Industry Segments and Geographic Areas

Since March 2011, our core business has been pharmaceuticals, in which we closely monitor the revenues and gross margins generated by our commercial products. We sell our products in the United States and throughout the rest of the world. The information required by Item 101(b) and 101(d) of Regulation S-K relating to financial information about industry segments and geographical areas, respectively, is contained in Note 17 —*Segment Information* to our consolidated financial statements included in this Report.

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* .

EXECUTIVE OFFICERS OF THE REGISTRANT

The following is a list, as of February 10, 2017, 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 A. Rothblatt, Ph.D., J.D., M.B.A.	62	Chairman, Chief Executive Officer and Director
Michael Benkowitz	45	President and Chief Operating Officer
James C. Edgemond	49	Chief Financial Officer and Treasurer
Paul A. Mahon, J.D.	53	Executive Vice President, General Counsel and Corporate Secretary

Martine A. Rothblatt, Ph.D., J.D., M.B.A ., founded United Therapeutics in 1996 and served as Chairman and Chief Executive Officer since its inception through January 2015, when she became Chairman and Co-Chief Executive Officer. She was promoted to her current role as Chairman and *soul* CEO in June 2016. Prior to United Therapeutics, she founded and served as Chairman and Chief Executive Officer of SiriusXM Satellite Radio. She is a co-inventor on six of our patents pertaining to treprostinil.

Michael Benkowitz joined United Therapeutics in 2011 as our Executive Vice President, Organizational Development. In this role, he was responsible for most companywide administrative functions, including human resources, information technology, corporate real estate and risk management, and was also responsible for many of our business development efforts and oversight of several of our key collaborations. He was promoted to President and Chief Operating Officer in June 2016, when he also became responsible for all of our commercial and medical affairs activities.

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 November 2008 through January 2013. He also served in a variety of roles at The Corporate Executive Board Company from 1998 to 2008, including most recently as Executive Director, Finance from 2005 to 2008. He began his career as a public accountant at KPMG Peat Marwick LLP, where he served in a variety of roles from 1990 through 1998, including most recently as a Senior Manager.

Paul A. Mahon, J.D., has served as General Counsel and Corporate Secretary of United Therapeutics since its inception in 1996. In June 2001, Mr. Mahon joined United Therapeutics full-time as Senior Vice President, General Counsel and Corporate Secretary. In November 2003, Mr. Mahon was promoted to Executive Vice President, General Counsel and Corporate Secretary. Prior to June 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

Forward-Looking Statements

This Report contains forward-looking statements made pursuant to the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 (the Exchange Act) and the Private Securities Litigation Reform Act of 1995. These statements, which are based on our beliefs and expectations as to future outcomes, include, among others, statements relating to the following:

- Expectations of revenues, expenses, profitability, and cash flows;
- The sufficiency of current and future working capital to support operations;
- Our ability to obtain financing on terms favorable to us or at all;
- The maintenance of domestic and international regulatory approvals;
- Our ability to maintain attractive pricing for our products, in light of increasing competition and pressure from government and other payers to decrease the costs associated with healthcare;
- The expected volume and timing of sales of our existing commercial products—Remodulin, Tyvaso, Orenitram, Adcirca and Unituxin—and potential future commercial products;
- The timing and outcome of clinical studies, other research and development efforts, and related regulatory filings and approvals, including those described in this Report relating to our FREEDOM-EV study of Orenitram, our BEAT study of Tysuberprost, our collaboration with DEKA to develop the RemUnity pump, and pending regulatory filings by Medtronic and us with respect to the Implantable System for Remodulin (RemoSynch);
- The outcome of potential future legal and regulatory actions, including audits and inspections, by the FDA and other regulatory and government enforcement agencies;
- The impact of competing therapies on sales of our commercial products, including the impact of generic products such as generic tadalafil, which may become available following patent expiry in November 2017; generic forms of Remodulin, which we expect three generic companies will launch in June 2018 and December 2018; and newly-developed therapies, such as Uptravi;
- 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 protections and the validity and expiration dates of the patents we own or license, as well as the regulatory exclusivity periods for our products;
- Our ability to defend our intellectual property relating to Remodulin, Tyvaso and Orenitram against generic and other challenges, including but not limited to the challenges described in this Report related to Remodulin, Tyvaso and Orenitram;
- 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.

These statements are subject to risks and uncertainties and our actual results may differ materially from anticipated results. Factors that may cause such differences include, but are not limited to, those

discussed below. We undertake no obligation to publicly update forward-looking statements, whether as a result of new information, future events or otherwise.

Risks Related to Our Business

We rely heavily on sales of Remodulin, Tyvaso, Orenitram and Adcirca to generate revenues and support our operations.

Sales of our current PAH therapies (Remodulin, Tyvaso, Orenitram and Adcirca) comprise the vast majority of our revenues. Decreased sales of any one 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 decline, or to grow more slowly than expected. Generic competition due to the current commercial availability of generic sildenafil, potential commercial availability of generic Adcirca following patent expiry in November 2017, as well as generic versions of Remodulin to be launched in the United States by Sandoz in June 2018 and by Teva and Par in December 2018, respectively, or earlier under certain circumstances, and other generic challenges against Remodulin, Tyvaso and Orenitram, may also decrease our revenues. In addition, the inability of any third party that manufactures, markets, distributes or sells any of our commercial products to perform these functions satisfactorily, or our inability to manage our internal manufacturing processes, could result in an inability to meet patient demand and decrease sales.

If our products fail in clinical trials, we will be unable to obtain or maintain FDA and international regulatory approvals and will be unable to sell those products.

To obtain regulatory approvals from the FDA and international regulatory agencies to sell new products, or to expand the product labeling for our existing products to new indications, we must conduct clinical trials demonstrating that our products are safe and effective. These regulators have substantial discretion over the approval process for our products, and may not agree that we have demonstrated the requisite level of product safety and efficacy to grant approval.

The FDA and other regulatory agencies may require us to amend ongoing trials or perform additional trials beyond those we planned, which could result in significant delays and additional costs or may be unsuccessful. For example, approval of an NDA or a BLA could be delayed if the FDA determines that it cannot review or approve the application as submitted. In such a case, the FDA may require substantial additional studies, testing or information in order to complete its review of the application. If our clinical trials are not successful, or we fail to address any identified deficiencies adequately, we will not obtain required approvals to market the new product or new indication.

In addition, we are enrolling two pivotal studies, referred to in this Report as *FREEDOM-EV* and *BEAT* , in which we are attempting to demonstrate that the drug combination being studied delays time to clinical worsening. We have not previously conducted a pivotal study with time to clinical worsening as its primary endpoint. The timing of enrollment and completion of these studies is subject to uncertainty, in part because study completion depends on the accrual of a pre-specified number of clinical worsening events, the pace of which is inherently difficult to predict. Our inexperience with this type of trial design may impact our ability to conduct these trials appropriately and achieve positive results, or complete the trials within our anticipated timetable. In particular, failure of the *FREEDOM-EV* study to meet its primary endpoint could materially limit the commercial potential of Orenitram and impede our growth.

We cannot predict with certainty the length of time it will take to complete necessary clinical trials or obtain regulatory approvals relating to our current or future products. The length of time we need to complete clinical trials and obtain regulatory approvals varies by product, indication and country.

Our clinical trials may be discontinued, delayed or disqualified for various reasons, including:

- The drug is ineffective, or physicians and/or patients believe that the drug is ineffective, or that other therapies are more effective or convenient;
- We fail to reach agreement with the applicable regulatory agencies regarding the scope or design of our clinical trials;
- Patients do not enroll, patients drop out, or we do not observe worsening events, at the rate we expect;
- Ongoing or new clinical trials conducted by drug companies in addition to our own clinical trials reduce the availability of patients for our trials;
- Our clinical trial sites, contracted clinical trial administrators or clinical studies conducted entirely by third parties do not adhere to trial protocols and required quality controls under GCP regulations and similar regulations outside the United States;
- Patients experience severe side effects during treatment or die during our trials because of adverse events related to the trial drug, advanced disease, or other medical complications; and
- The results of our clinical trials conducted in a particular country are not acceptable to regulators in other countries.

We may not compete successfully with established and newly developed drugs or products, or the companies that develop and market them.

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. Most of these competitors have substantially greater financial, marketing, manufacturing, sales, distribution and technical resources, and a larger number of approved products, than we do. 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, and others are under development. For example, for the treatment of PAH, we compete with Adempas ®, Flolan ®, Ilomedin ®, Letairis ®, Opsumit ®, Revatio ®, Tracleer ®, Uptravi ®, Ventavis ®, generic epoprostenol and generic sildenafil citrate. Our competitors may introduce new products that render all or some of our technologies and products obsolete or noncompetitive. For example, Uptravi was approved by the FDA in December 2015 for the treatment of PAH, and competes directly with Orenitram. Our commercial therapies may also have to compete with investigational products currently in development, such as Trevyent ®, which is a single-use, pre-filled pump being developed by SteadyMed to deliver a two-day supply of treprostinil subcutaneously using SteadyMed's PatchPump ® technology. SteadyMed announced plans to file an NDA for Trevyent during the second quarter of 2017, and launch the product in 2018. In January 2016, SteadyMed announced that Trevyent had been granted orphan drug designation by the FDA for the treatment of PAH. As a result, if Trevyent obtains FDA approval prior to FDA approval of RemUnity (our pre-filled, semi-disposable treprostinil pump) or RemoSynch (our implantable system for intravenous treprostinil), SteadyMed could have seven years of exclusivity during which the FDA may be prevented from approving these products except in limited circumstances such as a showing of clinical superiority. In addition, we may not compete successfully against generic competitors, as we anticipate generic tadalafil may be launched in late 2017, and generic treprostinil will be launched in 2018, as described elsewhere in this Report. It is unclear what revenues, if any, we will generate from Adcirca sales after patent expiry in November 2017.

Legislation such as the 21 st Century Cures Act, which was enacted in December 2016 and designed to encourage innovation and bring pharmaceutical products to market more quickly, may enable our

competitors to bring competing products to market on an expedited basis. In addition, alternative approaches to treating chronic diseases, such as gene therapy, cell therapy or transplantation technologies, may make our products obsolete or noncompetitive. 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. Alternatively, 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 Tyvaso and Remodulin, and the use of these products may delay or prevent initiation of Tyvaso or Remodulin therapy. Any of these circumstances could negatively impact our operating results.

Sales of our products are subject to reimbursement from government agencies and other third parties. Pharmaceutical pricing and reimbursement pressures may negatively impact our sales.

The commercial success of our products depends, in part, on the availability of reimbursements by governmental payers such as Medicare and Medicaid, and private insurance companies. An estimated 40-50 percent of Remodulin, Tyvaso, Adcirca and Orenitram sales in the United States are reimbursed under the Medicare and Medicaid programs. 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. In the United States, the European Union and other potentially significant markets for our products, government payers and/or third-party payers are increasingly attempting to limit or regulate the price of medicinal products and frequently challenge the pricing of new and expensive drugs. Financial pressures may cause United States government or other third-party payers to seek cost containment more aggressively through mandatory discounts or rebates on our products, policies requiring the automatic substitution of generic products, more rigorous requirements for initial reimbursement approvals for new products or other similar measures. For example, there have been proposals to reduce reimbursement rates and/or adopt mandatory rebates under Medicare Part B, which covers Remodulin and Tyvaso. More recently, in January 2017, the Medicare Prescription Drug Price Negotiation Act was proposed in Congress; this act would require the federal government to negotiate the price of Medicare prescription drugs with pharmaceutical companies. 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. Our prostacyclin analogue products (Remodulin, Tyvaso and Orenitram) and our oncology product (Unituxin) are expensive therapies. Consequently, it may be difficult for our distributors to obtain adequate reimbursement for our products from commercial and government payers to motivate such distributors to support our products. Alternatively, third-party payers may reduce the amount of reimbursement for our products based on changes in pricing of other therapies for the same disease. If commercial and/or government payers do not approve our products for reimbursement, or limit reimbursements, patients and physicians could choose competing products that are approved for reimbursement or provide 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 growing 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 on Minnetronix, Inc. as the sole manufacturer of the Tyvaso Inhalation System, and on Lilly as the sole manufacturer of Adcirca. In addition, if the RemoSynch system is approved, we will rely on Medtronic as the sole manufacturer of the SynchroMed II infusion system and related components.

If any of our third-party manufacturing and supply arrangements are interrupted for compliance issues or other reasons, we may not have sufficient inventory to meet future demand. In addition, any

change 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.

In addition, our internal manufacturing process also subjects us to risks as we engage in increasingly complex manufacturing processes. For example, Remodulin, Tyvaso and Unituxin are sterile solutions that must be prepared under highly-controlled environmental conditions, which are challenging to maintain on a commercial scale. In addition, Unituxin is a monoclonal antibody. As with all biologic products, monoclonal antibodies are inherently more difficult to manufacture than our treprostinil-based products and involve increased risk of viral and other contaminants. Finally, we have limited experience producing Orenitram and Unituxin on a commercial scale, and currently all Orenitram and Unituxin manufacturing is performed internally. It could take substantial time to establish an FDA-approved contract manufacturer as a back-up supplier of Orenitram, or this process may not be successful at all. Our limited internal manufacturing capacity has restricted our ability to supply Unituxin outside the United States. We are constructing a new facility to expand our manufacturing capacity for dinutuximab, the active ingredient in Unituxin, but this process will take several years and may not be successful at all. We presently have no plans to engage a third-party contract manufacturer for dinutuximab, although we are in the process of qualifying a third-party manufacturer for finished Unituxin drug product. Our long-term regenerative medicine and xenotransplantation programs will involve exceptionally complicated manufacturing processes, many of which have never been attempted on a clinical or commercial scale. It could take substantial time and resources to develop and implement such manufacturing processes, or we may never be able to do so successfully.

Additional risks we face with our manufacturing strategy include the following:

- We and our third-party manufacturers are subject to the FDA's cGMP regulations, current Good Tissue Practices, and similar international regulatory standards. 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;

- Even if we and our third-party manufacturers comply with applicable drug manufacturing regulations, the sterility and quality of our products could be substandard and such products could not be sold or used or subject to recalls;

- If we had to replace our own manufacturing operations or a third-party manufacturer, the FDA and its international counterparts would require new testing and compliance inspections. Furthermore, a new manufacturer would have to be familiarized with the processes necessary to manufacture and commercially validate our products, as producing our treprostinil-based and biologic products is complex;

- We may be unable to contract with needed manufacturers on satisfactory terms or at all; and

- 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. Products manufactured with substituted materials or components must be approved by the FDA and applicable international regulatory agencies before they could be sold.

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. Our ability to generate commercial sales or conduct clinical trials could suffer if our third-party suppliers and service providers fail to perform.

Third parties assist us in activities critical to our operations, such as: (1) producing our commercial products; (2) conducting clinical trials, preclinical studies and other research and development activities; (3) obtaining regulatory approvals; (4) conducting pharmacovigilance-related and product complaint activities, including drug safety, reporting adverse events and product complaints; and (5) marketing and distributing our products. For risks relating to the involvement of third parties in our manufacturing process, see the risk factor above, entitled *Our manufacturing strategy exposes us to significant risks* .

We rely on various distributors to market, distribute and sell Remodulin, Tyvaso, Orenitram and Unituxin. From time-to-time, we increase the price of products sold to our U.S.-based and international distributors. Our price increases may not be fully reimbursed by third-party payers. If our distributors do not achieve acceptable profit margins on our products, they may reduce or discontinue the sale of our products. Furthermore, if our distributors devote fewer resources to sell our products or are unsuccessful in 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.

We rely on Lilly to manufacture and supply Adcirca for us, and 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. In addition, Lilly has the right to determine the price of Adcirca. Changes in Lilly's prices could adversely impact demand or reimbursement for Adcirca, particularly in light of the commercial availability of generic sildenafil, the active ingredient in Revatio, which could be prescribed in lieu of Adcirca.

Any change in service providers could interrupt the distribution of our commercial products and our other products and services, and impede the progress of our clinical trials, commercial launch plans and related revenues.

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 particular, our research and development efforts into new indications for Unituxin are substantially outsourced to a contract research organization called Precision Oncology, LLC. In addition, the success of certain products we are developing will depend on clinical trials sponsored by third parties. Failure by any third party to conduct or assist us in conducting clinical trials in accordance with study protocols, quality controls and GCP, or other applicable U.S. or international requirements or to submit associated regulatory filings, could limit or prevent our ability to rely on results of those trials in seeking regulatory approvals.

We rely 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.

We rely heavily on Medtronic for the success of our program to develop an implantable pump to deliver intravenous Remodulin (the Implantable System for Remodulin, or RemoSynch). In particular, Medtronic is entirely responsible for regulatory approvals and all manufacturing and quality systems related to its infusion pump and related components. Medtronic has received a consent decree citing violations of the quality system regulation for medical devices and requiring it to stop manufacturing, designing and distributing SynchroMed II implantable infusion pump systems, except in limited circumstances until the FDA determines that Medtronic has met all the provisions listed in the consent

decree. It is unclear how this consent decree will impact our ability to obtain FDA approval for RemoSynch, or its commercial prospects if approved.

Finally, we rely heavily on DEKA for the development of RemUnity, our pre-filled, semi-disposable pump system for subcutaneous treprostinil.

Our operations must comply with extensive laws and regulations in the United States and other countries, including FDA regulations. Failure to obtain approvals on a timely basis or to achieve continued compliance could delay, disrupt or prevent the 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 is lengthy, expensive and uncertain. The regulatory approval process is particularly uncertain for our transplantation programs, which include the development of xenotransplantation, regenerative medicine 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 may fail to receive regulatory approval on a timely basis, or at all. 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. If data from post-marketing studies suggest that an approved product presents an unacceptable safety risk, regulatory authorities could withdraw the product's approval, suspend production or place other marketing restrictions on that product.

If we fail to comply with applicable regulatory requirements, we could be subject to penalties including fines, suspension of regulatory approvals that cause us to suspend production, distribution or marketing activities, product recalls, seizure of our products and/or criminal prosecution. If regulatory sanctions are applied or regulatory approval is delayed or withdrawn, our operating results and the value of our company may be adversely affected. In addition, our reputation could be harmed as a result of any such regulatory restrictions or actions, and patients and physicians may avoid the use of our products even after we have resolved the issues that led to such regulatory action.

Any investigation, inquiry or other legal proceeding relating to our operations may adversely affect our business, results of operations or reputation. For example, in May 2016, we received a subpoena from the U.S. Department of Justice requesting documents regarding our support of 501(c)(3) organizations that provide financial assistance to patients taking our medicines. We are cooperating with this inquiry. We are unable to predict how long this inquiry will continue or its outcome, but it may require significant management time and attention, and we may incur significant costs in connection with the investigation, regardless of the outcome.

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. If we are not able to obtain FDA approval for any desired future indications for our products, our ability to effectively market and sell our products may be reduced.

While physicians may choose to 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. If our promotional activities fail to comply with regulations or guidelines related to off-label promotion, we may be subject to warnings from, or enforcement action by, these authorities. In addition, failure to follow FDA rules and guidelines relating 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, fines, disgorgement of money, operating restrictions, civil lawsuits, injunctions or criminal prosecution.

We must comply with various laws in jurisdictions around the world that restrict certain marketing practices in the pharmaceutical and medical device industries. Failure to comply with such laws could result in penalties and have a material adverse effect on our business, financial condition and results of operations.

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 UK Bribery Act. Any penalties imposed upon us for failure to comply could have a material adverse effect on our business and financial condition.

In the United States, the federal health care program anti-kickback statute prohibits, among other activities, knowingly and willfully offering, paying, soliciting, or receiving compensation 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 health-care program. This statute has been interpreted broadly to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. The exemptions and safe harbors for this statute are narrow, and practices that involve compensation intended to induce prescriptions, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not always qualify for safe harbor protection.

The federal False Claims Act, as amended by the PPACA, prohibits any person from presenting or causing to be presented a false claim or making or causing a false statement material to a false claim. Several pharmaceutical and health care companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the free product. Other companies have been prosecuted for causing false claims to be submitted because of these companies' marketing of a product for unapproved and non-reimbursable uses. Potential liability under the federal False Claims Act includes mandatory treble damages and significant per-claim penalties. The majority of states also have statutes or regulations similar to the federal anti-kickback statute and False Claims Act. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's product from reimbursement under government programs, debarment, criminal fines, and imprisonment.

The PPACA imposed reporting requirements for pharmaceutical, biologic and device manufacturers regarding payments or other transfers of value made to physicians and teaching hospitals, investment interests in such manufacturers held by physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties, which may increase significantly for "knowing failures." Compliance with these and similar laws on a state-by-state basis is difficult and time consuming.

Government health care reform could adversely affect our revenue, costs and results of operations.

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. The PPACA is a broad measure intended to expand health care coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. The reforms imposed by the law will significantly impact the pharmaceutical industry; however, the full effects of the PPACA will be unknown until all of

these provisions are implemented and the Centers for Medicare and Medicaid Services and other federal and state agencies issue applicable regulations or guidance. Moreover, in the coming years, additional changes could be made to governmental health care programs that could significantly impact the success of our products or product candidates. In 2017, we may face uncertainties as a result of likely federal and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA. There is no assurance that the PPACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

Reports of actual or perceived side effects and adverse events associated with our products, such as sepsis, could cause physicians and patients to avoid or discontinue use of our products in favor of alternative treatments.

Reports of side effects and adverse events associated with our products could have a significant adverse impact on the sale of our products. An example of a known risk associated with intravenous Remodulin is sepsis, which is a serious and potentially life-threatening infection of the bloodstream caused by a wide variety of bacteria. Intravenous Remodulin is infused continuously through a catheter placed in a large vein in the patient's chest, and sepsis is a known risk associated with this type of delivery. 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. Concerns about side effects may affect a physician's decision to prescribe or a patient's willingness to use our products.

Negative attention from special interest groups may impair our business.

As is common with pharmaceutical and biotechnology companies, our early-stage research and development involves animal testing, 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 in the future could impede the operation of our business.

If any of the license or other agreements under which intellectual property rights are licensed to, or were acquired by us, are breached or terminated, our right to continue to develop, manufacture and sell the products covered by such agreements could be impaired or lost.

Our business depends upon our continuing ability to exploit our intellectual property rights acquired from third parties under product license and purchase agreements. Under each of our purchase agreements, we have rights to certain intellectual property covering a drug or other product 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 determine 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 Remodulin, Tyvaso and Orenitram, expire in October 2017, and a fourth will expire in 2028. We settled patent litigation with Sandoz, Teva and Par, which will permit them to launch generic versions of Remodulin in the United States in June 2018 (Sandoz) and December 2018 (Teva and Par), although they may be permitted to enter the market earlier under certain circumstances. Our patents relating to our individual treprostinil-based products expire at various times between 2018 and 2031. For further details, please see *Item 1.—Business—Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity—Remodulin, Tyvaso and Orenitram Proprietary Rights.* The U.S. patent for Adcirca for the treatment of pulmonary hypertension will expire in November 2017. We have no issued patents covering Unituxin.

We continue to conduct research into new methods to synthesize treprostinil and have pending U.S. and international patent applications and patents relating to such methods. We also have additional issued and pending patents covering the use of our existing commercial products in new indications and with new devices. However, 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. Upon the expiration of any of our patents, competitors may develop generic versions of our products and may market those generic versions 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 are currently, and may in the future, challenge the validity of our patents, through patent litigation and/or initiating proceedings, including re-examinations, *inter partes* reviews, post-grant reviews and interference proceedings, before the U.S. Patent and Trademark Office or other applicable patent filing office, or other means. We are currently involved in litigation challenging several of our patents related to Tyvaso and Orenitram as a result of ANDA filings by generic companies. If any company receives approval to sell a generic version of Tyvaso or Orenitram and/or prevailed in any patent litigation, the affected product would become subject to increased competition and our revenue could decrease. In addition, in October 2015, SteadyMed filed a petition for *inter partes* review with the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office seeking to invalidate the claims of one of our patents covering a method of making treprostinil that expires in 2028 and is listed in the Orange Book for Remodulin, Tyvaso, and Orenitram. For details on the status of these matters, please see Note 19— *Litigation* , to our consolidated financial statements.

Patent litigation can be time consuming, distracting to our operations, costly and may conclude unfavorably for us. In addition, the outcome of patent infringement litigation often is difficult to predict. If we are unsuccessful with respect to any future legal action in the defense of our patents and our patents are invalidated or determined to be unenforceable, our business could be negatively impacted. Even if our patents are determined to be valid or enforceable, it is possible that 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.

In addition to patent protection, we also rely on trade secrets to protect our proprietary know-how and other technological advances that we do not disclose to the public. We enter into confidentiality agreements with our employees and others to whom we disclose trade secrets and other confidential information. These agreements may not necessarily prevent our trade secrets from being used or disclosed without our authorization and confidentiality agreements may be difficult, time-consuming and expensive to enforce or may not provide an adequate remedy in the event of unauthorized disclosure. In addition, if any of 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. If any of our trade secrets were to be disclosed to or independently developed by a competitor, 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. Payment of royalties would negatively affect our profits; furthermore, if we chose to contest these allegations, we could be subject to costly and time-consuming litigation or could lose the ability to continue 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. In the case of 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. Otherwise, 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 could be compelled to 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 were to have any merit. We cannot be certain that we could prevail in the action, and an adverse judgment or settlement resulting from the action could require us to pay substantial amounts in damages for infringement or substantial amounts to obtain a license to continue to use the intellectual property that is the subject of the infringement claim.

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 claims or losses significantly exceed our liability insurance coverage, we may experience financial hardship or potentially be forced out of business. While we historically have had a limited number of product liability claims, the clinical testing and eventual marketing and sale of new products, reformulated versions of existing products, or existing products in new indications, could expose us to new product liability risks.

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, Chairman 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. In addition, effective succession

planning is important to our long-term success. 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 skilled scientific and technical personnel in the biotechnology and pharmaceutical industries is intense. Furthermore, our compensation arrangements may not be sufficient to attract new qualified scientific and technical employees or retain such core employees. If we fail to attract and retain such employees, we may not be successful in developing and commercializing new therapies for PAH and other diseases.

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 and we are expanding these activities in both scale and location. In addition, 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; furthermore, we can be subject to substantial fines and penalties in the event of noncompliance. The risk of accidental contamination or injury from these materials cannot be completely eliminated. Furthermore, once chemical and hazardous materials leave our facilities, we cannot control the manner in which such hazardous waste is disposed of by our contractors. In the event of an accident, we could be liable for substantial civil damages or costs associated with the cleanup of the release of hazardous materials. Any related liability could have a material adverse effect on our business.

We may encounter substantial difficulties managing our growth relative to product demand.

If we experience substantial sales growth, we may have difficulty managing inventory levels as marketing new therapies is complicated and gauging future demand can be difficult and uncertain until we possess sufficient post-launch sales experience. In addition, we have spent considerable resources building and expanding our offices, laboratories and manufacturing facilities. However, our facilities could be insufficient to meet future demand for our products. Conversely, we may have excess capacity at our facilities if future demand falls short of our projections, or if we do not receive regulatory approvals for the products we intend to manufacture at our facilities. Our ability to satisfactorily recover our investments in our facilities will depend on sales of the products manufactured at these facilities in sufficient volume.

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. In addition, we are parties to a credit agreement (the 2016 Credit Agreement), which provides an unsecured, revolving credit facility of up to $1.0 billion. The 2016 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 require additional financing to meet significant future obligations. For example, awards granted under our Share Tracking Awards Plans (which we collectively refer to as the STAP) entitle participants to receive in cash an amount equal to the appreciation in the price of our common stock, which is calculated as the positive difference between the closing price of our common stock on the date of exercise and the date of grant. Consequently, our STAP may require significant future cash payments to participants to the extent the price of our common stock appreciates and the number of vested STAP awards increases over time. If we do not have sufficient funds to meet such obligations or the ability to secure alternative sources of financing, we could be in default, face litigation and/or lose key employees, which could have a material adverse effect on our business.

We may not be able to generate sufficient cash to service our indebtedness, which may have a material adverse effect on our financial position, results of operations and cash flows. In addition, we may be forced to take other actions to satisfy our obligations in connection with our indebtedness, which actions may not be successful.

We may borrow up to $1.0 billion under the 2016 Credit Agreement, which matures in January 2022. Our ability to make payments on or refinance our debt obligations, including any future debt that we may incur, will depend on our financial condition and operating performance, which are subject to prevailing economic and competitive conditions and to certain financial, business, legislative, regulatory and other 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, premium, if any, 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 could 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, if necessary, on commercially reasonable terms or at all and, even if successful, such actions may not be sufficient for 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.

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. In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers, 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 in the United States and abroad, such as the Health Insurance Portability and Accountability Act of 1996 and European Union regulations related to data privacy, which require us to protect the privacy and security of certain types of information. Our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Such breaches could compromise sensitive and confidential information stored on our networks and expose such information to public disclosure, loss or theft. Any 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 which could adversely affect our business.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our products and the diseases our therapies are designed to treat. Social media practices in our industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. 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 were to 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 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, there can be significant price and volume fluctuations in the market that may not relate to operating performance. The following table sets forth the high and low closing prices of our common stock for the periods indicated:

	High	Low
January 1, 2016 - December 31, 2016	$ 155.54	$ 98.33
January 1, 2015 - December 31, 2015	$ 188.56	$ 119.57
January 1, 2014 - December 31, 2014	$ 136.16	$ 86.14

The price of our common stock could decline sharply due to the following factors, among others:

- Failure to meet our estimates or expectations, or those of securities analysts;
- Quarterly and annual financial results;
- Timing of enrollment and results of our clinical trials;
- Announcements regarding generic or other challenges to the intellectual property relating to our products, including developments with respect to the ANDAs filed by generic drug companies relating to certain of our Tyvaso and Orenitram patents and to our pending lawsuits defending our patent rights, and the *inter partes* review initiated by SteadyMed challenging the validity of one of the patents listed in the Orange Book for Remodulin, Tyvaso and Orenitram;
- 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 legislation and regulations affecting reimbursement of, our therapeutic products by Medicare, Medicaid or other government payers, and changes in reimbursement policies of private health 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 PAH 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 any other activity which could be viewed as being dilutive to our shareholders;
- Rumors among, 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 regulatory approvals from the FDA or international regulatory agencies;
- 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;
- 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; and
- General market conditions.

Provisions of Delaware law and our amended and restated certificate of incorporation, fourth amended and restated by-laws, shareholder rights plan 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 and our amended and restated certificate of incorporation, fourth amended and restated by-laws and shareholder rights plan 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, our amended and restated certificate of incorporation divides our Board of Directors into three classes. Members of each class are elected for staggered three-year terms. This provision may make it more difficult for shareholders to replace the majority of directors. It may also deter the accumulation of large blocks of our common stock by limiting the voting power of such blocks.

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 also result in an acceleration of the vesting of outstanding STAP awards, stock options and restricted stock units. This, together with any increase in our stock price resulting from the announcement of a change of control, could make an acquisition of our company significantly more expensive to the purchaser. We also have a broad-based change of control severance program, under which employees may be entitled to severance benefits in the event they are terminated without cause (or they terminate their employment for good reason) following a change of control. This program could also increase the cost of acquiring our company.

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 these 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 to these agreements 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, both Lilly and Toray have the right to terminate our license agreements relating to Adcirca and esuberaprost, 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.

Because we do not intend to pay cash dividends, our shareholders must rely on stock appreciation for any return on their investment in us.

We have never declared or paid cash dividends on our common stock. Furthermore, we do not intend to pay cash dividends in the future and our 2016 Credit Agreement contains covenants that may restrict us from doing so. As a result, the return on an investment in our common stock will depend entirely upon the future appreciation in the price of our common stock. There can be no assurances that our common stock will provide a return to investors.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Maryland—We own a 232,000 square foot combination laboratory and office building complex in Silver Spring, Maryland that serves as our co-headquarters and is used for commercial manufacturing. These manufacturing activities include the synthesis of treprostinil, the active ingredient in Remodulin and Tyvaso, and treprostinil diolamine, the active ingredient in Orenitram, as well as dinutuximab, the active ingredient in Unituxin. We also manufacture finished Remodulin, Tyvaso and Unituxin in our Silver Spring facilities. We own several other buildings in Silver Spring used principally for office and laboratory space.

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 tablets and we package, warehouse and distribute Remodulin, Tyvaso, Orenitram and Unituxin at this location. We also own a 132-acre property containing approximately 330,000 square feet of building space adjacent to our RTP facility, which we use for our research, development and manufacturing facilities relating to our lung regeneration program, office space and for future expansion.

Europe—We own an office building near London, England which serves as our European headquarters. In Germany, we lease a warehouse where we maintain inventory of components for our Tyvaso Inhalation System. The German facility includes office and laboratory space.

District of Columbia—We own two adjacent buildings in Washington, D.C., which serve as office space.

Florida—We own an office building in Satellite Beach, Florida and a facility in Melbourne, Florida used as a reimbursement support call center.

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

Please refer to Note 19— *Litigation* , to our consolidated financial statements contained elsewhere in this Report, 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 (and associated preferred stock purchase rights) trades on the NASDAQ Global Select Market under the symbol "UTHR". The table below sets forth the high and low closing prices for our common stock for the periods indicated:

	2016		2015	
	High	Low	High	Low
January 1 - March 31	$ 155.54	$ 108.47	$ 179.51	$ 124.93
April 1 - June 30	$ 121.03	$ 98.33	$ 188.56	$ 159.69
July 1 - September 30	$ 129.64	$ 107.73	$ 179.15	$ 131.24
October 1 - December 31	$ 145.38	$ 111.68	$ 160.91	$ 119.57

Number of Holders

As of February 10, 2017, there were 36 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 2016 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

Period	Total Number of Shares (or Units) Purchased	Average Price Paid Per Share (or Unit) [1]	Total Number of Shares (or Units) Purchased as Part of Publicly Announced Plans or Programs	Maximum Number (or Approximate Dollar Value) of Shares (or Units) That May Yet Be Purchased Under the Plans or Programs [2]
Beginning repurchase authority				$ 104,489,107
October 1, 2016 - October 31, 2016	384,267	$ 117.49	384,267	59,340,205
November 1, 2016 - November 30, 2016	349,392	127.02	349,392	14,961,537
December 1, 2016 - December 31, 2016	114,900	130.21	114,900	—
Total	848,559	$ 123.14	848,559	$ —

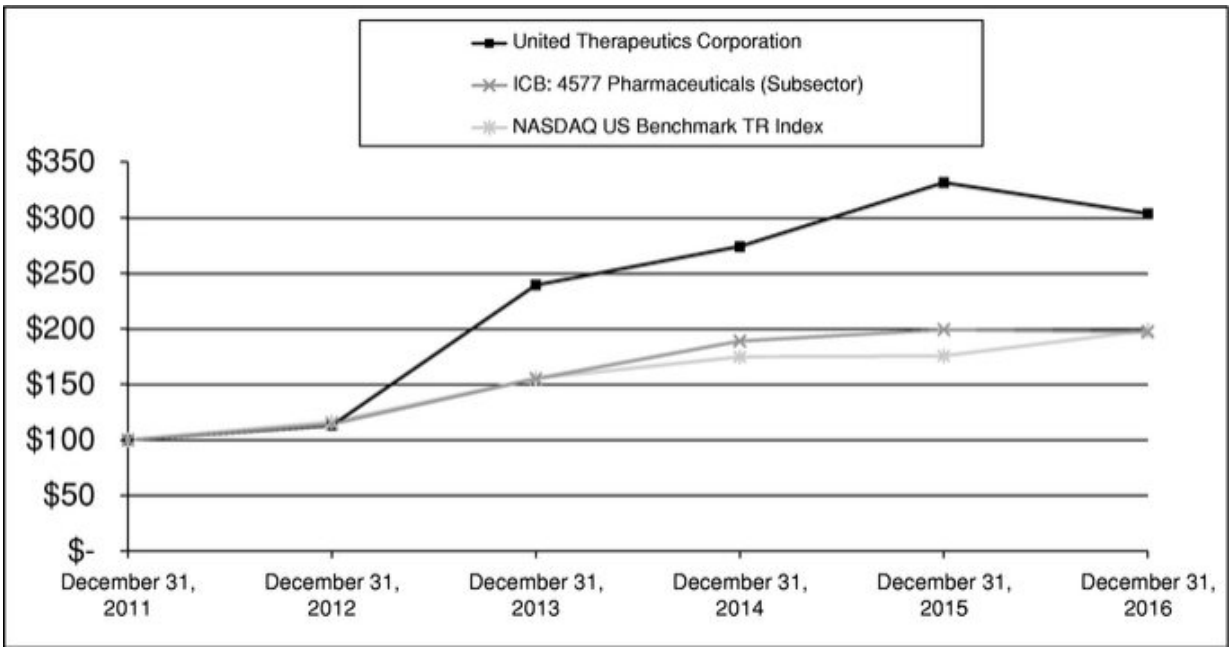
(1) Average price paid per share calculated at settlement, including commission.

(2) On October 15, 2015, we announced that our Board of Directors authorized a share repurchase program for up to $500.0 million in aggregate repurchases. This program was effective from January 1, 2016 through December 31, 2016. In the aggregate, we repurchased approximately 4.2 million shares of common stock under this program for $500.0 million.

Comparison of Five-Year Total Cumulative Shareholder Return

The following chart shows the performance from December 31, 2011 through December 31, 2016 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 ICB: 4577 Pharmaceutical Stock Index, assuming the investment of $100 at the beginning of the period and the reinvestment of dividends, if any.



ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with our consolidated financial statements and the notes accompanying the consolidated financial statements and *Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations* included in this Report. The historical results are not necessarily indicative of results to be expected for future periods. The following information is presented in millions, except per share data.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
Consolidated Statements of Operations Data:					
Revenues	$ 1,598.8	$ 1,465.8	$ 1,288.5	$ 1,117.0	$ 916.1
Operating income	$ 1,061.7	$ 699.0	$ 538.8	$ 292.5	$ 421.6
Net income	$ 713.7	$ 651.6	$ 340.1	$ 174.6	$ 304.4
Net income per common share:					
Basic [1]	$ 16.29	$ 14.17	$ 7.06	$ 3.49	$ 5.84
Diluted [1]	$ 15.25	$ 12.72	$ 6.28	$ 3.28	$ 5.71

	As of December 31,				
	2016	2015	2014	2013	2012
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable investments	$ 1,053.1	$ 991.8	$ 818.2	$ 1,142.0	$ 784.9
Total assets	$ 2,325.6	$ 2,184.4	$ 1,884.4	$ 2,087.6	$ 1,626.6
Other non-current liabilities	$ 130.9	$ 144.0	$ 114.5	$ 95.6	$ 355.0
Total stockholders' equity	$ 1,851.3	$ 1,588.6	$ 1,242.4	$ 1,259.3	$ 1,084.0

(1) Refer to Note 11— *Stockholders' Equity—Earnings Per Common Share* to our consolidated financial statements contained in this Report for the computation of basic and diluted net income per share.

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 the consolidated financial statements included in this Report.

Overview

Commercial Products

We currently market and sell the following commercial products:

- *Remodulin* , a continuously-infused formulation of the prostacyclin analogue treprostinil, approved by the FDA for subcutaneous and intravenous administration to diminish symptoms associated with exercise in PAH patients. Remodulin has also been approved in various countries outside of the United States.
- *Tyvaso* , an inhaled formulation of treprostinil, approved by the FDA to improve exercise ability in PAH patients.
- *Orenitram* , a tablet dosage form of treprostinil approved by the FDA to improve exercise capacity in PAH patients.
- *Adcirca* , an oral PDE-5 inhibitor approved by the FDA to improve exercise ability in PAH patients.

- *Unituxin* , approved by the FDA for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy.

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

Research and Development

We are engaged in research and development of new formulations, indications and delivery devices for our existing products. In particular, we are developing the RemoSynch and RemUnity delivery systems for intravenous and subcutaneous Remodulin. We are studying Tyvaso in patients with WHO Group 3 pulmonary hypertension (which we refer to as Tyvaso-ILD), and Orenitram in patients with WHO Groups 2 and 5 pulmonary hypertension (which we refer to as OreniLeft and OreniCell, respectively). We are also planning studies of Unituxin in new oncology indications. Finally, we are engaged in studies to improve the label for the use of Orenitram in PAH patients, including our FREEDOM-EV study of Orenitram in combination with background therapy, a project we refer to as OreniPlus.

In addition, we are developing new therapies for PAH (esuberaprost and eNOS gene therapy). We are also heavily engaged in early-stage research and development of a number of organ transplantation-related technologies including regenerative medicine, xenotransplantation and ex-vivo lung perfusion. Finally, we are engaged in additional, early-stage research and development efforts in PAH and other diseases. For additional detail regarding our research and development programs, see *Item 1 — Business — Research and Development.*

Revenues

Our net product sales consist entirely of sales of the five commercial products noted above. We have entered into separate, non-exclusive distribution agreements with Accredo and Caremark to distribute Remodulin, Tyvaso and Orenitram in the United States, and we have entered into an exclusive distribution agreement with ASD to distribute Unituxin in the United States. We also sell Remodulin, Tyvaso and Unituxin to distributors internationally. We sell Adcirca through Lilly's pharmaceutical wholesale network. To the extent we increase the price of any of these products, increases are in the single-digit percentages per year, except for Adcirca, the price of which is set by Lilly.

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

We recognize revenues net of: (1) estimated rebates; (2) prompt pay discounts; (3) allowances for sales returns; and (4) distributor fees. We derive our provisions for rebates from an analysis of historical levels of rebates for all government drug discount programs and commercial third-party payer contracts, relative to sales of each product. We provide prompt pay discounts to customers that pay amounts due within a specific time period and base related estimates on observed historical customer payment behavior. The allowance for exchanges for Remodulin, Tyvaso, Orenitram and Unituxin has been negligible and immaterial. Furthermore, we anticipate minimal exchange activity in the future for Remodulin, Tyvaso, Orenitram and Unituxin since we typically sell these products with a remaining shelf life in excess of one year and our distributors generally carry a thirty- to sixty-day supply of our products at any given time. As a result, we do not record reserves for exchanges for Remodulin, Tyvaso,

Orenitram and Unituxin at the time of sale. We derive estimates relating to our allowance for returns of Adcirca based on actual return data accumulated since the drug's launch in 2009. We also compare patient prescription data for Adcirca to product sales on a quarterly basis to ensure a reasonable relationship between prescription and sales trends. To date, we have not identified any unusual patterns in the volume of prescriptions relative to sales that would warrant reconsideration of our methodology for estimating Adcirca returns. Remodulin, Tyvaso and Orenitram are distributed in the United States under separate contracts with substantially similar terms, which include exchange rights in the event that product is damaged during shipment or expires. Lastly, we pay our distributors for contractual services rendered and accrue for related fees based on contractual rates applied to the estimated units of service provided by distributors for a given financial reporting period.

Operating Expenses

Since our inception, we have devoted 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 following costs:

Cost of Product Sales

Our cost of product sales primarily includes costs to manufacture and acquire products sold to customers, royalty payments under license agreements granting us rights to sell related products, direct and indirect distribution costs incurred in the sale of products, and the costs of inventory reserves for current and projected obsolescence. These costs generally 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.

We manufacture our primary supply of Remodulin, Tyvaso, Orenitram and Unituxin at our own facilities. In particular, we synthesize treprostinil, the active ingredient in Remodulin and Tyvaso, and treprostinil diolamine, the active ingredient in Orenitram, at our facility in Silver Spring, Maryland. We also manufacture finished Remodulin, Tyvaso, and Unituxin at our Silver Spring facility. We manufacture Orenitram and we package, warehouse and distribute Remodulin, Tyvaso, Orenitram and Unituxin, at our facility in Research Triangle Park, North Carolina. We intend to use our own facilities to manufacture our primary supply of Remodulin, Tyvaso, Orenitram and Unituxin. We utilize third-party contract manufacturers to supplement our Remodulin and Tyvaso manufacturing capacity and mitigate the risk of shortages and we are working to obtain FDA approval of a third party to serve as an additional manufacturer of Orenitram and Unituxin finished drug product, and are commencing construction of a new facility to expand our internal manufacturing capacity for Unituxin drug substance. We engage a third-party contract manufacturer to manufacture the Tyvaso Inhalation System. We began selling Orenitram during 2014 and Unituxin in 2015. Typical of the initial commercial activities of a newly-launched product, Orenitram's and Unituxin's cost of product sales as a percentage of its net product sales was initially significantly higher than that of our other commercial products. This percentage has decreased since the commercial launches of Orenitram and Unituxin, and we expect this trend to continue as sales of these products increase.

Lilly manufactures Adcirca. We take title to Adcirca upon its manufacture and bear any losses related to the storage, distribution and sale of Adcirca.

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 generally 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 pre-FDA approval payments to third-party contract manufacturers. Expenses also include costs for third-party arrangements, including upfront fees and milestone payments required under license arrangements for therapies under development. We expect to see increased clinical trial-related expenses in 2017, driven by enrollment in several large clinical studies of our existing products, including Orenitram (*SOUTHPAW* : 310 patients; *IRONS* : 226 patients; and *TAO* , a study of Orenitram in up-front combination with ambrisentan and tadalafil: 600 patients), Tyvaso (*INCREASE* : 314 patients) and Unituxin in new indications (likely to be large, international studies).

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 generally 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 include our core corporate support functions such as human resources, finance and legal, external costs such as insurance premiums, legal fees, grants to non-affiliated, not-profit organizations, and other professional service fees.

Share-Based Compensation

Historically, we granted stock options under our Amended and Restated Equity Incentive Plan (the 1999 Plan) and awards under our Share Tracking Awards Plans (STAP). In June 2015, our shareholders approved the United Therapeutics Corporation 2015 Stock Incentive Plan (the 2015 Plan), which authorizes the issuance of up to 6,150,000 shares of our common stock. Following approval of the 2015 Plan, we ceased granting awards under the STAP and the 1999 Plan, and we modified our equity compensation programs to grant stock options to employees who previously received STAP awards, and to grant stock options and restricted stock units to non-employee directors. The grant date fair value of stock options and restricted stock units are recognized as share-based compensation expense ratably over their vesting period.

Although we have ceased granting STAP awards, we still have a significant number of STAP awards outstanding. Our operating expenses and net income are often materially impacted by the recognition of share-based compensation (benefit) expense associated with outstanding STAP awards as the fair value of these awards varies with the changes in our stock price. The fair values of STAP awards and stock option grants are measured using inputs and assumptions under the Black-Scholes-Merton model that can materially impact the amount of share-based compensation (benefit) expense for a given period. The fair value of restricted stock units is measured using our stock price on the date of grant.

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 STAP-related liability resulting from such re-measurements are recorded as adjustments to share-based compensation (benefit) expense and can create substantial volatility within our operating expenses from financial reporting period to period. The following factors, among others, have a significant impact on the amount of share-based compensation (benefit) expense 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 STAP liability and related compensation expense, while decreases in our stock price will generally result in a reduction in our STAP liability and related compensation expense); (2) changes in the number of outstanding awards; and (3) changes in the number of vested and unvested awards.

Future Prospects

Our strategy is to continue to grow the revenues of our existing commercial products, including through approval of new and/or improved indications, formulations and delivery devices for our existing cardiopulmonary and oncology products. These efforts are designed to provide continued revenue growth in the near and medium term, while efforts are under way to develop technologies in organ transplantation in the longer term.

Our ability to achieve these objectives and sustain our growth and profitability will depend on many factors, including among others: (1) the timing and outcome of preclinical research, clinical trials and regulatory approvals for products we develop; (2) the timing and degree of success related to the commercial launch of 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; (5) the competition we face within our industry; (6) our ability to effectively manage our business in an increasingly complex legal and regulatory environment; (7) our ability to defend against generic competition and challenges to our patents; and (8) the risks identified in *Item 1A — Risk Factors* , included in this Report.

We will need to construct additional facilities to support the development and commercialization of our products and technologies. We have budgeted for capital expenditures of approximately $275 million over the next three years.

We operate in a highly competitive market in which a small number of 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

Revenues

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

	Year Ended December 31,			Percentage Change	
	2016	2015	2014	2016 v. 2015	2015 v. 2014
Net product sales:					
Remodulin	$ 602.3	$ 572.8	$ 553.7	5.2%	3.4%
Tyvaso	404.6	470.1	463.1	(13.9)%	1.5%
Adcirca	372.2	278.8	221.5	33.5%	25.9%
Orenitram	157.2	118.4	41.2	32.8%	187.4%
Unituxin	62.5	20.5	—	204.9%	100.0%
Other	—	5.2	9.0	(100.0)%	(42.2)%
Total revenues	$ 1,598.8	$ 1,465.8	$ 1,288.5	9.1%	13.8%

Revenues for the year ended December 31, 2016 increased by $133.0 million as compared to the same period in 2015. The growth in revenues primarily resulted from the following: (1) a $93.4 million

increase in Adcirca net product sales due to an increase in the number of Adcirca bottles sold and price increases, which were determined by Lilly; (2) a $42.0 million increase in Unituxin net product sales, which we launched in the third quarter of 2015; (3) a $38.8 million increase in Orenitram net product sales due to an increase in the number of patients being treated with Orenitram; and (4) a $29.5 million increase in Remodulin net product sales due to an increase in the number of patients being treated with Remodulin. These increases were partially offset by: (1) a $65.5 million decrease in Tyvaso net product sales due to a decrease in the number of patients being treated with Tyvaso; and (2) a $5.2 million decrease in other revenues as a result of the sale of our antiviral program in late 2015. We believe the decrease in Tyvaso sales resulted from the availability of oral prostacyclin-class therapies, and increased propensity to treat patients with multiple oral therapies earlier in their disease progression, which can delay the need to prescribe inhaled therapies.

Revenues for the year ended December 31, 2015 increased by $177.3 million as compared to the same period in 2014. The growth in revenues primarily resulted from the following: (1) a $77.2 million increase in Orenitram net product sales due to an increase in the number of patients being treated with Orenitram, which we launched in the second quarter of 2014; (2) a $57.3 million increase in Adcirca net product sales due to price increases, which were determined by Lilly, and to a lesser extent by an increase in the number of Adcirca bottles sold; (3) a $20.5 million increase in Unituxin net product sales, which we launched in the third quarter of 2015; and (4) a $19.1 million increase in Remodulin net product sales due to an increase in the number of patients being treated with Remodulin.

For the years ended December 31, 2016, 2015 and 2014 approximately 64 percent, 72 percent and 74 percent, respectively, of total revenues were derived from net product sales of Remodulin, Tyvaso and Orenitram to our U.S.-based specialty pharmaceutical distributors. Remaining revenues were derived primarily from net product sales of Adcirca and Unituxin and net product sales of Remodulin to our international distributors.

The potential launch of generic versions of Remodulin and Adcirca in 2018 and 2017, respectively, as described in *Item 1—Business—Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity—Generic Competition* , could materially reduce our revenues from those products.

We recognize revenues net of: (1) estimated rebates; (2) prompt pay discounts; (3) allowances for sales returns; and (4) distributor fees. These are referred to as gross-to-net deductions and are based on historical experiences and contractual and statutory requirements. The tables below include a reconciliation of the accounts associated with these deductions (in millions):

	Year Ended December 31, 2016				
	Rebates	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees	Total
Balance, January 1, 2016	$ 44.6	$ 3.9	$ 5.3	$ 2.6	$ 56.4
Provisions attributed to sales in:					
Current period	206.3	36.9	3.2	12.6	259.0
Prior periods	4.0	—	—	—	4.0
Payments or credits attributed to sales in:					
Current period	(164.7)	(32.7)	—	(9.8)	(207.2)
Prior periods	(44.2)	(3.8)	(0.8)	(2.6)	(51.4)
Balance, December 31, 2016	$ 46.0	$ 4.3	$ 7.7	$ 2.8	$ 60.8

	Year Ended December 31, 2015				
	Rebates	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees	Total
Balance, January 1, 2015	$ 31.6	$ 3.3	$ 4.0	$ 0.6	$ 39.5
Provisions attributed to sales in:					
Current period	171.6	33.5	2.7	9.8	217.6
Prior periods	—	—	0.3	(0.3)	—
Payments or credits attributed to sales in:					
Current period	(123.9)	(29.6)	—	(7.2)	(160.7)
Prior periods	(34.7)	(3.3)	(1.7)	(0.3)	(40.0)
Balance, December 31, 2015	$ 44.6	$ 3.9	$ 5.3	$ 2.6	$ 56.4

	Year Ended December 31, 2014				
	Rebates	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees	Total
Balance, January 1, 2014	$ 22.5	$ 2.5	$ 2.8	$ 1.1	$ 28.9
Provisions attributed to sales in:					
Current period	116.8	27.1	1.7	7.8	153.4
Prior periods	6.6	—	0.4	0.3	7.3
Payments or credits attributed to sales in:					
Current period	(85.8)	(24.0)	—	(7.1)	(116.9)
Prior periods	(28.5)	(2.3)	(0.9)	(1.5)	(33.2)
Balance, December 31, 2014	$ 31.6	$ 3.3	$ 4.0	$ 0.6	$ 39.5

Cost of Product Sales

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

	Year Ended December 31,			Percentage Change	
	2016	2015	2014	2016 v. 2015	2015 v. 2014
Category:					
Cost of product sales	$ 72.1	$ 60.2	$ 121.5	19.8%	(50.5)%
Share-based compensation expense [1]	0.6	8.8	4.4	(93.2)%	100.0%
Total cost of product sales	$ 72.7	$ 69.0	$ 125.9	5.4%	(45.2)%

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

Cost of Product Sales. The increase in cost of product sales of $11.9 million for the year ended December 31, 2016 as compared to the same period in 2015, was primarily attributable to increased sales.

The decrease in cost of product sales of $61.3 million for the year ended December 31, 2015 as compared to the same period in 2014, primarily resulted from the expiration of our royalty obligation to GlaxoSmithKline PLC (formerly Glaxo Wellcome, Inc.) (Glaxo) in October 2014. During the twelve months ended December 31, 2014, we incurred $72.5 million in royalty expense related to this obligation. This decrease was partially offset by an increase in the cost of product sales of $8.6 million relating to an increase in net product sales of Orenitram and Adcirca in 2015.

Research and Development Expense

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

	Year Ended December 31,			Percentage Change	
	2016	2015	2014	2016 v. 2015	2015 v. 2014
Category:					
Research and development projects	$ 157.6	$ 157.4	$ 169.8	0.1%	(7.3)%
Share-based compensation expense [1]	(10.0)	87.7	72.7	(111.4)%	20.6%
Total research and development expense	$ 147.6	$ 245.1	$ 242.5	(39.8)%	1.1%

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

Research and development expense. The decrease in research and development expense of $12.4 million for the year ended December 31, 2015 as compared to the same period in 2014, primarily resulted from a $6.4 million decrease in expenditures for our development of Unituxin, which was approved by the FDA in March of 2015.

Selling, General and Administrative Expense

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

	Year Ended December 31,			Percentage Change	
	2016	2015	2014	2016 v. 2015	2015 v. 2014
Category:					
General and administrative	$ 210.7	$ 174.6	$ 186.3	20.7%	(6.3)%
Sales and marketing	84.6	94.3	82.0	(10.3)%	15.0%
Share-based compensation expense [1]	21.5	183.8	113.0	(88.3)%	62.7%
Total selling, general and administrative expense	$ 316.8	$ 452.7	$ 381.3	(30.0)%	18.7%

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

General and administrative. The increase in general and administrative expenses of $36.1 million for the year ended December 31, 2016, as compared to the same period in 2015, primarily resulted from: (1) a $20.0 million increase in grants to a non-affiliated, non-profit organization that provides financial assistance to patients with PAH; and (2) $9.3 million of expenses in connection for disposition and write-down of various properties.

The decrease in general and administrative expenses of $11.7 million for the year ended December 31, 2015 as compared to the same period in 2014, primarily resulted from the following: (1) a $12.7 million decrease due to timing of grants to non-affiliated, non-profit organizations that provide financial assistance to patients with PAH; and (2) a $9.4 million decrease in legal expenses resulting from the April 2015 closure of an investigation by the Office of Inspector General of the Department of Health and Human Services related to our marketing practices; partially offset by (3) a $10.0 million increase in salaries and other compensation-related expenses driven by the general expansion of our business.

Sales and marketing. The decrease in sales and marketing expenses of $9.7 million for the year ended December 31, 2016, as compared to the same period in 2015, primarily resulted from an overall decrease in general spending on sales and marketing activities.

The increase in sales and marketing expenses of $12.3 million for the year ended December 31, 2015 as compared to the same period in 2014, primarily resulted from the following: (1) an $8.6 million increase in marketing activities for all of our commercial products, primarily for our most recently approved products, Orenitram and Unituxin; and (2) a $3.7 million increase in salaries and other compensation-related expenses driven by the expansion of our personnel in connection with the growth of our commercial product portfolio.

Share-based Compensation Expense

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

	Year Ended December 31,			Percentage Change	
	2016	2015	2014	2016 v. 2015	2015 v. 2014
Category:					
Share tracking awards plan	$ (15.2)	$ 274.2	$ 159.5	(105.5)%	71.9%
Stock options	24.8	4.9	29.5	406.1%	(83.4)%
Other [1]	2.5	1.2	1.1	108.3%	9.1%
Total share-based compensation expense	$ 12.1	$ 280.3	$ 190.1	(95.7)%	47.4%

(1) Includes expense related to restricted stock units for the year ended December 31, 2016 and employee stock purchase plan for the years ended December 31, 2016, 2015 and 2014.

The decrease in share-based compensation of $268.2 million for the year ended December 31, 2016, as compared to the same period in 2015 and the increase in share-based compensation of $90.2 million for the year ended December 31, 2015 as compared to the same period in 2014, was primarily due to changes in our stock price and number of share tracking awards and stock options outstanding during the periods.

Gain on Sale of Intangible Asset

In September 2015, we sold for $350.0 million in cash the Rare Pediatric Priority Review Voucher (PPRV) we received from the FDA in connection with the approval of Unituxin. The proceeds from the sale of the PPRV were recognized as a gain on the sale of an intangible asset, as the PPRV did not have a carrying value on our consolidated balance sheet at the time of sale.

Income Tax Expense

The provision for income taxes was $346.5 million for the year ended December 31, 2016 compared to $392.8 million for the same period in 2015. The decrease in the provision for income taxes corresponded primarily to a decrease in non-deductible compensation related to STAP awards, which in turn resulted from the decrease in our stock price. The provision for income taxes was $392.8 million for the year ended December 31, 2015 compared to $185.1 million for the year ended 2014. The increase corresponded to an increase in income before income taxes. For the years ended December 31, 2016, 2015 and 2014, the effective tax rates were approximately 33 percent, 38 percent and 35 percent, respectively. For additional details refer to Note 13— *Income Taxes* to the consolidated financial statements contained in this Report.

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 liquidity is sufficient to fund ongoing operations and future business plans as we expect demand for our commercial products to continue to grow. Furthermore, our customer base remains stable and we believe 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 January 2016, we entered into our 2016 Credit Agreement, which provides an unsecured, revolving line of credit of up to $1.0 billion. This line of credit remains undrawn at December 31, 2016 and matures in January 2022. See *Unsecured Revolving Credit Facility* below for further details.

Cash and Cash Equivalents and Marketable Investments

	Year Ended December 31,		Percentage Change
	2016	2015	2016 v. 2015
Cash and cash equivalents	$ 1,023.0	$ 831.8	23.0%
Marketable investments—current	27.8	122.0	(77.2)%
Marketable investments—non-current	2.3	38.0	(93.9)%
Total cash and cash equivalents and marketable investments	$ 1,053.1	$ 991.8	6.2%

The net increase in our cash and cash equivalents and marketable investments was primarily due to $643.6 million in cash generated from operations, partially offset by the use of $500.0 million in cash to repurchase shares of our common stock, $38.1 million in cash to purchase investments in privately-held companies, $38.0 million in cash paid to purchase property, plant and equipment and $15.6 million in cash for debt-related payments.

Cash Flows

	Year Ended December 31,			Percentage Change	
	2016	2015	2014	2016 v. 2015	2015 v. 2014
Net cash provided by operating activities	$ 643.6	$ 382.8	$ 355.3	68.1%	7.7%
Net cash provided by investing activities	$ 48.3	$ 503.6	$ 338.5	(90.4)%	48.8%
Net cash used in financing activities	$ (497.7)	$ (447.0)	$ (576.6)	11.3%	(22.5)%

Operating Activities

Our operating assets and liabilities consist primarily of accounts receivable, inventories, accounts payable and accrued expenses, which include share-based compensation arrangements.

The increase of $260.8 million in net cash provided by operating activities for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily due to: (1) a $133.0 million increase in revenues during the year, which resulted in higher cash collections; and (2) a $179.3 million increase in cash flows due to a decrease in cash paid to settle STAP award exercises, which were partially offset by a $69.1 million increase in cash paid for income taxes.

The increase of $27.5 million in net cash provided by operating activities for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily due to: (1) a $177.3 million increase in revenues during the year, which resulted in higher cash collections; (2) a $23.8 million increase in cash flows due to an increase in accounts payable and accrued expenses; (3) a $14.2 million increase in cash flows due to a decrease in payments for inventory, which were partially

offset by: (1) a $104.7 million increase in cash paid to settle STAP award exercises; and (2) a $97.7 million increase in cash paid for income taxes.

Investing Activities

The decrease of $455.3 million in net cash provided by investing activities for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily due to a decrease of $350.0 million of cash received in the prior year from the sale of our PPRV in September 2015 and a decrease of $128.0 million in cash provided from the net maturities of held-to-maturity investments, which were partially offset by a decrease of $16.1 million in cash paid to purchase investments in privately-held companies and a decrease of $11.8 million in cash paid to purchase property, plant and equipment.

The increase of $165.1 million in net cash provided by investing activities for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily due to $350.0 million of cash from the sale of our PPRV in September 2015, partially offset by a $173.3 million decrease of cash provided from the net maturities of held-to-maturity investments.

Financing Activities

The increase of $50.7 million in net cash used in financing activities for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily due to an increase of $105.5 million in repurchases of our common stock and a decrease of $63.1 million in proceeds from stock option exercises including excess tax benefits from share-based compensation, partially offset by a decrease of $117.6 million in debt-related payments.

In October 2015, our Board of Directors authorized a new program for the repurchase of up to $500.0 million of our common stock in open or privately negotiated transactions, at our discretion. This program was effective from January 1, 2016 to December 31, 2016. In the aggregate, we repurchased approximately 4.2 million shares of common stock under this program for $500.0 million.

The decrease of $129.6 million in net cash used in financing activities for the year ended December 31, 2015 compared to the year ended December 31, 2014 is primarily due to a decrease of $88.6 million in repurchases of our common stock, due to the completion of our repurchase program in August 2015, and a decrease of $44.6 million in principal payments of debt as a result of less early conversion requests on our Convertible Notes.

In June 2014, our Board of Directors authorized the repurchase of up to $500.0 million of our common stock. This program became effective on August 1, 2014, and remained open for one year. In the aggregate, we repurchased approximately 3.3 million shares of common stock under this program for $500.0 million, of which $394.5 million was used to repurchase shares during 2015.

Unsecured Revolving Credit Facility

In January 2016, we entered into the 2016 Credit Agreement, providing for an unsecured revolving credit facility of up to $1.0 billion, which is available to refinance certain of our existing indebtedness and/or for working capital and other general corporate purposes. In January 2017, the maturity date of the 2016 Credit Agreement was extended to January 2022.

At our option, amounts borrowed under the 2016 Credit Agreement will bear interest at either the LIBOR rate 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 2016 Credit Agreement).

The 2016 Credit Agreement contains customary events of default and customary affirmative and negative covenants. As of December 31, 2016, we were in compliance with such covenants and we had not drawn any amounts under the 2016 Credit Agreement. In addition, Lung Biotechnology PBC is our only subsidiary that guarantees our obligations under the 2016 Credit Agreement though, from time to time, one or more of our other subsidiaries may be required to guarantee such obligations.

Secured Line of Credit

In September 2013, we entered into a one-year credit agreement (the 2013 Credit Agreement) with Wells Fargo for a $75.0 million revolving loan facility. In each of July 2014 and July 2015, we amended the 2013 Credit Agreement solely to extend its maturity to September 30 of 2015 and 2017, respectively. In January 2016, we terminated and repaid in full all obligations under the 2013 Credit Agreement when we entered into the 2016 Credit Agreement.

Convertible Senior Notes

In October 2011, we issued the Convertible Notes with an aggregate principal value of $250.0 million. Upon maturity of the Convertible Notes in September 2016, we fulfilled all remaining settlement and repayment obligations.

Contractual Obligations

At December 31, 2016, 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	$ 7.2	$ 3.8	$ 3.2	$ 0.2	$ —
Obligations under the STAP [1]	279.9	174.5	105.4	—	—
Obligations under the SERP [2]	88.0	15.2	7.2	—	65.6
Purchase commitments [3]	167.9	87.0	74.8	6.1	—
Milestone payments under license and acquisition agreements [4]	21.8	9.8	3.9	2.2	5.9
Total	$ 564.8	$ 290.3	$ 194.5	$ 8.5	$ 71.5

(1) Estimated based on the intrinsic value of outstanding STAP awards vested and expected to vest, assuming that unvested awards will be exercised immediately upon vesting. Refer to Note 7 —*Share Tracking Awards Plans* to our consolidated financial statements included in this Report for further details.

(2) Consists of actuarially derived, estimated future payouts of benefits. Refer to Note 14— *Employee Benefit Plans—Supplemental Executive Retirement Plan* to our consolidated financial statements included in this Report for further details.

(3) Purchase commitments primarily include: (i) commitments related to research and development (including clinical trials) for new and existing products; and (ii) open purchase orders for the acquisition of goods and services in the ordinary course of business. Our obligation to pay certain of these amounts may be reduced based on certain future events.

(4) Amount represents contingent consideration and future payments that are recorded within other liabilities (current and non-current) on the consolidated balance sheet as of December 31, 2016. The amounts and timing of future milestone payments may vary depending on when related milestones will be attained, if at all.

Toray License Obligations

In 2000, we entered into an agreement with Toray to obtain exclusive rights to develop and market beraprost, a chemically stable oral prostacyclin analogue, in a sustained release formulation in the United States and Canada for the treatment of all cardiovascular indications. Pursuant to a March 2007 amendment to our license agreement with Toray, we issued 200,000 shares of our common stock to Toray. Toray has the right to request that we repurchase these shares (which have since split into 400,000 shares) upon 30 days prior written notice at the price of $27.21 per share. To date, Toray has not notified us that it intends to require us to repurchase these shares. In 2011, we amended our license agreement with Toray to reduce the royalty rates in exchange for a total of $50.0 million in equal, non-refundable payments to Toray over the five-year period ending in 2015. As of December 31, 2015, this obligation was fully satisfied.

Obligations Under License and Assignment Agreements

We pay Lilly a five percent royalty on net product sales of Adcirca and 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 rights arrangements 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 related licensed technology.

Off-Balance Sheet Arrangements

We do not have any 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

Remodulin, Tyvaso, Orenitram and Unituxin

We market Remodulin, Tyvaso, Orenitram and Unituxin to specialty distributors in the United States and other distributors internationally under materially similar contractual arrangements. Net product sales of Remodulin, Tyvaso, Orenitram and Unituxin are recognized when title and risk of ownership pass to our distributors upon satisfactory delivery to our distributors' facilities—i.e., when all of our performance obligations under these distributor arrangements have been satisfied. We record sales of Remodulin, Tyvaso, Orenitram and Unituxin net of: (1) estimated rebates; (2) prompt payment discounts; (3) service fees we pay to distributors; and (4) an allowance for return rights. Determining sales allowances involves the use of significant estimates and judgment and may involve the use of information from external sources.

We derive our provisions for estimated rebates from an analysis of historical levels of rebates for all government drug discount programs and commercial third-party payer contracts, relative to sales of

each product. In formulating our estimates, we also consider the impact of anticipated changes in product prices, sales trends and government and commercial rebate programs.

We estimate prompt pay discounts based on our experience with sales to eligible distributors. Our distributors have routinely taken advantage of these discounts and we expect them to continue to do so.

We pay our distributors for contractual services rendered and accrue for related fees based on contractual rates applied to the estimated units of service provided by distributors for a given financial reporting period.

Our distributors do not possess return rights for Remodulin, Tyvaso and Orenitram; however, the sales terms for Unituxin include return rights that extend throughout the distribution channel. The financial impact of return rights for Unituxin is not material. We also provide exchange rights for all products in the event that a product is damaged during shipment or expires. Exchanges for damaged product are highly infrequent and the impact of expired product is not material. We do not record a reserve for estimated exchange rights for any of these products in the period of sale.

Adcirca

Adcirca is manufactured for us by Eli Lilly and Company (Lilly) and distributed through Lilly's pharmaceutical wholesaler network. 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. In addition, the sales terms for Adcirca include return rights that extend throughout the distribution channel. We recognize sales of Adcirca on a gross basis (net of allowances) upon delivery to customers due to the following factors: (1) we are responsible for the acceptability of the product purchased by wholesalers; (2) we bear all inventory risk, as title and risk of loss pass to us at the shipping point from Lilly's manufacturing facility; (3) we assume credit risk if Lilly is unable to collect amounts due from customers; and (4) we assume the risk and cost of a product recall, if required.

We recognize sales of Adcirca net of: (1) estimated rebates; (2) prompt pay discounts; (3) allowances for product returns; and (4) wholesaler fees. We estimate our liability for rebates based on an analysis of historical levels of rebates for all government drug discount programs and commercial third-party payer contracts, relative to sales of each product, changes in government and commercial rebate programs and changes in Adcirca's pricing. Prompt pay discounts are estimated based on our experience with sales to eligible distributors. We estimate our allowance for returns based on historical return experience for expired products. Wholesaler fees are based on contractual percentages of sales to wholesalers.

Share-Based Compensation

Our share-based awards are classified as either equity (stock options, restricted stock units and our employee stock purchase plan) or as liabilities (STAP awards). We recognize related share-based compensation expense based on the grant date fair value of stock options and restricted stock units, and based on the fair value of outstanding STAP awards on the grant date and at the end of each reporting period. We estimate the fair value of all share-based awards using the Black-Scholes-Merton valuation model. 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, among others, the expected volatility of our stock price, the expected term of awards and the expected forfeiture rate. Developing these assumptions requires the use of judgment. The fair value of the STAP awards is measured at the end of each financial reporting period because the awards are settled in cash. The STAP liability is adjusted based on the closing price of our common stock at the end of each period, resulting in increased sensitivity to the

price of our common stock. At December 31, 2016, a one dollar change in our stock price would have a $3.5 million impact on our STAP liability and the related share-based compensation expense.

Pension Benefit Obligation

Accounting for our Supplemental Executive Retirement Plan (SERP) requires that we recognize in our consolidated balance sheets a liability equal to the unfunded status of the SERP (the projected benefit obligation, as we do not fund the SERP) and measure our projected benefit obligation as of the end of our fiscal year. Estimating the SERP obligation involves the use of judgment and estimates. The SERP obligation and related pension expense are derived from actuarial valuations that are developed using a number of assumptions. A key assumption underlying the valuation is the discount rate. The discount rate should be representative of the rate associated with high-quality, fixed-income debt securities. We must consider prevailing economic conditions and outlook, the state of the credit markets and other economic factors when determining an appropriate discount rate to employ. Changes in the discount rate can significantly increase or decrease our SERP obligation. For instance, a reduction in the discount rate of one percent would increase our projected benefit obligation by $2.9 million as of December 31, 2016 and result in an actuarial loss. Consequently, we could be required to recognize additional pension expense in our consolidated statements of operations related to the actuarial loss in future periods if certain thresholds are met. Conversely, an increase in the discount rate of one percent would decrease our projected benefit obligation by $2.6 million as of December 31, 2016 and could result in pension benefit recognized in our consolidated statements of operations in future periods if certain thresholds are met. Other actuarial assumptions include participant demographics such as the expected date of retirement, rate of salary increases and withdrawal rates, among other factors. Not only can actual experience differ from actuarial assumptions, but changes in any of these assumptions can also materially affect the measurement of the SERP obligation.

Income Taxes

Income taxes are accounted for in accordance with the asset and liability method. Accordingly, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their tax bases. Deferred tax assets and liabilities are measured using the enacted tax rates that are expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. Deferred tax assets are reduced by a valuation allowance when, in our opinion, it is more likely than not that some or all of the deferred tax assets will not be realized. Evaluating whether deferred assets will be realized requires us to review forecasts of earnings and taxable income, among other considerations. Accordingly, the evaluation of deferred tax assets requires us to make significant judgments and forward-looking assessments regarding the amounts and availability of future taxable income.

Financial statement recognition of a tax position taken or expected to be taken in a tax return is determined based on a more likely than not threshold of that position being sustained. If the tax position meets this threshold, the benefit to be recognized is measured as the largest amount that is more than 50 percent likely to be realized upon ultimate settlement. Accounting for uncertain tax positions involves considerable judgment in assessing the future tax consequences of amounts that have been recognized in our financial statements or tax returns. The ultimate resolution of uncertain tax positions could result in amounts different from those recognized in 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

As of December 31, 2016, we have invested $30.1 million in corporate-debt securities and federally-sponsored agencies. 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. To date, we have not experienced significant volatility in the value of these investments. However, to address market risk, we invest in debt securities with terms no longer than three years and 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, 2016 (in millions, except percentages):

	Expected Maturity	
	2017	2018
Held-to-maturity investments	$ 27.8	$ 2.3
Weighted average interest rate	0.8%	1.4%

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 we take prudent measures to mitigate investment related risks, such risks cannot be fully eliminated, as circumstances can occur that are beyond our control.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

UNITED THERAPEUTICS CORPORATION
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of
United Therapeutics Corporation

We have audited the accompanying consolidated balance sheets of United Therapeutics Corporation as of December 31, 2016 and 2015, and 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, 2016. Our audits also included the financial statement schedule listed in the Index at Item 15(a)(2). These financial statements and schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of United Therapeutics Corporation at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly in all material respects the information set forth therein.

We also have audited, in accordance with the Standards of the Public Company Accounting Oversight Board (United States), United Therapeutics Corporation's internal control over financial reporting as of December 31, 2016, 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, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

McLean, Virginia
February 22, 2017

Report of Independent Registered Public Accounting Firm on

Internal Control over Financial Reporting

The Board of Directors and Shareholders of
United Therapeutics Corporation

We have audited United Therapeutics Corporation's internal control over financial reporting as of December 31, 2016, 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). United Therapeutics Corporation'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 conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). 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.

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.

In our opinion United Therapeutics Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of United Therapeutics Corporation as of December 31, 2016 and 2015 and 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, 2016 and our report dated February 22, 2017, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

McLean, Virginia
February 22, 2017

UNITED THERAPEUTICS CORPORATION

Consolidated Balance Sheets

(In millions, except share and per share data)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 1,023.0	$ 831.8
Marketable investments	27.8	122.0
Accounts receivable, no allowance for 2016 and 2015	214.5	192.8
Inventories, net	100.0	81.3
Other current assets	59.5	47.4
Total current assets	1,424.8	1,275.3
Marketable investments	2.3	38.0
Goodwill and other intangible assets, net	33.8	28.4
Property, plant and equipment, net	489.3	495.8
Deferred tax assets, net	178.3	192.7
Other non-current assets	197.1	154.2
Total assets	$ 2,325.6	$ 2,184.4
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 104.2	$ 103.4
Share tracking awards plan	194.8	274.5
Other current liabilities	33.5	62.8
Total current liabilities	332.5	440.7
Other non-current liabilities	130.9	144.0
Total liabilities	463.4	584.7
Commitments and contingencies—Note 9		
Temporary equity	10.9	11.1
Stockholders' equity:		
Preferred stock, par value $.01, 10,000,000 shares authorized, no shares issued	—	—
Series A junior participating preferred stock, par value $.01, 100,000 shares authorized, no shares issued	—	—
Common stock, par value $.01, 245,000,000 shares authorized, 69,340,985 and 68,987,919 shares issued, and 42,965,856 and 45,760,845 shares outstanding at December 31, 2016 and 2015, respectively	0.7	0.7
Additional paid-in capital	1,813.5	1,790.6
Accumulated other comprehensive loss	(16.8)	(20.4)
Treasury stock, 26,375,129 and 23,227,074 shares at December 31, 2016 and 2015, respectively	(2,379.6)	(1,902.1)
Retained earnings	2,433.5	1,719.8
Total stockholders' equity	1,851.3	1,588.6
Total liabilities and stockholders' equity	$ 2,325.6	$ 2,184.4

See accompanying notes to consolidated financial statements.

UNITED THERAPEUTICS CORPORATION

Consolidated Statements of Operations

(In millions, except per share data)

	Year Ended December 31,		
	2016	2015	2014
Revenues:			
Net product sales	$ 1,598.8	$ 1,460.6	$ 1,279.5
Other	—	5.2	9.0
Total revenues	1,598.8	1,465.8	1,288.5
Operating expenses:			
Cost of product sales	72.7	69.0	125.9
Research and development	147.6	245.1	242.5
Selling, general and administrative	316.8	452.7	381.3
Total operating expenses	537.1	766.8	749.7
Operating income	1,061.7	699.0	538.8
Other (expense) income:			
Interest expense	(3.9)	(4.7)	(17.6)
Gain on sale of intangible asset	—	350.0	—
Other, net	2.4	0.1	4.0
Total other (expense) income, net	(1.5)	345.4	(13.6)
Income before income taxes	1,060.2	1,044.4	525.2
Income tax expense	(346.5)	(392.8)	(185.1)
Net income	$ 713.7	$ 651.6	$ 340.1
Net income per common share:			
Basic	$ 16.29	$ 14.17	$ 7.06
Diluted	$ 15.25	$ 12.72	$ 6.28
Weighted average number of common shares outstanding:			
Basic	43.8	46.0	48.2
Diluted	46.8	51.2	54.2

See accompanying notes to consolidated financial statements.

UNITED THERAPEUTICS CORPORATION

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME

(In millions)

	Year Ended December 31,		
	2016	2015	2014
Net income	$ 713.7	$ 651.6	$ 340.1
Other comprehensive income (loss):			
Foreign currency translation losses	(3.0)	(5.3)	(4.8)
Defined benefit pension plan:			
Prior service cost arising during period, net of tax	—	—	(2.4)
Actuarial gain arising during period, net of tax	6.0	0.7	3.0
Amortization of actuarial gain and prior service cost included in net periodic pension cost, net of tax	0.6	0.9	0.9
Total defined benefit pension plan, net of tax	6.6	1.6	1.5
Unrealized loss on available-for-sale securities, net of tax	—	—	(0.3)
Other comprehensive income (loss), net of tax	3.6	(3.7)	(3.6)
Comprehensive income	$ 717.3	$ 647.9	$ 336.5

See accompanying notes to consolidated financial statements.

UNITED THERAPEUTICS CORPORATION

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, 2013	63.0	$ 0.6	$ 1,057.2	$ (13.1)	$ (513.4)	$ 728.1	$ 1,259.4
Net income	—	—	—	—	—	340.1	340.1
Foreign currency translation adjustments	—	—	—	(4.8)	—	—	(4.8)
Unrealized gain on available-for-sale securities	—	—	—	(0.3)	—	—	(0.3)
Defined benefit pension plan	—	—	—	1.5	—	—	1.5
Shares issued under employee stock purchase plan	—	—	3.3	—	—	—	3.3
Conversion of 2016 convertible notes	1.5	0.1	192.9	—	(189.3)	—	3.7
Equity component—2016 convertible notes	—	—	11.1	—	—	—	11.1
Repurchase of shares	—	—	—	—	(483.1)	—	(483.1)
Exercise of stock options	1.5	—	50.2	—	—	—	50.2
Tax benefit from exercises of non-qualified stock options	—	—	30.8	—	—	—	30.8
Share-based compensation	—	—	30.6	—	—	—	30.6
Balance, December 31, 2014	66.0	0.7	1,376.1	(16.7)	(1,185.8)	1,068.2	1,242.5
Net income	—	—	—	—	—	651.6	651.6
Foreign currency translation adjustments	—	—	—	(5.3)	—	—	(5.3)
Defined benefit pension plan	—	—	—	1.6	—	—	1.6
Shares issued under employee stock purchase plan	—	—	4.0	—	—	—	4.0
Conversion of 2016 convertible notes	2.0	—	324.7	—	(321.8)	—	2.9
Equity component—2016 convertible notes	—	—	3.0	—	—	—	3.0
Repurchase of shares	—	—	—	—	(394.5)	—	(394.5)
Exercise of stock options	1.0	—	39.3	—	—	—	39.3
Tax benefit from exercises of non-qualified stock options	—	—	37.4	—	—	—	37.4
Share-based compensation	—	—	6.1	—	—	—	6.1
Balance, December 31, 2015	69.0	0.7	1,790.6	(20.4)	(1,902.1)	1,719.8	1,588.6
Net income	—	—	—	—	—	713.7	713.7
Foreign currency translation adjustments	—	—	—	(3.0)	—	—	(3.0)
Defined benefit pension plan	—	—	—	6.6	—	—	6.6
Shares issued under employee stock purchase plan	—	—	4.3	—	—	—	4.3
Conversion of 2016 convertible notes	0.1	—	7.6	—	(7.5)	—	0.1
Equity component—2016 convertible notes	—	—	0.1	—	—	—	0.1
Shares issued upon expiration of warrants	—	—	(30.0)	—	30.0	—	—
Repurchase of shares	—	—	—	—	(500.0)	—	(500.0)
Exercise of stock options	0.2	—	7.7	—	—	—	7.7
Tax benefit from exercises of non-qualified stock options	—	—	5.9	—	—	—	5.9
Share-based compensation	—	—	27.3	—	—	—	27.3
Balance, December 31, 2016	69.3	$ 0.7	$ 1,813.5	$ (16.8)	$ (2,379.6)	$ 2,433.5	$ 1,851.3

See accompanying notes to consolidated financial statements.

UNITED THERAPEUTICS CORPORATION

Consolidated Statements of Cash Flows

(In millions)

	Year Ended December 31,		
	2016	2015	2014
Cash flows from operating activities:			
Net income	$ 713.7	$ 651.6	$ 340.1
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation and amortization	31.6	32.9	32.2
Share-based compensation expense	12.1	280.3	190.1
Gain on sale of intangible asset	—	(350.0)	—
Other	9.5	7.5	24.2
Excess tax benefits from share-based compensation	(5.9)	(37.4)	(30.8)
Changes in operating assets and liabilities:			
Accounts receivable	(21.7)	(30.5)	(35.7)
Inventories	(24.5)	(6.8)	(21.0)
Accounts payable and accrued expenses	0.6	17.0	(6.8)
Other assets and liabilities	(71.8)	(181.8)	(137.0)
Net cash provided by operating activities	643.6	382.8	355.3
Cash flows from investing activities:			
Purchases of property, plant and equipment	(38.0)	(49.8)	(47.4)
Purchases of held-to-maturity investments	(0.8)	(62.8)	(118.7)
Maturities of held-to-maturity investments	130.4	320.4	549.6
Gain on sale of intangible asset	—	350.0	—
Purchase of investments held at cost	(36.0)	(54.2)	(45.0)
Purchase of investments under the equity method	(2.1)	—	—
Intangible assets acquired, net	(5.2)	—	—
Net cash provided by investing activities	48.3	503.6	338.5
Cash flows from financing activities:			
Principal payments of debt	(8.8)	(133.2)	(177.8)
Payments of debt issuance costs	(6.8)	—	—
Payments to repurchase common stock	(500.0)	(394.5)	(483.1)
Proceeds from line of credit	—	—	140.0
Payments on line of credit	—	—	(140.0)
Proceeds from exercise of stock options	7.7	39.3	50.2
Issuance of stock under employee stock purchase plan	4.3	4.0	3.3
Excess tax benefits from share-based compensation	5.9	37.4	30.8
Net cash used in financing activities	(497.7)	(447.0)	(576.6)
Effect of exchange rate changes on cash and cash equivalents	(3.0)	(5.3)	(3.8)
Net increase in cash and cash equivalents	191.2	434.1	113.4
Cash and cash equivalents, beginning of year	831.8	397.7	284.3
Cash and cash equivalents, end of year	$ 1,023.0	$ 831.8	$ 397.7
Supplemental cash flow information :			
Cash paid for interest	$ 1.5	$ 1.0	$ 5.5
Cash paid for income taxes	$ 362.4	$ 293.3	$ 195.6
Non-cash investing and financing activities:			
Acquisitions—non-cash consideration	$ —	$ —	$ 5.2
Non-cash additions to property, plant and equipment	$ 2.9	$ 1.1	$ 3.2
Issuance of common stock upon conversion of convertible notes	$ 7.5	$ 321.8	$ 189.3

See accompanying 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.

We have approval from the U.S. Food and Drug Administration (FDA) to market the following therapies: Remodulin ® (treprostinil) Injection (Remodulin), Tyvaso ® (treprostinil) Inhalation Solution (Tyvaso), Adcirca ® (tadalafil) Tablets (Adcirca), Orenitram ® (treprostinil) Extended-Release Tablets (Orenitram) and Unituxin ® (dinutuximab) Injection (Unituxin). Our only significant revenues outside the United States are derived from sales of Remodulin in Europe. We commenced commercial sales of Orenitram and Unituxin during the second quarter of 2014 and third quarter of 2015, respectively.

As used in these notes to the 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 wholly owned 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.

In the current liabilities section of our balance sheet, we reclassified the prior period amount within "convertible notes" to "other current liabilities" to conform with the current period presentation.

Use of Estimates

The preparation of the 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 the 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. Our significant accounting policies that require use of subjective and/or complex judgment and estimates impact the following financial statement areas: revenue recognition, share-based compensation, marketable investments, fair value measurements (including those relating to our acquisitions), income taxes, goodwill and other intangible assets, and obligations related to our Supplemental Executive Retirement Plan.

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, 1.0 percent Convertible Senior Notes which matured in September 2016 (Convertible Notes) and contingent consideration are reported in Note 4 —*Investments* and Note 5 —*Fair Value Measurements* , respectively.

2. Summary of Significant Accounting Policies (Continued)

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* to these consolidated financial statements.

Cash Equivalents

Cash equivalents consist of highly liquid investments with maturities of three months or less from the date of acquisition and include money market funds, commercial paper, and certificates of deposit.

Marketable Investments

Substantially all of our marketable investments are debt securities that we classify as held-to-maturity because of our positive intent and ability to hold the securities until maturity. Held-to-maturity securities are classified as either current or non-current assets on our consolidated balance sheets based on their contractual maturity dates and 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.

We monitor our investment portfolio for impairment quarterly or more frequently if circumstances warrant. In the event that the carrying value of an investment exceeds its fair value and the decline in value is determined to be other-than-temporary, we record an impairment charge within earnings attributable to the estimated credit loss. In determining whether a decline in the value of an investment is other-than-temporary, we evaluate currently available factors that may include, among others: (1) general market conditions; (2) the duration and extent to which fair value has been less than the carrying value; (3) the investment issuer's financial condition and business outlook; and (4) our assessment as to whether it is more likely than not that we will be required to sell a security prior to recovery of its amortized cost basis.

Trade Receivables

Trade receivables consist of short-term amounts due from customers and are stated at the amount we expect to collect. We establish an allowance for doubtful accounts, if any, based on our assessment of the collectability of specific customer accounts.

2. Summary of Significant Accounting Policies (Continued)

Inventories

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

	As of December 31,	
	2016	2015
Raw materials	$ 25.4	$ 23.1
Work-in-progress	24.9	22.5
Finished goods	49.7	35.7
Total inventories	$ 100.0	$ 81.3

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). If the carrying amount of the reporting unit exceeds its fair value, then the amount of an impairment loss, if any, is measured as the excess of the recorded amount of goodwill over its implied fair value (Step 2 of the goodwill impairment test). We used a qualitative assessment for our goodwill impairment testing for 2016 and 2015. Our evaluation of goodwill completed during the years ended December 31, 2016 and 2015, resulted in no 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 projects, which were measured at their estimated fair values as of their acquisition dates. We used a qualitative assessment for our indefinite-lived intangible asset impairment testing. Our evaluation of indefinite-lived intangible assets completed during the years ended December 31, 2016 and 2015, resulted in no impairment losses.

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, 2016 and 2015.

2. Summary of Significant Accounting Policies (Continued)

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

	As of December 31, 2016			As of December 31, 2015		
	Gross	Accumulated Amortization	Net	Gross	Accumulated Amortization	Net
Goodwill	$ 10.3	$ —	$ 10.3	$ 10.3	$ —	$ 10.3
Other intangible assets:						
Technology, patents and trade names	6.5	(4.8)	1.7	6.5	(4.7)	1.8
In-process research and development	21.5	—	21.5	15.5	—	15.5
Customer relationships and non-compete agreements	4.3	(4.0)	0.3	4.3	(3.5)	0.8
Total	$ 42.6	$ (8.8)	$ 33.8	$ 36.6	$ (8.2)	$ 28.4

Related amortization expense for the years ended December 31, 2016, 2015 and 2014, was $0.6 million, $1.1 million and $1.4 million, respectively. As of December 31, 2016, aggregate amortization expense relating to definite-lived intangible assets for each of the five succeeding years and thereafter is estimated at less than $1.0 million per year.

In September 2015, we sold for $350.0 million in cash the Rare Pediatric Priority Review Voucher (PPRV) we received from the FDA in connection with the approval of Unituxin. The proceeds from the sale of the PPRV were recognized as a gain on the sale of an intangible asset as the PPRV did not have a carrying value on our consolidated balance sheet at the time of sale.

Property, Plant and Equipment

Property, plant and equipment is recorded at cost and depreciated over its estimated useful life using the straight-line method. The estimated useful lives of property, plant and equipment 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

2. Summary of Significant Accounting Policies (Continued)

Property, plant and equipment consists of the following (in millions):

	As of December 31,	
	2016	2015
Land and land improvements	$ 60.1	$ 61.1
Buildings, building improvements and leasehold improvements	409.9	418.2
Buildings under construction	44.6	26.5
Furniture, equipment and vehicles	149.7	144.9
	664.3	650.7
Less—accumulated depreciation	(175.0)	(154.9)
Property, plant and equipment, net	$ 489.3	$ 495.8

Depreciation expense for the years ended December 31, 2016, 2015 and 2014, was $31.0 million, $31.8 million and $30.8 million, respectively.

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

Treasury Stock

Repurchased treasury stock is recorded at cost, including commissions and fees. Treasury stock acquired in connection with the convertible note hedge on our Convertible Notes is recorded at the fair value on the acquisition date, which is the closing price of our common stock on that date. 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

Remodulin, Tyvaso, Orenitram and Unituxin

We sell Remodulin, Tyvaso, Orenitram and Unituxin to distributors under similar contractual arrangements. We recognize sales of these products when title and risk of ownership pass to our distributors upon satisfactory delivery— *i.e.,* when all of our performance obligations under our distribution agreements have been satisfied. We record sales of these products net of various product sales allowances in the period that associated revenues are recognized. These sales allowances include estimated rebates, prompt payment discounts and service fees paid to our distributors. Calculating these sales allowances involves the use of significant estimates and judgments and information obtained from external sources.

We derive our provisions for estimated rebates from an analysis of historical levels of rebates to both state Medicaid agencies and commercial third-party payers by product, relative to sales of each product. In addition, for Orenitram patients, we determine our obligation for prescription drug discounts required by Medicare Part D for patients within the coverage gap based on estimations of the number of patients and the period that such patients will remain within the coverage gap. In formulating our estimates, we also consider the impact of anticipated changes in our product pricing, if any, sales trends and government rebate programs, particularly as they relate to eligibility requirements and/or rebate pricing.

2. Summary of Significant Accounting Policies (Continued)

Prompt pay discounts are estimated based on our experience with sales to eligible distributors. Our distributors have routinely taken advantage of these discounts and we expect them to continue to do so.

We pay our distributors for contractual services rendered and accrue for related fees based on contractual rates applied to the estimated units of service provided by distributors for a given financial reporting period.

Our distributors do not possess return rights for Remodulin, Tyvaso and Orenitram; however, the sales terms for Unituxin include return rights that extend throughout the distribution channel. The financial impact of return rights for Unituxin is not material. We also provide exchange rights for all products in the event that a product is damaged during shipment or expires. Exchanges for damaged product are highly infrequent and the impact of expired product is not material. We do not record a reserve for estimated exchange rights for any of these products in the period of sale.

Adcirca

Adcirca is manufactured for us by Eli Lilly and Company (Lilly) and distributed through Lilly's pharmaceutical wholesaler network. 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. In addition, the sales terms for Adcirca include return rights that extend throughout the distribution channel. We recognize sales of Adcirca on a gross basis (net of allowances) upon delivery to customers due to the following factors: (1) we are responsible for the acceptability of the product purchased by wholesalers; (2) we bear all inventory risk, as title and risk of loss pass to us at the shipping point from Lilly's manufacturing facility; (3) we assume credit risk if Lilly is unable to collect amounts due from customers; and (4) we assume the risk and cost of a product recall, if required.

We recognize sales of Adcirca net of: (1) estimated rebates under government drug discount programs and commercial third-party payer contracts; (2) prompt pay discounts; (3) allowances for product returns; and (4) wholesaler fees. We estimate our liability for rebates based on an analysis of historical levels of rebates to both Medicaid and commercial third-party payers and we consider the impact of sales trends, changes in government and commercial rebate programs and anticipated changes in Adcirca's pricing. Prompt pay discounts are estimated based on our experience with sales to eligible distributors. We derive our allowance for returns based on historical return rates accumulated since the commercial launch of Adcirca in 2009. Wholesaler fees are based on contractual percentages of sales to wholesalers.

Research and Development

Research and development costs are expensed as incurred except for refundable 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 and amounts paid to third parties for services and materials relating to drug development and clinical trials.

2. Summary of Significant Accounting Policies (Continued)

We recognize the following 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

Our share tracking awards plans 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.

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.

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.

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

Income taxes are accounted for in accordance with the asset and liability method. Accordingly, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their tax bases. Deferred tax assets and liabilities are measured using the enacted tax rates that are expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in the period that includes the enactment date. Deferred tax assets are reduced by a valuation allowance when, in our judgment, it is more likely than not that some or all of the deferred tax assets will not be realized.

Financial statement recognition of a tax position taken or expected to be taken in a tax return is determined based on a more likely than not threshold of that position being sustained. If the tax position meets this threshold, the benefit to be recognized is measured as the largest amount that is

2. Summary of Significant Accounting Policies (Continued)

more likely than not to be realized upon ultimate settlement. It is our policy to record interest and penalties related to uncertain tax positions as a component of income tax expense.

Earnings (Loss) 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 is 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, commercial paper, marketable investments, 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 federally-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 on our consolidated balance sheets.

3. Recently Issued Accounting Standards

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2014-09, *Revenue from Contracts with Customers* and subsequent clarifying guidance. This guidance eliminates transaction-specific and industry-specific revenue recognition guidance under current GAAP and replace it with a principle-based approach for determining revenue recognition. This guidance requires that companies recognize revenue based on the value of transferred goods or services as they occur in the contract. In addition, disclosure is required about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. This guidance is effective for annual reporting periods beginning after December 15, 2017, and allows for either full retrospective or modified retrospective adoption. We are evaluating the transition method we will elect and the effects of the adoption of this ASU on our financial statements. An assessment of our customer arrangements has been initiated and we are currently evaluating the impact on our financial statements.

3. Recently Issued Accounting Standards (Continued)

In July 2015, the FASB issued ASU No. 2015-11, *Simplifying the Measurement of Inventory* (ASU 2015-11), which requires that inventory be measured at the lower of cost or net realizable value for entities using first-in, first-out or average cost methods. ASU 2015-11 should be applied prospectively and will be effective for fiscal years beginning after December 15, 2016, and for interim periods within those fiscal years, with early adoption permitted. We adopted this standard on January 1, 2017. The provisions of this standard do not have a material impact on our financial statements.

In January 2016, the FASB issued ASU No. 2016-01, *Financial Instruments—Overall: Recognition and Measurement of Financial Assets and Financial Liabilities* (ASU 2016-01), which requires equity investments to be measured at fair value through net income. Equity investments that are accounted for under the equity method are not impacted. ASU 2016-01 provides that equity investments without readily determinable fair values can be valued at cost minus impairment with a simplified impairment assessment using qualitative assessments. ASU 2016-01 requires separate presentation of the financial assets and liabilities by category and form. ASU 2016-01 should be applied prospectively and will be effective for fiscal years beginning after December 15, 2017, and for interim periods within those fiscal years. Early adoption is not permitted except in limited circumstances. We are evaluating the effect of adoption on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (ASU 2016-02), which requires that organizations recognize lease assets and lease liabilities on the balance sheet. ASU 2016-02 also requires additional quantitative and qualitative disclosures that provide the amount, timing, and uncertainty of cash flows relating to lease arrangements. ASU 2016-02 is effective for annual reporting periods beginning after December 15, 2018, using a modified retrospective approach. The modified retrospective approach requires retrospective application to the earliest period presented in the respective financial statements, provides certain practical expedients related to leases that commenced prior to the effective date and allows the use of hindsight when evaluating lease options. Early adoption is permitted. We are evaluating the effect of adoption on our financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation* (ASU 2016-09), which serves to simplify the accounting for share-based payment transactions. ASU 2016-09 includes guidance on several aspects of the accounting for share-based payments, including the income tax consequences, forfeitures and classification on the statement of cash flows. ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, and for interim periods within those fiscal years. We adopted this standard on January 1, 2017. Upon adoption of ASU 2016-09, we will recognize excess tax benefits as income tax benefits and expenses on the consolidated statements of operations. Previously, such amounts were recognized as increases and decreases in additional paid-in capital on the consolidated balance sheets. On January 1, 2017, we also established an accounting policy election to account for forfeitures when they occur. As a result, we will recognize a cumulative-effect adjustment to reduce retained earnings for the effect of the forfeiture estimate on awards that were in the process of vesting as of December 31, 2016. Although it is difficult to predict the impact of adopting ASU 2016-09 because the impact depends on the timing of when employees exercise stock options, when employees forfeit stock options and the fair value of our stock price at such time, we do not anticipate a material impact on our financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows—Classification of Certain Cash Receipts and Cash Payments* (ASU 2016-15), which reduces existing diversity in the classification of certain cash receipts and cash payments on the statements of cash flows. ASU 2016-15

3. Recently Issued Accounting Standards (Continued)

is effective for fiscal years beginning after December 15, 2017, and for interim periods within those fiscal years. Early adoption is permitted. We are evaluating the effect of adoption on our financial statements.

In October 2016, the FASB issued ASU No. 2016-16, *Income Taxes—Intra-Entity Transfers of Assets Other Than Inventory* (ASU 2016-16), which requires that an entity recognize the income tax consequences of an intra-entity transfer of assets other than inventory when the transfer occurs. ASU 2016-16 is effective for annual reporting periods beginning after December 15, 2017 using a modified retrospective approach through a cumulative adjustment in retained earnings as of the beginning of the period of adoption. Early adoption is permitted. We are evaluating the effect of adoption on our financial statements.

4. Investments

Marketable Investments

Held-to-Maturity Investments

Marketable investments classified as held-to-maturity consist of the following (in millions):

As of December 31, 2016	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Government-sponsored enterprises	$ 19.3	$ —	$ —	$ 19.3
Corporate notes and bonds	10.8	—	—	10.8
Total	$ 30.1	$ —	$ —	$ 30.1
Reported under the following captions on the consolidated balance sheet:				
Current marketable investments	$ 27.8			
Non-current marketable investments	2.3			
	$ 30.1			

As of December 31, 2015	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Government-sponsored enterprises	$ 53.3	$ —	$ (0.2)	$ 53.1
Corporate notes and bonds	106.7	—	—	106.7
Total	$ 160.0	$ —	$ (0.2)	$ 159.8
Reported under the following captions on the consolidated balance sheet:				
Current marketable investments	$ 122.0			
Non-current marketable investments	38.0			
	$ 160.0			

4. Investments (Continued)

The following table summarizes gross unrealized losses and the length of time marketable investments have been in a continuous unrealized loss position (in millions):

	As of December 31,			
	2016		2015	
	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss
Government-sponsored enterprises:				
Continuous unrealized loss position less than one year	$ —	$ —	$ 48.1	$ (0.2)
Continuous unrealized loss position greater than one year	—	—	—	—
	—	—	48.1	(0.2)
Corporate notes and bonds:				
Continuous unrealized loss position less than one year	—	—	63.8	—
Continuous unrealized loss position greater than one year	—	—	—	—
	—	—	63.8	—
Total	$ —	$ —	$ 111.9	$ (0.2)

We attributed the unrealized losses on held-to-maturity securities as of December 31, 2015, to the variability in related market interest rates. We did not intend to sell these securities, nor was it more likely than not that we were required to sell them prior to the end of their contractual terms. Furthermore, we did not believe that these securities exposed us to undue market risk or counterparty credit risk. As such, we did not consider these securities to be other than temporarily impaired.

The following table summarizes the contractual maturities of held-to-maturity marketable investments (in millions):

	As of December 31, 2016	
	Amortized Cost	Fair Value
Due in less than one year	$ 27.8	$ 27.8
Due in one to two years	2.3	2.3
Due in three to five years	—	—
Due after five years	—	—
Total	$ 30.1	$ 30.1

Investments Held at Cost

As of December 31, 2016, we maintain in the aggregate, non-controlling equity investments of approximately $173.2 million in privately-held companies, including a $100.0 million investment in the preferred stock of Synthetic Genomics, Inc. (SGI), which we purchased in two separate $50.0 million transactions in May 2014 and September 2015. These investments are held at cost since we do not have the ability to exercise significant influence over these companies and their fair values are not readily determinable. The fair value of these investments has not been estimated at December 31, 2016, as we

4. Investments (Continued)

have not identified any events or developments indicating that their carrying amounts may be impaired. We include these investments within other non-current assets on our accompanying consolidated balance sheets.

In addition to the SGI investments noted above, we entered into a separate multi-year research and development collaboration agreement with SGI in May 2014, whereby SGI will develop engineered primary pig cells with modified genomes for use in our xenotransplantation program. This collaboration was initially focused primarily on lungs and was expanded in September 2015 to include an additional focus on kidneys. Under this agreement, each party assumes its own research and development costs and SGI may receive royalties and milestone payments from development and commercialization of organs. During the year ended December 31, 2016, we made payments of $36.0 million for investments held at cost.

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 rank these assets and liabilities within the fair value hierarchy. Other current assets and other current liabilities have fair values that approximate their carrying values.

5. Fair Value Measurements (Continued)

Assets and liabilities subject to fair value measurements are as follows (in millions):

	As of December 31, 2016			
	Level 1	Level 2	Level 3	Balance
Assets				
Money market funds [1]	$ 534.4	$ —	$ —	$ 534.4
Federally-sponsored and corporate debt securities [2]	—	30.1	—	30.1
Total assets	$ 534.4	$ 30.1	$ —	$ 564.5
Liabilities				
Contingent consideration [4]	—	—	10.4	10.4
Total liabilities	$ —	$ —	$ 10.4	$ 10.4

	As of December 31, 2015			
	Level 1	Level 2	Level 3	Balance
Assets				
Money market funds [1]	$ 496.4	$ —	$ —	$ 496.4
Federally-sponsored and corporate debt securities [2]	—	159.8	—	159.8
Total assets	$ 496.4	$ 159.8	$ —	$ 656.2
Liabilities				
Convertible notes due 2016 [3]	$ 16.0	$ —	$ —	$ 16.0
Contingent consideration [4]	—	—	9.4	9.4
Total liabilities	$ 16.0	$ —	$ 9.4	$ 25.4

(1) Included in cash and cash equivalents on the accompanying consolidated balance sheets.

(2) Included in current and non-current marketable investments on the accompanying consolidated balance sheets. The fair value of these securities is principally measured or corroborated by trade data for identical securities in which related trading activity is not sufficiently frequent to be considered a Level 1 input or comparable securities that are more actively traded. See also Note 4— *Investments—Marketable Investments—Held-to-Maturity Investments* to these consolidated financial statements.

(3) Included in other current liabilities on the accompanying consolidated balance sheets. The Convertible Notes matured on September 15, 2016. The carrying value of the Convertible Notes as of December 31, 2015 was $5.4 million. The fair value of our Convertible Notes was estimated using Level 1 observable inputs since our Convertible Notes were trading with sufficient frequency such that we believed related pricing could be used as the primary basis for measuring their fair value. As of December 31, 2015, the fair value of the Convertible Notes was substantially higher than their book value. This was primarily due to the excess conversion value of the Convertible Notes compared to the Convertible Notes' par value, and the fact that any such excess would be paid in shares of our common stock.

(4) Included in other non-current liabilities on the accompanying consolidated balance sheets. The fair value of contingent consideration has been estimated using probability weighted discounted cash flow models (DCF). The DCF incorporates 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. We analyze and evaluate these fair value measurements quarterly to determine whether valuation inputs continue to be relevant and appropriate or whether current period developments warrant adjustments to valuation inputs and related measurements.

6. Accounts Payable and Accrued Expenses

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

	As of December 31,	
	2016	2015
Accounts payable	$ 8.1	$ 7.5
Accrued expenses:		
Sales related (royalties, rebates and fees)	$ 55.7	$ 52.8
Payroll related	30.6	31.4
Other	9.8	11.7
Total accrued expenses	$ 96.1	$ 95.9
Total accounts payable and accrued expenses	$ 104.2	$ 103.4

7. Share Tracking Awards Plans

We previously issued awards under the United Therapeutics Corporation Share Tracking Awards Plan, adopted in June 2008 (2008 STAP) and the United Therapeutics Corporation 2011 Share Tracking Awards Plan, adopted in March 2011 (2011 STAP). We refer to the 2008 STAP and the 2011 STAP collectively as the "STAP" and awards granted and/or outstanding under either of these plans 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. 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. The STAP liability includes vested awards and awards that are expected to vest. We recognize expense for awards that are expected to vest during the vesting period. We discontinued the issuance of STAP awards in June 2015, when our shareholders approved the United Therapeutics Corporation 2015 Stock Incentive Plan (the 2015 Plan), a broad-based stock incentive plan enabling us to grant stock options and other forms of equity compensation to our employees. See Note 11— *Stockholders' Equity* to these consolidated financial statements for information on the 2015 Plan.

The aggregate balance of the STAP liability was $268.9 million and $354.7 million at December 31, 2016 and 2015, respectively, of which $74.1 million and $80.2 million, respectively, has been classified as other non-current liabilities on our consolidated balance sheets based on their vesting terms.

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, the expected forfeiture rate 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.

7. Share Tracking Awards Plans (Continued)

A description of the key inputs, requiring estimates, used in determining the fair value of the awards is provided 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 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 term —The expected term reflects the estimated time period we expect an award to remain outstanding. For the years ended December 31, 2016, 2015 and 2014, we used historical data to develop this input.

Expected forfeiture rate —The expected forfeiture rate is an estimated percentage of awards granted that are expected to be forfeited or canceled on an annual basis prior to becoming fully vested. We derive our estimate based on historical forfeiture experience for similar classes of employees.

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

	As of December 31,		
	2016	2015	2014
Expected volatility	36.1%	35.3%	34.0%
Risk-free interest rate	1.4%	1.4%	1.3%
Expected term of awards (in years)	2.5	3.4	4.0
Expected forfeiture rate	8.8%	8.8%	9.3%
Expected dividend yield	0.0%	0.0%	0.0%

The closing price of our common stock was $143.43, $156.61, and $129.49 on December 31, 2016, 2015, and 2014, respectively.

7. Share Tracking Awards Plans (Continued)

A summary of the status and activity of the STAP is presented below:

	Number of Awards	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in millions)
Outstanding at January 1, 2016	6,845,163	$ 86.86		
Granted	—	—		
Exercised	(1,139,612)	61.08		
Forfeited	(591,713)	96.32		
Outstanding at December 31, 2016	5,113,838	$ 91.51	6.5	$ 290.3
Exercisable at December 31, 2016	2,564,858	$ 88.46	6.1	$ 151.3
Expected to vest at December 31, 2016	2,315,483	$ 93.41	6.9	$ 128.6

The weighted average grant-date fair value of STAP awards granted during the years ended December 31, 2015 and 2014 was $58.52 and $33.82, respectively.

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

	Year Ended December 31,		
	2016	2015	2014
Cost of product sales	$ —	$ 8.7	$ 4.3
Research and development	(11.8)	87.4	72.3
Selling, general and administrative	(3.4)	178.1	82.9
Share-based compensation (benefit) expense before tax	(15.2)	274.2	159.5
Related income tax expense (benefit)	5.6	(103.5)	(56.6)
Share-based compensation (benefit) expense, net of tax	$ (9.6)	$ 170.7	$ 102.9
Share-based compensation capitalized as part of inventory	$ —	$ 7.1	$ 2.0

Cash paid to settle STAP exercises during the years ended December 31, 2016, 2015 and 2014 was $69.5 million, $248.8 million, and $144.1 million, respectively.

8. Debt

Unsecured Revolving Credit Facility

In January 2016, we entered into a credit agreement (the 2016 Credit Agreement) with Wells Fargo Bank, National Association (Wells Fargo), as administrative agent and a swingline lender, and various other lender parties, providing for an unsecured revolving credit facility of up to $1.0 billion. In accordance with the terms of the 2016 Credit Agreement, we extended the maturity date by one year effective in January 2017. As a result, the 2016 Credit Agreement will mature in January 2022.

8. Debt (Continued)

At our option, amounts borrowed under the 2016 Credit Agreement will bear interest at either the LIBOR rate 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 2016 Credit Agreement).

The 2016 Credit Agreement contains customary events of default and customary affirmative and negative covenants. As of December 31, 2016, we were in compliance with such covenants and we had not drawn any amounts. Lung Biotechnology PBC is our only subsidiary that guarantees our obligations under the 2016 Credit Agreement though, from time to time, one or more of our other subsidiaries may be required to guarantee such obligations.

Secured Line of Credit

In September 2013, we entered into a one-year credit agreement (the 2013 Credit Agreement) with Wells Fargo for a $75.0 million revolving loan facility. In each of July 2014 and July 2015, we amended the 2013 Credit Agreement solely to extend its maturity to September 30 of 2015 and 2017, respectively. In January 2016, we terminated and repaid in full all obligations under the 2013 Credit Agreement when we entered into the 2016 Credit Agreement.

Convertible Notes Due 2016

In October 2011, we issued $250.0 million in aggregate principal value 1.0 percent Convertible Senior Notes due September 15, 2016 (Convertible Notes). Upon maturity of the Convertible Notes on September 15, 2016, we fulfilled all remaining settlement and repayment obligations.

The Convertible Notes were unsecured, unsubordinated debt obligations that ranked equally with all of our other unsecured and unsubordinated indebtedness. We paid interest semi-annually on March 15 and September 15 of each year. The initial conversion price was $47.69 per share and the number of underlying shares used to determine the aggregate consideration upon conversion was approximately 5.2 million shares.

Upon conversion, holders of our Convertible Notes were entitled to receive: (1) cash equal to the lesser of the par value of the notes or the conversion value (the number of shares underlying the Convertible Notes multiplied by the then current conversion price per share); and (2) to the extent the conversion value exceeded the par value of the notes, shares of our common stock.

During the year ended December 31, 2016, we settled conversion requests representing $5.6 million in principal value of our Convertible Notes. We paid $5.6 million in principal and issued 0.1 million shares of our common stock during the settlement process. We received 0.1 million shares of our common stock under our convertible note hedge (discussed below under *Convertible Note Hedge and Warrant Transactions*) from Deutsche Bank AG London (DB London) which we placed into our treasury stock account.

Convertible Note Hedge and Warrant Transactions

In connection with the issuance of our Convertible Notes, we entered into separate convertible note hedge and warrant transactions with DB London to reduce the potentially dilutive impact of the conversion of our convertible notes. Pursuant to the convertible note hedge, we purchased call options to acquire up to approximately 5.2 million shares of our common stock with a strike price of $47.69.

8. Debt (Continued)

The call options became exercisable upon any conversions and the maturity of the Convertible Notes, and terminated upon the maturity of the Convertible Notes. The call options offset on a share for share basis, any shares of our common stock that we issued upon any conversion of our Convertible Notes.

We also sold DB London warrants to acquire up to approximately 5.2 million shares of our common stock with a strike price of $67.56. The warrants expired incrementally on a series of expiration dates that began in December 2016 and ended in January 2017. The warrants were settled on a net-share basis. As the price of our common stock exceeded the strike price of the warrants on the series of related incremental expiration dates, we issued 2.8 million shares of our common stock to DB London during the term of the warrant, of which, 1.1 million shares were issued during 2016.

Interest Expense

Details of interest expense presented on our consolidated statements of operations are as follows (in millions):

	Year Ended December 31,		
	2016	2015	2014
Contractual coupon rate of interest—convertible notes	$ —	$ 0.4	$ 2.1
Discount amortization—convertible notes	0.1	3.0	11.1
Interest expense—convertible notes	0.1	3.4	13.2
Other interest expense [1]	3.8	1.3	4.4
Total interest expense	$ 3.9	$ 4.7	$ 17.6

(1) Represents interest expense related to debt and amortization of issuance costs.

9. Commitments and Contingencies

Operating Leases

We lease facilities and equipment under operating lease arrangements that have terms expiring at various dates through 2020. 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.

9. Commitments and Contingencies (Continued)

Future minimum lease payments under non-cancelable operating leases as of December 31, 2016, are as follows (in millions):

Year Ending December 31,	
2017	$ 3.8
2018	2.8
2019	0.4
2020	0.2
Total	$ 7.2

Total rent expense was $4.4 million, $3.8 million and $3.6 million for the years ended December 31, 2016, 2015 and 2014, respectively.

Milestone Payments

We are party to certain license agreements as described in Note 15— *Assignment and License Agreements* and acquisition agreements. 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.

Future milestone payments based on our estimates of the timing and probability of achieving milestones specified under these arrangements are as follows (in millions):

Year Ending December 31,	(1)
2017	$ 9.8
2018	1.6
2019	2.3
2020	1.5
2021	0.7
Thereafter	5.9
Total	$ 21.8

(1) The amounts and timing of future milestone payments may vary depending on when related milestones will be attained, if at all.

10. Temporary Equity

Temporary equity includes securities that: (1) have redemption features that are outside our control; (2) are not classified as an asset or liability; (3) are excluded from permanent stockholders' equity; and (4) are not mandatorily redeemable. Amounts included in temporary equity relate to securities that are redeemable at a fixed or determinable price.

10. Temporary Equity (Continued)

Components comprising the carrying value of temporary equity include the following (in millions):

	As of December 31,	
	2016	2015
Reclassification of Equity Component [1]	$ —	$ 0.2
Common stock subject to repurchase [2]	10.9	10.9
Total	$ 10.9	$ 11.1

(1) Represents the reclassification of the Equity Component equal to the unamortized debt discount of our Convertible Notes as of December 31, 2015 from additional paid-in capital to temporary equity. Our Convertible Notes were convertible at the election of the holders as noted in Note 8— *Debt — Convertible Notes Due 2016* . The Convertible Notes matured in September 2016.

(2) In connection with our license agreement with Toray Industries Inc. (Toray), we issued 200,000 shares of our common stock (which have since split into 400,000 shares) to Toray in 2007, and provided Toray the right to require us to repurchase the shares at a price of $27.21 per share.

11. Stockholders' Equity

Earnings Per Common 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 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 other securities if such securities were converted or exercised.

11. Stockholders' Equity (Continued)

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

	Year Ended December 31,		
	2016	2015	2014
Numerator:			
Net income	$ 713.7	$ 651.6	$ 340.1
Denominator:			
Weighted average outstanding shares—basic	43.8	46.0	48.2
Effect of dilutive securities [1]:			
Convertible notes	—	0.9	2.6
Warrants	2.3	3.0	1.9
Stock options, restricted stock units and employee stock purchase plan	0.7	1.3	1.5
Weighted average shares—diluted [2]	46.8	51.2	54.2
Earnings per common share:			
Basic	$ 16.29	$ 14.17	$ 7.06
Diluted	$ 15.25	$ 12.72	$ 6.28
Stock options and warrants excluded from calculation [2]	5.2	3.8	9.3

(1) Calculated using the treasury stock method.

(2) Certain convertible notes, stock options and warrants have been excluded from the computation of diluted earnings per share because their impact would be anti-dilutive. Under our convertible note hedge agreement, we were entitled to receive shares required to be issued to investors upon conversion of our Convertible Notes. Since related shares used to compute dilutive earnings per share would be anti-dilutive, they have been excluded from the calculation above.

Equity Incentive Plans

As of December 31, 2016, 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 2015 Stock Incentive Plan (the 2015 Plan). The 2015 Plan was approved by our shareholders in June 2015 and provides for the issuance of up to 6,150,000 shares of our common stock pursuant to awards granted under the 2015 Plan. As a result of the approval of the 2015 Plan, no further awards will be granted under the 1999 Plan. During the years ended December 31, 2016 and December 31, 2015, we granted 1.6 million and 0.2 million stock options under the 2015 Plan, respectively.

Employee Stock Options

We estimate the fair value of stock options using the Black-Scholes-Merton valuation model. Option-pricing models, including the Black-Scholes-Merton model, require the use of judgment and subjective assumptions that can materially impact the estimation of fair value and share-based

11. Stockholders' Equity (Continued)

compensation. Share-based compensation expense is recorded ratably over the vesting period of the stock option.

Inputs included in estimating the fair value of a stock option 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, the expected forfeiture rate and the expected dividend yield.

A description of the key inputs, requiring estimates, used in determining the fair value of stock options is provided 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 a stock option grant that is equal to the expected term of the grant (up to a maximum of five years). We believe the volatility of the price of our common stock measured over the preceding five years 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 a given stock option grant.

Expected term —The expected term reflects the estimated time period we expect an option grant to remain outstanding. We use historical data to develop this input.

Expected forfeiture rate —The expected forfeiture rate is the estimated percentage of options granted that are expected to be forfeited or canceled on an annual basis prior to becoming fully vested. We derive our estimate based on historical forfeiture experience for similar classes of employees.

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

The following weighted-average assumptions were used in estimating the fair value of stock options granted to employees:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	34.8%	33.1%	32.6%
Risk-free interest rate	1.6%	2.0%	1.7%
Expected term of options (in years)	5.8	5.8	5.0
Expected forfeiture rate [1]	5.4%	1.5%	0.0%
Expected dividend yield	0.0%	0.0%	0.0%

(1) During 2016 we issued stock options to all employees, which resulted in an increase in the forfeiture rate compared to prior years.

11. Stockholders' Equity (Continued)

A summary of the status and activity of stock options is presented below:

	Options	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in millions)
Outstanding at January 1, 2016	3,247,438	$ 93.09		
Granted	1,630,552	119.38		
Exercised	(243,624)	31.71		
Forfeited	(175,075)	120.79		
Outstanding at December 31, 2016	4,459,291	$ 104.97	7.0	$ 176.7
Exercisable at December 31, 2016	3,231,814	$ 99.46	6.1	$ 147.1
Expected to vest at December 31, 2016	1,150,003	$ 119.35	9.2	$ 27.9

The weighted average fair value of a stock option granted during each of the years in the three-year period ended December 31, 2016, was $42.59, $60.70 and $40.70, respectively. The total fair value of stock options that vested for each of the years in the three-year period ended December 31, 2016, was $19.9 million, $0.0 million and $29.5 million, respectively.

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

	Year Ended December 31,		
	2016	2015	2014
Cost of product sales	$ 0.5	$ —	$ —
Research and development	1.4	—	—
Selling, general and administrative	22.9	4.9	29.5
Share-based compensation expense before tax	24.8	4.9	29.5
Related income tax benefit	(9.1)	(1.8)	(10.4)
Share-based compensation expense, net of tax	$ 15.7	$ 3.1	$ 19.1

Selling, general and administrative expense for the year ended December 31, 2016 includes approximately $9.8 million of costs related to the accelerated vesting of stock options associated with the departure of a corporate officer during the second quarter of 2016.

As of December 31, 2016, the unrecognized compensation cost was $39.2 million. Unvested outstanding stock options as of December 31, 2016 had a weighted average remaining vesting period of 3.2 years.

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

	Year Ended December 31,		
	2016	2015	2014
Number of options exercised	243,624	985,583	1,462,369
Cash received from options exercised	$ 7.7	$ 39.3	$ 50.2
Total intrinsic value of options exercised	$ 21.9	$ 120.3	$ 108.4
Tax benefits realized from options exercised	$ 5.9	$ 37.4	$ 30.8

11. Stockholders' Equity (Continued)

Restricted Stock Units

In June 2016, we began issuing restricted stock units under the 2015 Plan to non-employee directors. Each restricted stock unit entitles the director to receive one share of our common stock upon vesting, subject to the director's election to defer receipt of shares to a later date. We measure the fair value of restricted stock units using the stock price on the date of grant.

During the year ended December 31, 2016, we granted 20,960 restricted stock units under the 2015 Plan with a weighted average grant date fair value of $101.80. The restricted stock units have an aggregate grant date fair value of $2.1 million. Share-based compensation expense is recorded ratably over the vesting period of the restricted stock unit. We recorded $1.1 million in share-based compensation expense for the year ended December 31, 2016 related to restricted stock units. The share-based compensation expense related to restricted stock units granted is reflected in selling, general and administrative expense on the statements of operations.

As of December 31, 2016, unrecognized compensation cost related to the grant of restricted stock units was $1.0 million. Unvested outstanding restricted stock units as of December 31, 2016 had a weighted average remaining vesting period of 0.5 years.

Employee Stock Purchase Plan

In June 2012, our shareholders approved the United Therapeutics Corporation Employee Stock Purchase Plan (ESPP), which has been 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 September 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.

Share Repurchases

In June 2014, our Board of Directors authorized the repurchase of up to $500.0 million of our common stock. This program became effective on August 1, 2014, and remained open for one year. During the years ended December 31, 2015, and 2014, we repurchased approximately 2.4 million and 0.9 million shares of our common stock, respectively, at an aggregate cost of $394.5 million and $105.5 million, respectively, under this repurchase program. We completed this repurchase program in September 2015.

In October 2015, our Board of Directors authorized a new program for the repurchase of up to $500.0 million of our common stock in open or privately negotiated transactions, at our discretion. This program was effective from January 1, 2016 through December 31, 2016. During the year ended December 31, 2016, we repurchased approximately 4.2 million shares of our common stock at an aggregate cost of $500.0 million.

11. Stockholders' Equity (Continued)

Shareholder Rights Plan

In June 2008, we entered into an Amended and Restated Rights Agreement with The Bank of New York as Rights Agent (the Plan), which amended and restated our original Rights Agreement dated December 17, 2000. The Plan, as amended and restated, extended the expiration date of the Preferred Share Purchase Rights (Rights) from December 29, 2010 to June 26, 2018, and increased the purchase price of each Right from $64.75 to $400.00, respectively. Each Right entitles holders to purchase one one-thousandth of a share of our Series A Junior Participating Preferred Stock. Rights are exercisable only upon our acquisition by another company, or commencement of a tender offer that would result in ownership of 15 percent or more of the outstanding shares of our voting stock by a person or group (as defined under the Plan) without our prior express written consent. As of December 31, 2016, we have not issued any shares of our Series A Preferred Stock.

12. 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 (2)	Total
Balance, January 1, 2016	$ (5.3)	$ (15.1)	$ (20.4)
Other comprehensive income (loss) before reclassifications	6.0	(3.0)	3.0
Amounts reclassified from accumulated other comprehensive loss	0.6	—	0.6
Net current-period other comprehensive income (loss)	6.6	(3.0)	3.6
Balance, December 31, 2016	$ 1.3	$ (18.1)	$ (16.8)

	Defined Benefit Pension Plan (1)	Foreign Currency Translation Losses	Total
Balance, January 1, 2015	$ (6.9)	$ (9.8)	$ (16.7)
Other comprehensive income (loss) before reclassifications	0.7	(5.3)	(4.6)
Amounts reclassified from accumulated other comprehensive loss	0.9	—	0.9
Net current-period other comprehensive income (loss)	1.6	(5.3)	(3.7)
Balance, December 31, 2015	$ (5.3)	$ (15.1)	$ (20.4)

(1) Refer to Note 14— *Employee Benefit Plans — Supplemental Executive Retirement Plan* , which identifies the captions within our consolidated statement of operations where reclassification adjustments were recognized and their associated tax impact.

(2) In the fourth quarter of 2016, we changed the functional currency for our foreign entities to the U.S. dollar. The loss on foreign currency translation attributable to each foreign entity at the time of this change will remain in accumulated other comprehensive loss until the sale or substantial liquidation of the foreign entity.

13. Income Taxes

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

	Year Ended December 31,		
	2016	2015	2014
Current:			
Federal	$ 311.9	$ 351.2	$ 166.4
State	24.1	37.0	21.4
Total current	336.0	388.2	187.8
Deferred			
Federal	8.3	(2.7)	(3.1)
State	2.2	7.3	0.4
Total deferred	10.5	4.6	(2.7)
Total income tax expense	$ 346.5	$ 392.8	$ 185.1

Presented below is a reconciliation of income tax expense computed at the statutory federal tax rate to income tax expense as reported (in millions):

	Year Ended December 31,		
	2016	2015	2014
Federal taxes at 35%	$ 371.1	$ 365.5	$ 183.8
State taxes, net of federal benefit	17.1	28.7	12.9
General business credits	(10.5)	(6.9)	(12.2)
Section 199 deduction	(22.0)	(21.8)	(11.7)
Nondeductible compensation expense	(11.4)	29.3	13.0
Other	2.2	(2.0)	(0.7)
Total income tax expense	$ 346.5	$ 392.8	$ 185.1

13. Income Taxes (Continued)

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

	As of December 31,	
	2016	2015
Deferred tax assets:		
Intangible assets	$ 48.1	$ 53.4
Nonqualified stock options	44.7	37.4
SERP	18.9	17.1
STAP awards	80.1	95.2
Other	22.9	27.4
Total deferred tax assets	214.7	230.5
Deferred tax liabilities:		
Plant and equipment principally due to differences in depreciation	(23.5)	(26.5)
Other	(8.2)	(7.9)
Net deferred tax assets before valuation allowance	183.0	196.1
Valuation allowance	(4.7)	(3.4)
Net deferred tax assets	$ 178.3	$ 192.7

We do not provide for U.S. income taxes on undistributed earnings of our foreign operations that are intended to be invested indefinitely outside the United States. At December 31, 2016, the cumulative amount of undistributed foreign earnings was approximately $13 million. If these earnings were repatriated to the United States, we would be subject to U.S. income taxes (after application of foreign tax credits). It is not practicable to estimate the tax cost of repatriating the cumulative undistributed taxable earnings of these foreign subsidiaries to the United States.

A reconciliation of the beginning and ending balances of unrecognized tax benefits is as follows (in millions):

	As of December 31,	
	2016	2015
Unrecognized tax benefits at the beginning of year	$ 0.5	$ 1.4
Lapse of statute of limitations	—	(0.9)
Unrecognized tax benefits at the end of year	$ 0.5	$ 0.5

Unrecognized tax benefits at both December 31, 2016 and 2015, included $0.3 million of tax benefits that, if recognized, would impact our effective tax rate. We record interest and penalties related to uncertain tax positions as a component of income tax expense. As of both December 31, 2016 and 2015, we have not accrued any interest expense relating to uncertain tax positions. We are unaware of any positions for which it is reasonably possible that the total amount of unrecognized tax benefits will significantly increase or decrease within the next twelve months.

13. Income Taxes (Continued)

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 substantially all other major jurisdictions for tax years prior to 2011. At December 31, 2016, we had no federal net operating loss carryforwards and approximately $55 million of state net operating loss carryforwards which will expire at various dates between the years 2028 and 2036, if not utilized.

14. 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 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, 2016 and 2015, 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.

We recognize the unfunded balance of the SERP as a liability on our consolidated balance sheets. Since we do not fund the SERP, the liability is equal to the projected benefit obligation as measured at the end of each fiscal year. Expenses related to the SERP are reported under the captions, "Research and development expense" and "Selling, general and administrative expense" in the accompanying consolidated statements of operations.

14. Employee Benefit Plans (Continued)

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

	Year Ended December 31,	
	2016	2015
Projected benefit obligation at the beginning of the year	$ 54.8	$ 58.0
Service cost	2.7	3.5
Interest cost	1.5	1.8
Plan amendments	2.0	—
Benefits paid	—	(7.1)
Actuarial gain [1]	(11.5)	(1.4)
Projected benefit obligation at the end of the year	$ 49.5	$ 54.8
Fair value of plan assets at the end of the year	—	—
Unfunded at end of the year	$ 49.5	$ 54.8
Amount included in Other current liabilities [2]	$ 15.2	$ 14.7

(1) During the second quarter of 2016, certain participants in the SERP departed before retirement age under the terms of the SERP. As a result, we remeasured the benefit obligation under the SERP as of June 30, 2016, and recorded a reduction to the benefit obligation with a corresponding increase to "Actuarial gain arising during period, net of tax" within "Accumulated other comprehensive loss" of $7.1 million. As part of the re-measurement of the benefit obligation, we updated the discount rate we used to measure our SERP obligation to 3.36 percent. The discount rate as of December 31, 2015 was 3.82 percent.

(2) The amount included under the caption "Other current liabilities" on our consolidated balance sheet represents the benefit obligation due to participants who are eligible to retire.

The accumulated benefit obligation, a measure that does not consider future increases in participants' salaries, was $37.5 million and $42.3 million at December 31, 2016 and 2015, 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,	
2017	$ 15.2
2018	—
2019	7.2
2020	—
2021	—
Thereafter	65.6
Total	$ 88.0

14. Employee Benefit Plans (Continued)

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

	Year Ended December 31,	
	2016	2015
Discount Rate	3.67%	3.82%
Salary Increases	4.00%	4.00%

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

	Year Ended December 31,		
	2016	2015	2014
Service cost	$ 2.7	$ 3.5	$ 5.5
Interest cost	1.5	1.8	2.4
Amortization of prior service cost	1.4	1.2	1.2
Amortization of net actuarial (gain) loss	(0.4)	0.2	0.2
Total	$ 5.2	$ 6.7	$ 9.3

Reclassification adjustments related to the SERP from accumulated other comprehensive loss to the statements of operations by line item and the tax impact of these reclassifications is presented below (in millions):

Components Reclassified from Accumulated Other Comprehensive Loss [1]	As of December 31, 2016	As of December 31, 2015
Prior service cost:		
Research and development	$ 0.3	$ 0.4
Selling, general and administrative	1.1	0.8
Total	1.4	1.2
Amortization of net actuarial (gain) loss:		
Research and development	(0.1)	—
Selling, general and administrative	(0.3)	0.2
Total	(0.4)	0.2
Total prior service cost and amortization of net actuarial (gain) loss	1.0	1.4
Tax benefit	(0.4)	(0.5)
Total, net of tax	$ 0.6	$ 0.9

(1) Refer to Note 12— *Accumulated Other Comprehensive Loss* .

14. Employee Benefit Plans (Continued)

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

	Year Ended December 31,		
	2016	2015	2014
Net unrecognized actuarial gain	$ 11.0	$ 1.6	$ 5.0
Net unrecognized prior service (benefit) cost	(0.6)	1.2	(2.6)
Total	10.4	2.8	2.4
Tax benefit	(3.8)	(1.2)	(0.9)
Total, net of tax	$ 6.6	$ 1.6	$ 1.5

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

	Year Ended December 31,		
	2016	2015	2014
Net unrecognized actuarial (gain) loss	$ (9.8)	$ 1.2	$ 2.8
Net unrecognized prior service cost	7.7	7.1	8.3
Total	(2.1)	8.3	11.1
Tax expense (benefit)	0.8	(3.0)	(4.2)
Total, net of tax	$ (1.3)	$ 5.3	$ 6.9

Estimated amounts included in accumulated other comprehensive loss as of December 31, 2016, that are expected to be recognized as components of net periodic pension cost on our statements of operations for the year ended December 31, 2017, comprise the following (in millions):

Amortization of prior service cost	$ 1.5
Amortization of net actuarial gain	(0.6)
Total	$ 0.9

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 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.

15. Assignment and License Agreements

GlaxoSmithKline plc

In 1997, GlaxoSmithKline plc (Glaxo) assigned to us patents and patent applications covering treprostinil for the treatment of PAH and congestive heart failure. Under the agreement, Glaxo was entitled to receive royalties on sales exceeding a specified threshold for a minimum period of ten years (or until expiration of the licensed patents) following the date of the first commercial sale of any initial product containing treprostinil. Pursuant to these terms, our royalty obligation ended in October 2014.

Supernus Pharmaceuticals, Inc.

In June 2006, we entered into an exclusive license agreement with Supernus Pharmaceuticals, Inc. (Supernus) for the use of certain technologies developed by Supernus in our Orenitram tablet. Under this 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. Additionally, we pay a single digit royalty under this agreement, based on net product sales of Orenitram. Royalties will be paid for approximately twelve years commencing with the first commercial sale, which occurred in the second quarter of 2014.

Eli Lilly and Company

In November 2008, we acquired from Lilly exclusive rights to develop, market, promote and commercialize Adcirca for the treatment of pulmonary hypertension in the United States. In exchange for these license rights, we agreed to pay Lilly, among other fees, royalties of five percent of our net product sales of Adcirca as a pass through of Lilly's third-party royalty obligations for as long as Lilly is required to make such royalty payments. Pursuant to the terms of our license arrangement, Lilly manufactures Adcirca for us and distributes Adcirca via its wholesaler network in the same manner that it distributes its own pharmaceutical products. We purchase Adcirca from Lilly at a fixed manufacturing cost, which is adjusted by Lilly from time to time. The terms of this licensing arrangement will continue generally until the later of: (1) the expiration or lapse of the last to expire claim within a Lilly patent covering commercialization of Adcirca; or (2) the expiration of any government conferred exclusivity rights to Adcirca. In addition, at Lilly's discretion the license agreement may be terminated in the event that we undergo a change in control.

National Cancer Institute and The Scripps Research Institute

In July 2010, we entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) of the United States National Institutes for Health (NIH) to collaborate on the late-stage development and regulatory approval process for Unituxin for children with high-risk neuroblastoma and patients with other forms of cancer. In lieu of a royalty payment to the NCI, we have an obligation to provide the NCI with Unituxin for certain of its studies free of charge. Under a non-exclusive license agreement with The Scripps Research Institute, we pay a royalty of one percent of Unituxin's net sales.

Toray Industries, Inc.

In 2000, we entered into an agreement with Toray to obtain exclusive rights to develop and market beraprost, a chemically stable oral prostacyclin analogue, in a sustained release formulation in the

15. Assignment and License Agreements (Continued)

United States and Canada for the treatment of all cardiovascular indications. In 2007, we amended the agreement to expand our rights to commercialize modified release formulations of beraprost, which include esuberaprost. As part of the 2007 amendment, we issued 200,000 shares of our common stock (which have since split into 400,000 shares) to Toray with certain put rights. These put rights provide Toray the ability to request at its discretion that we repurchase these shares at a price of $27.21 per share upon 30 days' prior written notice. Accordingly, we classified the value of the shares within temporary equity on our consolidated balance sheets. In the event that Toray requests that we repurchase these shares, we will reclassify the repurchase value of the stock as a liability until settlement. The 2007 amendment also provided for certain milestone payments during the development period and upon receipt of regulatory approval in the United States or the European Union.

In July 2011, we amended our license agreement with Toray. The amendment did not materially change the terms of our license agreement, except for a reduction in royalty rates in exchange for a total of $50.0 million in equal, non-refundable payments to Toray over the five-year period ending in 2015. As of December 31, 2015, we have fulfilled this obligation to Toray.

Medtronic Inc.

In 2009, we entered into an agreement with Medtronic, Inc. (Medtronic) providing us exclusive rights in the United States and certain other countries to develop Medtronic's proprietary intravascular infusion catheter to be used with its SynchroMed ® II implantable infusion pump and related infusion system components (together referred to as the Implantable System for Remodulin) in order to deliver Remodulin for the treatment of PAH. If this development program is successful, our agreement provides that, upon commercialization, we will purchase infusion pumps and supplies from Medtronic and will also pay a ten percent royalty to Medtronic based on net product sales of Remodulin for use in the Implantable System for Remodulin within the exclusive territories, subject to certain adjustments specified in the agreement. The Implantable System for Remodulin will be exclusive to Remodulin so long as we purchase a minimum percentage of our annual requirement for implantable pump systems from Medtronic. We will be solely responsible for all marketing and promotion of the Implantable System for Remodulin for the treatment of PAH in the exclusive territories.

DEKA Research & Development Corp.

In December 2014, we entered into an exclusive agreement with DEKA Research & Development Corp. (DEKA) to develop a pre-filled, semi-disposable pump system for subcutaneous delivery of Remodulin. Under the terms of the agreement, we will fund the development costs related to the semi-disposable pump system and will pay product fees and a single-digit royalty to DEKA based on commercial sales of the system and the Remodulin sold for use with the system.

Other

We are party to various other license agreements relating to therapies 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.

16. Distribution Agreements

U.S.-Based Specialty Distributors

We are party to separate distribution agreements for Remodulin, Tyvaso and Orenitram with two U.S.-based specialty pharmaceutical distributors, Accredo and CVS Caremark. The distribution agreements are similar to one another, and generally have one-year terms that renew automatically for additional one-year periods, unless terminated earlier. The agreements contain contractual responsibilities relating to ordering specifications, inventory requirements and exchange rights. We also have agreements with these distributors to perform certain services for us on a fee-for-service basis. If any of our distribution agreements expire or terminate, we may be required under certain circumstances to repurchase any unsold inventory held by our distributors. In the second quarter of 2015, we entered into an exclusive distribution agreement with ASD Specialty Healthcare, Inc. (ASD), an affiliate of AmerisourceBergen Corporation, to distribute Unituxin in the United States. 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.

International Distributors

We currently sell Remodulin, Tyvaso and Unituxin internationally through various distributors. The financial terms and conditions relating to these distributor arrangements are generally structured in a manner substantially similar to those of our U.S. distribution agreements described above.

17. Segment Information

We currently 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 the overall level of resources available and how to best deploy these resources across functions, therapeutic areas, and research and development projects that are in line with our long-term company-wide strategic goals.

17. Segment Information (Continued)

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

	Remodulin	Tyvaso	Adcirca	Orenitram	Unituxin	Total
Year Ended December 31, 2016						
Net product sales	$ 602.3	$ 404.6	$ 372.2	$ 157.2	$ 62.5	$ 1,598.8
Cost of product sales	10.5	19.6	21.4	13.7	7.5	72.7
Gross profit	$ 591.8	$ 385.0	$ 350.8	$ 143.5	$ 55.0	$ 1,526.1
Year Ended December 31, 2015 (1)						
Net product sales	$ 572.8	$ 470.1	$ 278.8	$ 118.4	$ 20.5	$ 1,460.6
Cost of product sales	12.4	23.9	16.5	12.5	3.7	69.0
Gross profit	$ 560.4	$ 446.2	$ 262.3	$ 105.9	$ 16.8	$ 1,391.6
Year Ended December 31, 2014 (2)						
Net product sales	$ 553.7	$ 463.1	$ 221.5	$ 41.2	$ —	$ 1,279.5
Cost of product sales	47.3	57.5	13.5	7.6	—	125.9
Gross profit	$ 506.4	$ 405.6	$ 208.0	$ 33.6	$ —	$ 1,153.6

(1) We commenced sales of Unituxin during the third quarter of 2015.

(2) We commenced sales of Orenitram during the second quarter of 2014.

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,	2016	2015	2014
United States	$ 1,461.9	$ 1,353.0	$ 1,180.8
Rest-of-World (1)	136.9	112.8	107.7
Total (2)	$ 1,598.8	$ 1,465.8	$ 1,288.5

(1) Primarily Europe.

(2) Total includes other revenue of $5.2 million and $9.0 million for the years ended December 31, 2015 and 2014, respectively.

We recorded revenue from two specialty pharmaceutical distributors comprising 50 percent and 14 percent of total revenues in 2016, 55 percent and 16 percent of total revenues in 2015, and 58 percent and 15 percent of total revenues in 2014, respectively. All of our revenues for Adcirca are distributed through Lilly's pharmaceutical wholesaler network.

17. Segment Information (Continued)

Long-lived assets (property, plant and equipment) located by geographic area are as follows (in millions):

Year Ended December 31,	2016	2015	2014
United States	$ 481.1	$ 481.2	$ 462.4
Rest-of-World	8.2	14.6	16.0
Total	$ 489.3	$ 495.8	$ 478.4

18. Quarterly Financial Information (Unaudited)

Summarized quarterly financial information for each of the years ended December 31, 2016 and 2015 are as follows (in millions, except per share amounts):

	Quarter Ended			
	December 31, 2016	September 30, 2016	June 30, 2016	March 31, 2016
Total revenues	$ 409.0	$ 408.2	$ 412.6	$ 369.0
Cost of product sales	28.4	23.6	20.0	0.7
Gross profit	380.6	384.6	392.6	368.3
Net income [(1)]	110.3	161.8	206.1	235.5
Net income per share—basic	$ 2.61	$ 3.75	$ 4.65	$ 5.19
Net income per share—diluted	$ 2.43	$ 3.50	$ 4.39	$ 4.84

	Quarter Ended			
	December 31, 2015	September 30, 2015	June 30, 2015	March 31, 2015
Total revenues	$ 404.9	$ 386.2	$ 347.2	$ 327.5
Cost of product sales	25.3	6.9	16.0	20.8
Gross profit	379.6	379.3	331.2	306.7
Net income (loss) [(2) (3)]	104.6	464.4	99.2	(16.6)
Net income (loss) per share—basic	$ 2.29	$ 10.20	$ 2.15	$ (0.36)
Net income (loss) per share—diluted	$ 2.10	$ 9.24	$ 1.91	$ (0.36)

(1) Operating results for the quarter ended December 31, 2016, September 30, 2016, June 30, 2016 and March 31, 2016 include $64.2 million, $28.7 million, $(7.0) million and $(95.5) million net of tax expense (benefit) to operating expenses for STAP related share-based compensation expense, respectively.

(2) Operating results for the quarter ended December 31, 2015, September 30, 2015, June 30, 2015 and March 31, 2015 include $73.9 million, $(75.7) million, $27.5 million and $145.0 million net of tax expense (benefit) to operating expenses for STAP related share-based compensation expense, respectively.

(3) Operating results for the quarter ended September 30, 2015, include a gain on sale of the PPRV we received from the FDA in connection with the approval of Unituxin, for $350.0 million in cash. The proceeds from the sale of the PPRV were recognized as a gain on the sale of an intangible asset, as the PPRV did not have a carrying value on our consolidated balance sheet at the time of sale.

19. Litigation

Watson Laboratories, Inc.

In June 2015, we received a Paragraph IV certification notice letter from Watson Laboratories, Inc. (Watson) indicating that Watson has submitted an abbreviated new drug application (ANDA) to the FDA to market a generic version of Tyvaso. In its notice letter, Watson states that it intends to market a generic version of Tyvaso before the expiration of U.S. Patent Nos. 6,521,212 and 6,756,033, each of which expires in November 2018; and U.S. Patent No. 8,497,393, which expires in December 2028. Watson's notice letter states that the ANDA 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 the proposed product described in Watson's ANDA submission. We responded to the Watson notice letter by filing a lawsuit on July 22, 2015 against Watson in the U.S. District Court for the District of New Jersey alleging infringement of U.S. Patent Nos. 6,521,212, 6,756,033, and 8,497,393. Under the Hatch-Waxman Act, the FDA is automatically precluded from approving Watson's ANDA for up to 30 months from receipt of Watson's notice letter or until the issuance of a U.S. District Court decision that is adverse to us, whichever occurs first. In September 2015, Watson filed (1) a motion to dismiss some, but not all, counts of the complaint; (2) its answer to the complaint; and (3) certain counterclaims against us. The Court granted Watson's motion to dismiss certain counts of our complaint. In September 2015, we filed our answer to Watson's counterclaims. In June 2016, Watson sent a second Paragraph IV certification notice letter addressing two new patents, U.S. Patent Nos. 9,339,507 and 9,358,240. In June 2016, we filed an amended complaint against Watson asserting these two additional patents. The parties are currently engaged in discovery, and trial on all of the asserted patents is currently scheduled to take place in September 2017.

We intend to vigorously enforce our intellectual property rights relating to Tyvaso.

Actavis Laboratories FL, Inc.

In February 2016, we received a Paragraph IV certification notice letter (the First Actavis Notice Letter) from Actavis Laboratories FL, Inc. (Actavis) indicating that Actavis has submitted an ANDA to the FDA to market a generic version of the 2.5 mg strength of Orenitram. The First Actavis Notice Letter states that Actavis intends to market a generic version of the 2.5 mg strength of Orenitram before the expiration of the following patents, all of which are listed in the Orange Book:

U.S. Patent No.	Expiration Date
8,252,839	May 2024
9,050,311	May 2024
7,544,713	July 2024
7,417,070	July 2026
8,497,393	December 2028
8,747,897	October 2029
8,410,169	February 2030
8,349,892	January 2031

The First Actavis Notice Letter states that the ANDA 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 the proposed product described in Actavis' ANDA submission. We responded to the First Actavis Notice Letter by filing a lawsuit (the First Actavis Action) against

19. Litigation (Continued)

Actavis in March 2016 in the U.S. District Court for the District of New Jersey alleging infringement of each of the patents noted above and one additional patent, U.S. Patent No. 9,278,901 (the '901 patent), which expires in May 2024 and is also now listed in the Orange Book. Under the Hatch-Waxman Act, the FDA is automatically precluded from approving Actavis' ANDA with respect to the 2.5 mg strength of Orenitram for up to 30 months from receipt of Actavis' notice letter or until the issuance of a U.S. District Court decision that is adverse to us with respect to all of the eight patents listed in the table above, whichever occurs first. In June 2016, we filed an amended complaint against Actavis, Actavis filed its answer and counterclaims to that amended complaint, and we filed our answer to those counterclaims.

In May 2016, we received a second Paragraph IV certification notice letter from Actavis (the Second Actavis Notice Letter) indicating that Actavis has amended its ANDA to include its generic version of the 0.25 mg and 1.0 mg strengths of Orenitram, in addition to the 2.5 mg strength identified in the First Actavis Notice Letter. We responded to the Second Actavis Notice Letter by filing an additional lawsuit against Actavis (the Second Actavis Action) on June 17, 2016 in the U.S. District Court for the District of New Jersey alleging infringement of the same patents asserted in the First Actavis Action. The Second Actavis Action triggered an additional 30-month stay with respect to the 0.25 mg and 1.0 mg strengths. Specifically, the FDA is automatically precluded from approving Actavis' ANDA with respect to the 0.25 mg and 1.0 mg strengths of Orenitram for up to 30 months from receipt of the Second Actavis Notice Letter or until the issuance of a U.S. District Court decision that is adverse to us with respect to all of the eight patents listed in the table above and the '901 patent, whichever occurs first. The Court has consolidated the First Actavis Action and the Second Actavis Action. The parties are currently engaged in discovery, and trial is scheduled for February 2018.

We intend to vigorously enforce our intellectual property rights relating to Orenitram.

SteadyMed Ltd.

On October 1, 2015, SteadyMed Ltd. (SteadyMed) filed a petition with the Patent Trial and Appeal Board (PTAB) of the U.S. Patent and Trademark Office for *inter partes* review (the IPR Petition) of U.S. Patent No. 8,497,393 (the '393 Patent), which is owned by United Therapeutics. In its IPR Petition, SteadyMed seeks to invalidate '393 Patent, which expires in December 2028 and covers a method of making treprostinil, the active pharmaceutical ingredient in our Remodulin, Tyvaso and Orenitram products. The '393 Patent was also the subject of now-settled litigation with generic companies relating to ANDAs to market generic versions of Remodulin, and remains the subject of our pending litigation with Watson and Actavis, described above. The PTAB granted the petition for review, and subsequently, the parties made a number of submissions to the PTAB with their supporting evidence and arguments. Oral argument was held in November 2016. We are currently awaiting the PTAB's final decision, which we expect in or before April 2017. SteadyMed has announced that it is developing a product called Trevyent™, which is a single-use, pre-filled pump for which it plans to seek FDA approval for delivery of a two-day supply of treprostinil subcutaneously using its PatchPump ® technology.

Department of Justice Subpoena

In May 2016, we received a subpoena from the U.S. Department of Justice requesting documents regarding our support of 501(c)(3) organizations that provide financial assistance to patients taking our medicines. Other companies have received similar inquiries. We are cooperating with this inquiry.

United Therapeutics Corporation
Schedule II—Valuation and Qualifying Accounts
Years Ended December 31, 2016, 2015 and 2014
(In millions)

	Valuation Allowance on Deferred Tax Assets			
	Balance at Beginning of Year	Additions Charged to Expense	Deductions	Balance at End of Year
Year Ended December 31, 2016	$ 3.4	$ 1.3	$ —	$ 4.7
Year Ended December 31, 2015	$ 3.0	$ 0.4	$ —	$ 3.4
Year Ended December 31, 2014	$ 2.5	$ 0.5	$ —	$ 3.0

	Reserve for Inventory Obsolescence			
	Balance at Beginning of Year	Additions Charged to Expense	Deductions	Balance at End of Year
Year Ended December 31, 2016	$ 12.1	$ 8.2	$ (2.8)	$ 17.5
Year Ended December 31, 2015	$ 10.5	$ 7.9	$ (6.3)	$ 12.1
Year Ended December 31, 2014	$ 18.3	$ 3.4	$ (11.2)	$ 10.5

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 Chairman 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, 2016. Based on that evaluation, our Chairman and Chief Executive Officer and Chief Financial Officer and Treasurer concluded that our disclosure controls and procedures were effective as of December 31, 2016.

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, 2016, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) 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, 2016, 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, 2016 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

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 2017 annual meeting of shareholders currently scheduled for June 28, 2017 (the 2017 Proxy Statement) is hereby incorporated herein by this reference. Information regarding our executive officers appears in *Item 1* of this Report under the heading *Executive Officers of the Registrant* . Information regarding the Audit Committee and the Audit Committee's financial expert appearing under the heading *Committees of our Board of Directors—Audit Committee* in our 2017 Proxy Statement is hereby incorporated herein by this reference.

Information appearing under the heading *Section 16(a) Beneficial Ownership Reporting Compliance* in our 2017 Proxy Statement is hereby incorporated herein by this 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.cfm* . 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.
Principal, Causey Consortium
Raymond Dwek, F.R.S.
Director of the Glycobiology Institute and Professor Emeritus, University of Oxford
Richard Giltner
Private Investor
Katherine Klein, Ph.D.
Vice-Dean and Professor, The Wharton School of the University of Pennsylvania
Ray Kurzweil
Director of Engineering, Google Inc.
Judy D. Olian, Ph.D.
Dean, UCLA Anderson School of Management and John E. Anderson Chair in Management
Christopher Patusky, J.D., M.G.A.
Founding Principal, Patusky Associates, LLC
Martine Rothblatt, Ph.D., J.D., M.B.A.
Chairman and Chief Executive Officer of United Therapeutics
Louis Sullivan, M.D.
Former Secretary, U.S. Department of Health and Human Services
Tommy Thompson, J.D.
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, Summary Compensation Table and Grants of Plan-Based Awards in 2016, Narratives to Summary Compensation Table and Grants of Plan-Based Awards Table, Summary of Terms of Plan-Based Awards, Supplemental Executive Retirement Plan, Rabbi Trust, Potential Payments Upon Termination or Change in Control, and Director Compensation* in our 2017 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 2017 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 2017 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, 2016, regarding our securities authorized for issuance under equity compensation plans:

Plan category	Number of securities to be issued upon exercise of outstanding options (a)	Weighted average exercise price of outstanding options	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plan approved by security holders	4,459,291	$ 104.97	7,344,794
Equity compensation plans not approved by security holders	—	—	N/A
Total	4,459,291	$ 104.97	7,344,794

All outstanding stock options were issued under our two equity incentive plans approved by security holders in 1999 (the 1999 Plan) and 2015 (the 2015 Plan). In addition, our employees have outstanding rights to purchase our common stock at a discount as part of our ESPP. Information regarding these plans is contained in Note 11 —*Stockholders' Equity* to the consolidated financial statements included in this Report. Aside from stock options issued under the 1999 Plan and the 2015 Plan and shares issued under the ESPP, we do not have any outstanding stock options, warrants or rights that are outstanding or available for issuance as described in Regulation S-K Item 201(d). No further awards will be issued under the 1999 Plan.

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, Board of Directors, Committees, Corporate Governance—Director Independence and Committees of our Board of Directors* in our 2017 Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING 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 *Report of the Audit Committee and Information on our Independent Auditors* in our 2017 Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, 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 factual or disclosure 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 the 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.

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 A. ROTHBLATT

Martine A. Rothblatt, Ph.D.
Chairman and Chief Executive Officer

February 22, 2017

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
/s/ MARTINE A. ROTHBLATT Martine A. Rothblatt	Chairman and Chief Executive Officer (Principal Executive Officer)	February 22, 2017
/s/ JAMES C. EDGEMOND James C. Edgemond	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	February 22, 2017
/s/ CHRISTOPHER CAUSEY Christopher Causey	Director	February 22, 2017
/s/ RAYMOND DWEK Raymond Dwek	Director	February 22, 2017
/s/ RICHARD GILTNER Richard Giltner	Director	February 22, 2017
/s/ KATHERINE KLEIN Katherine Klein	Director	February 22, 2017
/s/ RAYMOND KURZWEIL Raymond Kurzweil	Director	February 22, 2017
/s/ JUDY D. OLIAN Judy D. Olian	Director	February 22, 2017
/s/ CHRISTOPHER PATUSKY Christopher Patusky	Director	February 22, 2017
/s/ LOUIS W. SULLIVAN Louis W. Sullivan	Director	February 22, 2017
/s/ TOMMY G. THOMPSON Tommy Thompson	Director	February 22, 2017

EXHIBIT INDEX

Exhibit No.	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant, incorporated by reference to Exhibit 3.1 of the Registrant's Registration Statement on Form S-1 (Registration No. 333-76409).
3.2	Certificate of Amendment to Amended and 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 on June 28, 2010.
3.3	Fifth Amended and Restated By-laws of the Registrant, incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K filed on February 3, 2017.
3.4	Form of Certificate of Designation, Preferences and Rights of Series A Junior Participating Preferred Stock of the Registrant, incorporated by reference to Exhibit A to Exhibit 4 to the Registrant's Current Report on Form 8-K, filed December 18, 2000.
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3 and 3.4.
4.2	First Amended and Restated Rights Agreement, incorporated by reference to Exhibit 4.1 of the Registrant's Current Report on Form 8-K filed on July 3, 2008.
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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2009.
10.2**	Amended and Restated Executive Employment Agreement dated as of January 1, 2009, between the Registrant and Martine A. 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.

Exhibit No.	Description
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 Agreements 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**	Form of terms and conditions for awards granted to Non-Employees by the Registrant under the Amended and Restated Equity Incentive Plan, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed on December 17, 2004.
10.19**	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.
10.20	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.
10.21**	United Therapeutics Corporation 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 June 30, 2008.
10.22**	First Amendment to the United Therapeutics Corporation Share Tracking Awards Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on September 18, 2009.

Exhibit No.	Description
10.23**	Second Amendment to the United Therapeutics Corporation Share Tracking Awards Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on February 6, 2012.
10.24**	Form of terms and conditions for awards granted to non-employees by the Registrant under the United Therapeutics Corporation Share Tracking Awards Plan, incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2008.
10.25**	Form of terms and conditions for awards granted to employees by the Registrant prior to January 1, 2010, under the United Therapeutics Corporation Share Tracking Awards Plan, incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2008.
10.26**	Form of terms and conditions for awards granted to employees by the Registrant on or after January 1, 2010, under the United Therapeutics Corporation Share Tracking Awards Plan, incorporated by reference to Exhibit 10.48 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2009.
10.27**	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.
10.28**	Form of grant letter used by Registrant under the United Therapeutics Corporation Share Tracking Awards Plan, incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2008.
10.29	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.
10.30**	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.
10.31**	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.
10.32**	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.
10.33**	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.
10.34**	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.

Exhibit No.	Description
10.35**	Form of terms and conditions for awards granted to employees by the Registrant on or after March 15, 2011 under the United Therapeutics Corporation Share Tracking Awards Plan or 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 March 18, 2011.
10.36**	Form of terms and conditions for awards granted to non-employees by the Registrant on or after March 15, 2011 under the United Therapeutics Corporation Share Tracking Awards Plan or the United Therapeutics Corporation 2011 Share Tracking Awards Plan, incorporated by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed on March 18, 2011.
10.37**	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.
10.38**	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.
10.39**	United Therapeutics Corporation Section 162(m) Bonus Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed June 27, 2014.
10.40**	United Therapeutics Corporation 2015 Stock Incentive Plan, incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on June 29, 2015.
10.41**	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 on June 29, 2015.
10.42**	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 on June 29, 2015.
10.43**	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 on June 29, 2015.
10.44**	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.
10.45*	License Agreement, dated as of November 14, 2008, by and between Eli Lilly and Company and the Registrant, incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed on December 24, 2008.
10.46*	Manufacturing and Supply Agreement, dated as of November 14, 2008, by and between Eli Lilly and Company, Lilly del Caribe, Inc. and the Registrant incorporated by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed on December 24, 2008.

Exhibit No.	Description
10.47*	Amended and Restated Distribution Agreement relating to Remodulin, dated as of February 21, 2011, between the Registrant and Accredo Health Group, Inc., incorporated by reference to Exhibit 10.38 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2010.
10.48	First Amendment to Amended and Restated Distribution Agreement relating to Remodulin, dated as of December 18, 2013, between the Registrant, Accredo Health Group, Inc., CuraScript, Inc. and Priority Healthcare Distribution, Inc., incorporated by reference to Exhibit 10.49 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2013.
10.49***	Second Amendment to Amended and Restated Distribution Agreement relating to Remodulin, dated as of November 1, 2016, between the Registrant, Accredo Health Group, Inc. and Priority Healthcare Distribution, Inc.
10.50***†	Third Amendment to Amended and Restated Distribution Agreement relating to Remodulin, dated as of December 27, 2016, between the Registrant, Accredo Health Group, Inc. and Priority Healthcare Distribution, Inc.
10.51	Distribution Agreement relating to Tyvaso, dated as of August 17, 2009 between the Registrant and Accredo Health Group, Inc., incorporated by reference to Exhibit 10.47 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2009.
10.52	First Amendment to Distribution Agreement relating to Tyvaso, dated as of September 1, 2011, between the Registrant and Accredo Health Group, Inc., incorporated by reference to Exhibit 10.44 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2013.
10.53	Second Amendment to Distribution Agreement relating to Tyvaso, dated as of December 18, 2013, between the Registrant, Accredo Health Group, Inc., CuraScript, Inc. and Priority Healthcare Distribution, Inc., incorporated by reference to Exhibit 10.45 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2013.
10.54*	Third Amendment to Distribution Agreement relating to Tyvaso, dated October 20, 2014, by and among the Registrant, Accredo Health Group, Inc., CuraScript, Inc., and Priority Healthcare Distribution, Inc., incorporated by reference to Exhibit 10.54 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2014.
10.55***	Fourth Amendment to Distribution Agreement relating to Tyvaso, dated as of November 1, 2016, between the Registrant, Accredo Health Group, Inc. and Priority Healthcare Distribution, Inc.
10.56*	Settlement Agreement, dated September 29, 2015, between the Registrant and Sandoz Inc., incorporated by reference to Exhibit 10.2 to Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2015.
10.57	Credit Agreement, dated as of January 29, 2016, 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 of the Registrant's Current Report on Form 8-K filed on February 1, 2016.
10.58	Asset Purchase Agreement, dated as of August 18, 2015, by and between the Registrant and AbbVie Ireland Unlimited Company, incorporated by reference to Exhibit 2.1 of the Registrant's Current Report on Form 8-K filed on August 19, 2015.

Exhibit No.	Description
10.59***	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.
21	Subsidiaries of the Registrant.
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.
32.1	Certification of Principal Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial information from our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on February 22, 2017, formatted in Extensible Business Reporting Language (XBRL): (i) Consolidated Balance Sheets as of December 31, 2016 and 2015, (ii) Consolidated Statements of Operations for each of three years in the period ended December 31, 2016, (iii) Consolidated Statements of Comprehensive Income for each of the three years in the period ended December 31, 2016, (iv) Consolidated Statements of Stockholders' Equity for each of the three years in the period ended December 31, 2016, (v) Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2016, and (vi) Notes to Consolidated Financial Statements.

* Confidential treatment has been granted 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.

† Confidential treatment has been requested with respect to certain portions of this exhibit pursuant to 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.

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.

QuickLinks

Exhibit 10.49

Second Amendment to Amended and Restated Distribution Agreement
(*REMODULIN* ®)

THIS SECOND AMENDMENT TO AMENDED AND RESTATED DISTRIBUTION AGREEMENT (this " **Second Amendment** ") is made and effective November 1, 2016 (the " **Second Amendment Effective Date** ") by and among, **United Therapeutics Corporation** , a Delaware corporation having offices at 1040 Spring Street, Silver Spring, Maryland (" **UT** "), **Accredo Health Group, Inc.** , a Delaware corporation having offices at 6272 Lee Vista Boulevard, Orlando FL, 32822 (" **Accredo** "), and **Priority Healthcare Distribution, Inc** ., doing business as CuraScript SD Specialty Distribution, a Florida corporation with offices at 255 Technology Park, Lake Mary, Florida, 32746 (" **SD** "). SD and Accredo are collectively referred to herein as the " **Distributor** ".

WHEREAS , UT and Accredo entered into an Amended and Restated Distribution Agreement on February 21, 2011 (as amended from time to time, the " **Agreement** ") relating to the distribution of Remodulin ® (treprostinil) Inhalation Solution; and

WHEREAS , the parties desire to amend the Agreement as provided herein.

NOW, THEREFORE , in consideration of the mutual agreements and covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto, intending to be legally bound, agree as follows:

1. CuraScript, Inc. is no longer providing services under the Agreement and is, therefore, being removed as a party.

2. **AMENDMENT.** The Agreement is hereby amended by deleting Attachment C in its entirety, and amending Section 1.1(u) to read as follows:

   "(u) **"PAP Patient"** shall mean any Included Patient who is enrolled in the Patient Assistance Program as established by UT from time to time and operating in accordance with guidelines developed by UT. UT shall provide DISTRIBUTOR with the eligibility criteria for this program, which UT may update from time to time in its discretion, upon written notice to DISTRIBUTOR."

3. **COUNTERPARTS** . This Amendment may be executed in any number of counterparts and via facsimile, email or other electronic form of transmission, and each of such counterparts shall for all purposes be deemed original, and all such counterparts shall together constitute one and the same instrument.

4. **EFFECT OF AMENDMENT.** Except as specifically amended hereby or by any previous amendments duly executed in accordance with the Agreement, all other terms and conditions of the Agreement remain in full force and effect. To the extent that any of the terms in the underlying agreement are inconsistent with the terms of this Amendment, the terms of this Amendment shall control.

[Signature page follows]

IN WITNESS WHEREOF, the parties hereto have caused this Second Amendment to be executed by their duly authorized representatives.

UNITED THERAPEUTICS CORPORATION

/s/ Kevin Gray

Name: Kevin Gray

Title: Senior Vice President, Strategic Operations

Date: 1/3/2017

ACCREDO HEALTH GROUP, INC.

/s/ Bill Martin

Name: Bill Martin

Title: VP

Date: 12/28/16

PRIORITY HEALTHCARE DISTRIBUTION, INC.

/s/ Gayle C. Johnston

Name: Gayle C. Johnston

Title: President

Date: 12/28/16

Exhibit 10.50

Pursuant to 17 C.F.R §240.24b-2, confidential information (indicated as [***]) has been omitted and has been filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Application filed with the Commission.

3RD AMENDMENT TO AMENDED AND RESTATED DISTRIBUTION AGREEMENT
(*Remodulin* ®)

THIS 3RD AMENDMENT TO AMENDED AND RESTATED DISTRIBUTION AGREEMENT (this " **Third Amendment** ") is made and effective this 27th Day of December, 2016 (the " **Third Amendment Effective Date** "), by and among **Accredo Health Group, Inc** ., a Delaware corporation having offices at 6272 Lee Vista Boulevard, Orlando FL, 32822, (" **Accredo** "), **United Therapeutics Corporation** , a Delaware corporation, having offices at 1040 Spring Street, Silver Spring, Maryland (" **UT** "), and **Priority Healthcare Distribution, Inc** ., doing business as CuraScript SD Specialty Distribution, a Florida corporation with offices at 255 Technology Park, Lake Mary, Florida, 32746 (" **SD** "). SD and Accredo are collectively referred to herein as the " **Distributor** ".

WHEREAS , UT and Accredo are parties to that certain Amended and Restated Distribution Agreement dated February 21, 2011, as amended (the " **Agreement** "), which relates to the distribution of Remodulin ® (treprostinil) Injection (" **UT Product** ");

WHEREAS , the Parties wish to amend the Agreement as provided herein;

WHEREAS , pursuant to Section 18.4 of the Agreement, the Agreement may be amended by the parties by a written instrument signed by a duly authorized representative of each of the Parties; and

WHEREAS , capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

NOW THEREFORE , in consideration of the mutual agreements and covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereto, intending to be legally bound, hereby agree as follows:

1.0 Attachment A will be deleted in its entirety and replaced with the revised Attachment A, attached hereto..

(SIGNATURE PAGE TO FOLLOW)

Pursuant to 17 C.F.R §240.24b-2, confidential information (indicated as [***]) has been omitted and has been filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Application filed with the Commission.

IN WITNESS WHEREOF , the parties hereto have caused this Third Amendment to be executed as of the Third Amendment Effective Date set forth above by their duly authorized representatives.

ACCREDO HEALTH GROUP, INC.

By: /s/ Bill Martin

Name: Bill Martin

Title: VP

Date: 1/3/17

UNITED THERAPEUTICS CORPORATION

By: /s/ Kevin T. Gray

Name: Kevin T. Gray

Title: SVP, Strategic Operations

Date: 1/5/2017

PRIORITY HEALTHCARE DISTRIBUTION, INC.

By: /s/ Gayle C. Johnston

Name: Gayle C. Johnston

Title: President

Date: 12.30.16

Pursuant to 17 C.F.R §240.24b-2, confidential information (indicated as [***]) has been omitted and has been filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Application filed with the Commission.

Attachment A

Prices

UT Product

UT Product Name	NDC	Strength	Price	
Remodulin 1mg	66302-0101-01	1mg/20ml	$	[***]
Remodulin 2.5mg	66302-0102-01	2.5mg/20ml	$	[***]
Remodulin 5 mg	66302-0105-01	5mg/20ml	$	[***]
Remodulin 10 mg	66302-0110-01	10mg/20ml	$	[***]
Remodulin Diluent	(NDC 66302-150-50).	50 mL vial, carton of 1	$	[***]

UT shall notify the DISTRIBUTOR in writing of any change (and the amount of the change) in the Price of any respective UT Product during the term of this Agreement in the same time and manner as it notifies other similarly situated distributors.

UT shall provide DISTRIBUTOR with a current list of Remodulin prices to Discounted Entities, including FSS prices, Federal Ceiling Prices, and prices to section 340B entities, and shall promptly notify Distributor of any and all changes in such prices as well as the effective dates of such changes.

Fourth Amendment to Distribution Agreement
(*TYVASO* ®)

THIS FOURTH AMENDMENT TO DISTRIBUTION AGREEMENT (this " **Third Amendment** ") is made and effective November 1, 2016 (the " **Fourth Amendment Effective Date** ") by and among, **United Therapeutics Corporation** , a Delaware corporation having offices at 1040 Spring Street, Silver Spring, Maryland (" **UT** "), **Accredo Health Group, Inc.** , a Delaware corporation having offices at 6272 Lee Vista Boulevard, Orlando FL, 32822 (" **Accredo** "), and **Priority Healthcare Distribution, Inc** ., doing business as CuraScript SD Specialty Distribution, a Florida corporation with offices at 255 Technology Park, Lake Mary, Florida, 32746 (" **SD** "). SP, SD and Accredo are collectively referred to herein as the " **Distributor** ".

WHEREAS , UT and Accredo entered into a Distribution Agreement on August 17, 2009 (as amended from time to time, the " **Agreement** ") relating to the distribution of Tyvaso ® (treprostinil) Inhalation Solution; and

WHEREAS , the parties desire to amend the Agreement as provided herein.

NOW, THEREFORE , in consideration of the mutual agreements and covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto, intending to be legally bound, agree as follows:

1. CuraScript, Inc. is no longer providing services under the Agreement and is, therefore, being removed as a party.

2. **AMENDMENT.** The Agreement is hereby amended by deleting Attachment C in its entirety, and amending Section 1.1(r) to read as follows:

   "(r) **"PAP Patient"** shall mean any Included Patient who is enrolled in the Patient Assistance Program as established by UT from time to time and operating in accordance with guidelines developed by UT. UT shall provide DISTRIBUTOR with the eligibility criteria for this program, which UT may update from time to time in its discretion, upon written notice to DISTRIBUTOR."

3. **COUNTERPARTS** . This Amendment may be executed in any number of counterparts and via facsimile, email or other electronic form of transmission, and each of such counterparts shall for all purposes be deemed original, and all such counterparts shall together constitute one and the same instrument.

4. **EFFECT OF AMENDMENT.** Except as specifically amended hereby or by any previous amendments duly executed in accordance with the Agreement, all other terms and conditions of the Agreement remain in full force and effect. To the extent that any of the terms in the underlying agreement are inconsistent with the terms of this Amendment, the terms of this Amendment shall control.

[Signature page follows]

IN WITNESS WHEREOF, the parties hereto have caused this Fourth Amendment to be executed by their duly authorized representatives.

UNITED THERAPEUTICS CORPORATION

/s/ Kevin T. Gray

Name: Kevin Gray

Title: Senior Vice President, Strategic Operations

Date: 1/3/2017

ACCREDO HEALTH GROUP, INC.

/s/ Bill Martin

Name: Bill Martin

Title: VP

Date: 12/28/16

PRIORITY HEALTHCARE DISTRIBUTION, INC.

Name: /s/ Gayle C. Johnston

Title: President

Date: 12/28/16

UNITED THERAPEUTICS CORPORATION
GRANT NOTICE FOR 2015 STOCK INCENTIVE PLAN
NONQUALIFIED STOCK OPTIONS
FOR EMPLOYEES
(PERFORMANCE VESTING)

FOR GOOD AND VALUABLE CONSIDERATION, United Therapeutics Corporation (the "Company"), hereby grants to Participant named below the nonqualified stock option (the "Option") to purchase any part or all of the number of shares of its par value common stock (the "Shares"), that are covered by this Option, as specified below, at the Exercise Price per share specified below and upon the terms and subject to the conditions set forth in this Grant Notice, the United Therapeutics Corporation 2015 Stock Incentive Plan (the "Plan") and the Standard Terms and Conditions for Employees (the "Standard Terms and Conditions") promulgated under such Plan, each as amended from time to time. This Option is granted pursuant to the Plan and is subject to and qualified in its entirety by the Standard Terms and Conditions.

Name of Participant:	
Grant Date:	
Number of Shares covered by Option:	
Exercise Price Per Share:	$
Expiration Date:	
Vesting Schedule:	[To be Inserted]

This Option is not intended to qualify as an incentive stock option under Section 422 of the Internal Revenue Code of 1986, as amended.

By accepting this Grant Notice, Participant acknowledges that he or she has received and read, and agrees that this Option shall be subject to, the terms of this Grant Notice, the Plan and the Standard Terms and Conditions. Such acceptance shall be effected by such method(s) as determined by the Company, which may include acceptance by electronic means.

UNITED THERAPEUTICS CORPORATION
STANDARD TERMS AND CONDITIONS FOR
NONQUALIFIED STOCK OPTIONS
FOR EMPLOYEES
(PERFORMANCE VESTING)

These Standard Terms and Conditions for Employees (these "Standard Terms and Conditions") apply to the Option (as defined below) granted to an employee of the Company (as defined below) pursuant to the United Therapeutics Corporation 2015 Stock Incentive Plan (the "Plan"), which are identified as nonqualified stock options and are evidenced by a Grant Notice or an action of the Administrator that specifically refers to these Standard Terms and Conditions. In addition to these Standard Terms and Conditions, the Option shall be subject to the terms of the Plan, which are incorporated into these Standard Terms and Conditions by this reference. Capitalized terms not otherwise defined herein shall have the meaning set forth in the Plan.

1. **TERMS OF OPTION**

United Therapeutics Corporation (the "Company"), has granted to the Participant named in the Grant Notice provided to said Participant herewith (the "Grant Notice") a nonqualified stock option (the "Option") to purchase up to the number of shares of the Company's par value common stock (the "Shares"), set forth in the Grant Notice. The exercise price per share and the vesting schedule of the Option are set forth in the Grant Notice, and the Option is subject to the terms and conditions of the Grant Notice, these Standard Terms and Conditions (as amended from time to time), and the Plan. For purposes of these Standard Terms and Conditions and the Grant Notice, any reference to the Company shall include a reference to any Subsidiary or Affiliate of the Company.

2. **NONQUALIFIED STOCK OPTION**

The Option is not intended to be an incentive stock option under Section 422 of the Internal Revenue Code of 1986, as amended (the "Code") and will be interpreted accordingly.

3. **EXERCISE OF OPTION**

The Option shall not be exercisable as of the Grant Date set forth in the Grant Notice. After the Grant Date, to the extent not previously exercised, and subject to termination or acceleration as provided in these Standard Terms and Conditions and the Plan, the Option shall be exercisable only to the extent it becomes vested, as described in the Grant Notice, the terms of the Plan and these Standard Terms and Conditions, to purchase up to that number of Shares as set forth in the Grant Notice, provided that (except as set forth in Section 4.A, Section 5 and Section 6 below) the Participant remains employed with the Company and does not experience a Termination of Employment prior to the end of the applicable performance period. The vesting period and/or exercisability of an Option may be adjusted by the Administrator to reflect the decreased level of employment during any period in which the Participant is on an approved leave of absence or is employed on a less than full time basis. Notwithstanding any provision of any employment or other

agreement between the Company and the Participant, in no event shall any portion of the Option vest or become exercisable prior to the first anniversary of the Grant Date, other than as provided in these Standard Terms and Conditions in connection with the Participant's death or Disability or the occurrence of a Change in Control.

To exercise the Option (or any part thereof), the Participant shall deliver to the Company a "Notice of Exercise" in a form specified by the Administrator, specifying the number of whole Shares the Participant wishes to purchase and how the Participant's Shares should be registered (in the Participant's name only or in the Participant's and the Participant's spouse's names as community property or as joint tenants with right of survivorship). This may also be accomplished via the Company's electronic Plan administration system.

The exercise price (the "Exercise Price") of the Option is set forth in the Grant Notice. The Company shall not be obligated to issue any Shares until the Participant shall have paid the total Exercise Price for that number of Shares. The Exercise Price shall be paid pursuant to an irrevocable commitment by a broker to pay over such amount from a sale of the Shares issuable under the Option unless the Participant elects to pay such Exercise Price in Shares, cash or a combination thereof, including through the delivery of previously owned Shares, or in such other manners as may be permitted by the Administrator.

Fractional shares may not be exercised. Shares will be issued as soon as practical after exercise. Notwithstanding the above, the Company shall not be obligated to deliver any Shares during any period when the Company determines that the exercisability of the Option or the delivery of Shares hereunder would violate any federal, state or other applicable laws.

4. **EXPIRATION OF OPTION**

The Option shall expire and cease to be exercisable as of the earlier of (a) the Expiration Date set forth in the Grant Notice or (b) the date specified below in connection with the Participant's Termination of Employment:

A. If the Participant's Termination of Employment is by reason of death or Disability, the Option shall fully vest and become exercisable, and the Participant (or the Participant's estate, beneficiary or legal representative, as applicable) may exercise the Option (regardless of whether then vested or exercisable) until the date that is twelve months following the date of such Termination of Employment.

B. If the Participant's Termination of Employment is for any reason other than death, Disability, or pursuant to Section 4.C. below, the Participant may exercise any portion of the Option that is vested and exercisable at the time of such Termination of Employment until the date that is ninety (90) days following the date of such Termination of Employment. Any portion of the Option that is not vested and exercisable at the time of such Termination of Employment (after taking into account any accelerated vesting under Section 5 below or any other

agreement between the Participant and the Company) shall be forfeited and canceled as of the date of such Termination of Employment.

C. Notwithstanding any provision of these Standard Terms & Conditions or the Plan to the contrary other than with respect to a Qualifying Termination described in Section 5.C. below, the Option shall expire and shall no longer be exercisable on the date of Participant's Termination of Employment by the Company for gross misconduct (which includes, without limitation, commission of a felony, misdemeanor or similar crime or offense, the Participant's failure to follow lawful directions of the person to whom he or she reports, and such other circumstances as reasonably determined by the Administrator).

D. Notwithstanding any other provision of any employment agreement between the Participant and the Company that would permit the Participant to become a senior advisor to the Company and fully vest in the Option, if such senior advisor status becomes effective before the first anniversary of the Grant Date, the Option shall not vest until the first anniversary of the Grant Date and such vesting shall be subject to the Participant continuing to provide services to the Company as a senior advisor through such anniversary. The Participant's service as a senior advisor to the Company shall be treated as continued employment for purposes hereof, and the Participant's Termination of Employment shall occur at the termination of such senior advisor status.

5. **CHANGE IN CONTROL**

Notwithstanding any other provision in the Plan or these Standard Terms & Conditions to the contrary, the Option shall vest and become fully exercisable (a) upon a Change in Control if the Option is not assumed by, or a substitute award granted, in connection with such Change of Control, (b) upon a Qualifying Termination of the employment of the Participant within twelve (12) months following a Change in Control if the Award is assumed, or a new award substituted, in connection with the Change in Control. If so determined by the Committee or the Board, in connection with a Change in Control, all or a portion of the Option may be cancelled in connection with the Change in Control for a cash payment equal to the per-Share payment less the Exercise Price of the Option.

6. **VESTING ACCELERATION**

Where the Plan, these Standard Terms and Conditions, or any employment agreement to which the Participant is a party, provides for the acceleration of the vesting of the Option prior to the end of the relevant performance period (in connection with a Change in Control, a Termination of Employment, or otherwise), the number of shares subject to such Option, upon such acceleration, shall be determined assuming the relevant performance criteria were met at the "Target" level of performance. The remaining unvested portion of the Option, following such acceleration, shall automatically be forfeited upon the applicable Termination of Employment, consummation of the Change in Control, or occurrence of such other event.

7. **RESTRICTIONS ON RESALES OF SHARES ACQUIRED PURSUANT TO OPTION EXERCISE**

The Company may impose such restrictions, conditions or limitations as it determines appropriate as to the timing and manner of any resales by the Participant or other subsequent transfers by the Participant of any Shares issued as a result of the exercise of the Option, including without limitation (a) restrictions under an insider trading policy, (b) restrictions designed to delay and/or coordinate the timing and manner of sales by Participant and other optionholders and (c) restrictions as to the use of a specified brokerage firm for such resales or other transfers.

8. **INCOME TAXES**

The Company shall not deliver Shares in respect of the exercise of any Option unless and until the Participant has made arrangements satisfactory to the Administrator to satisfy applicable withholding tax obligations. The Company shall withhold Shares issuable in connection with the exercise of the Option (provided that Shares may be withheld only to the extent that such withholding will not result in adverse accounting treatment for the Company) to pay the minimum required withholding taxes unless the Participant pays the withholding tax obligations to the Company by cash or check. The Participant acknowledges that the Company shall have the right to deduct any taxes required to be withheld by law in connection with the exercise of the Option from any amounts payable by it to the Participant (including, without limitation, future cash wages).

9. **NON-TRANSFERABILITY OF OPTION**

Except as permitted by the Administrator or as permitted under the Plan, the Participant may not assign or transfer the Option to anyone other than by will or the laws of descent and distribution and the Option shall be exercisable only by the Participant during his or her lifetime. The Company may cancel the Participant's Option if the Participant attempts to assign or transfer it in a manner inconsistent with this Section 9.

10. **OTHER AGREEMENTS SUPERSEDED**

The Grant Notice, these Standard Terms and Conditions and the Plan constitute the entire understanding between the Participant and the Company regarding the Option. Any prior

agreements, commitments or negotiations concerning the Option are superseded (provided that, if the Participant is party to an employment agreement with the Company that specifically addresses treatment of stock options, such employment agreement shall control except as otherwise provided herein).

11. **LIMITATION OF INTEREST IN SHARES SUBJECT TO OPTION**

Neither the Participant (individually or as a member of a group) nor any beneficiary or other person claiming under or through the Participant shall have any right, title, interest, or privilege in or to any Shares allocated or reserved for the purpose of the Plan or subject to the Grant Notice or these Standard Terms and Conditions except as to such Shares, if any, as shall have been issued to such person upon exercise of the Option or any part of it. Nothing in the Plan, in the Grant Notice, these Standard Terms and Conditions or any other instrument executed pursuant to the Plan shall confer upon the Participant any right to continue in the Company's employ or service nor limit in any way the Company's right to terminate the Participant's employment at any time for any reason.

12. **GENERAL**

In the event that any provision of these Standard Terms and Conditions is declared to be illegal, invalid or otherwise unenforceable by a court of competent jurisdiction, such provision shall be reformed, if possible, to the extent necessary to render it legal, valid and enforceable, or otherwise deleted, and the remainder of these Standard Terms and Conditions shall not be affected except to the extent necessary to reform or delete such illegal, invalid or unenforceable provision.

The headings preceding the text of the sections hereof are inserted solely for convenience of reference, and shall not constitute a part of these Standard Terms and Conditions, nor shall they affect its meaning, construction or effect.

These Standard Terms and Conditions shall inure to the benefit of and be binding upon the parties hereto and their respective permitted heirs, beneficiaries, successors and assigns.

These Standard Terms and Conditions shall be construed in accordance with and governed by the laws of the State of Delaware, without regard to principles of conflicts of law.

In the event of any conflict between the Grant Notice, these Standard Terms and Conditions and the Plan, the Grant Notice and these Standard Terms and Conditions shall control. In the event of any conflict between the Grant Notice and these Standard Terms and Conditions, the Grant Notice shall control.

All questions arising under the Plan or under these Standard Terms and Conditions shall be decided by the Administrator in its total and absolute discretion.

13. **ELECTRONIC DELIVERY**

By executing the Grant Notice, the Participant hereby consents to the delivery of information (including, without limitation, information required to be delivered to the Participant pursuant to applicable securities laws) regarding the Company and the Subsidiaries, the Plan, the Option and the Shares via Company web site or other electronic delivery.

14. **DEFINITIONS**

A. "Cause" has the meaning specified in the Plan.

B. "Good Reason" means any of the following actions upon or after a Change in Control, without the Participant's express prior written approval, other than due to the Participant's Disability or death: (i) (a) an adverse change in the Participant's status, title, position or responsibilities (including reporting responsibilities) from the Participant's status, title, position or responsibilities as in effect immediately prior to the Change in Control; (b) the assignment to the Participant of any duties or responsibilities which are inconsistent with the Participant's status, title, position or responsibilities as in effect immediately prior to the Change in Control; or (c) any removal of the Participant from or failure to reappoint or reelect the Participant to any of the offices or positions held by the Participant immediately prior to the Change in Control, except in the case of (a), (b) or (c) in connection with the termination of the Participant's employment for Cause, as a result of the Participant's Disability or death, or by the Participant other than for Good Reason; (ii) a reduction in the Participant's base salary or any failure to pay the Participant any compensation or benefits to which the Participant is entitled within five days of the date due; (iii) a reduction in the Participant's annual cash bonus opportunity or equity-type incentive opportunity; (iv) the Company requiring the Participant to relocate to any place outside a 50 mile radius of the location serving as the Participant's principal work site immediately prior to the Change in Control, except for reasonably required travel on the business of the Company or an Affiliate which is not materially greater than such travel requirements in effect immediately prior thereto; (v) the failure by the Company to continue in effect employee benefits for the Participant no less favorable in the aggregate as in effect immediately prior to the Change in Control; or (vi) any material breach by the Company of any provision of an agreement between the Company and the Participant. With respect to (i) through (vi) above, Good Reason shall not be deemed to have occurred unless the Participant shall have notified the Company in writing of his or her intent to resign for Good Reason within thirty (30) days following occurrence of the event constituting Good Reason and the Company shall not have cured the grounds for Good Reason within five (5) days following the provision of such notice.

C. "Qualifying Termination" means termination of the Participant's employment by the Company without Cause or resignation by the Participant for Good Reason.

Exhibit 21

SUBSIDIARIES OF THE REGISTRANT

Lung Bioengineering Inc., a Delaware corporation
Lung Biotechnology Hong Kong Limited, a Hong Kong company
Lung Biotechnology (Nanjing) Co., Ltd., a Chinese Wholly Foreign-Owned Entity
Lung Biotechnology PBC, a Delaware public benefit corporation
Revivicor, Inc., a Delaware corporation
United Therapeutics Europe, Ltd., a company incorporated under the laws of England and Wales
Unither Biotech Inc., a Canadian corporation
Unither Pharma, LLC, a Delaware limited liability company
Unither Pharmaceuticals, LLC, a Delaware limited liability company
Unither Telmed, Ltd., a Delaware corporation
Unither Therapeutik GmbH, a German company
Unither.com, Inc., a Delaware corporation
UTASIA Inc., a Delaware corporation
1109 Spring Managing Holdings, LLC, a Delaware limited liability company
1109 Spring Managing Member, LLC, a Delaware limited liability company

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-108169) pertaining to the United Therapeutics Corporation's Equity Incentive Plan,

(2) Registration Statement (Form S-8 No. 333-56922) pertaining to Employee Options and Consultant Options Granted Outside the United Therapeutics Corporation's Equity Incentive Plan,

(3) Registration Statement (Form S-8 No. 333-95419) pertaining to the United Therapeutics Corporation's Equity Incentive Plan,

(4) Registration Statement (Form S-8 No. 333-153695) pertaining to the United Therapeutics Corporation's Share Tracking Awards Plan,

(5) Registration Statement (Form S-8 No. 333-173858) pertaining to the United Therapeutics Corporation's 2011 Share Tracking Awards Plan,

(6) Registration Statement (Form S-4 No. 333-173857) pertaining United Therapeutics Corporation common stock,

(7) Registration Statement (Form S-8 No. 333-179746) pertaining to the United Therapeutics Corporation 2011 Share Tracking Awards Plan,

(8) Registration Statement (Form S-8 No. 333-182851) pertaining to the United Therapeutics Corporation Employee Stock Purchase Plan,

(9) Registration Statement (Form S-8 No. 333-188241) pertaining to the United Therapeutics Corporation 2011 Share Tracking Awards Plan,

(10) Registration Statement (Form S-8 No. 333-197685) pertaining to the United Therapeutics Corporation 2011 Share Tracking Awards Plan, and

(11) Registration Statement (Form S-8 No. 333-205309) pertaining to the United Therapeutics Corporation 2015 Stock Incentive Plan.

of our reports dated February 22, 2017, with respect to the consolidated financial statements and schedule of United Therapeutics Corporation and the effectiveness of United Therapeutics Corporation's internal control over financial reporting, included in this Annual Report (Form 10-K) for the year ended December 31, 2016.

/s/ Ernst & Young LLP

McLean, Virginia
February 22, 2017

Exhibit 31.1

CERTIFICATION PURSUANT TO RULE 13a-14(a)
OF THE SECURITIES EXCHANGE ACT OF 1934

I, Martine A. Rothblatt, certify that:

1. I have reviewed this annual report on Form 10-K of United Therapeutics Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 22, 2017

/s/ MARTINE A. ROTHBLATT

By: Martine A. Rothblatt, Ph.D.
Title: *Chairman and Chief Executive Officer*
(Principal Executive Officer)

QuickLinks

Exhibit 31.2

CERTIFICATION PURSUANT TO RULE 13a-14(a)
OF THE SECURITIES EXCHANGE ACT OF 1934

I, James C. Edgemond, certify that:

1. I have reviewed this annual report on Form 10-K of United Therapeutics Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 22, 2017

/s/ JAMES C. EDGEMOND

By: James C. Edgemond
Title: *Chief Financial Officer and Treasurer*
(Principal Financial Officer)

QuickLinks

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the annual report of United Therapeutics Corporation (the "Company") on Form 10-K for the period ended December 31, 2016 as filed with the Securities and Exchange Commission (the "Report"), I, Martine A. Rothblatt, Chairman and Chief Executive Officer of the Company, certify, to the best of my knowledge, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ MARTINE A. ROTHBLATT

Martine A. Rothblatt
Chairman and Chief Executive Officer
(Principal Executive Officer)
United Therapeutics Corporation
February 22, 2017

THE FOREGOING CERTIFICATION IS BEING FURNISHED SOLELY PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 AND IS NOT BEING FILED AS PART OF THE FORM 10-K OR AS A SEPARATE DISCLOSURE DOCUMENT.

A SIGNED ORIGINAL OF THIS WRITTEN STATEMENT REQUIRED BY SECTION 906, OR OTHER DOCUMENT AUTHENTICATING, ACKNOWLEDGING, OR OTHERWISE ADOPTING THE SIGNATURE THAT APPEARS IN TYPED FORM WITHIN THE ELECTRONIC VERSION OF THIS WRITTEN STATEMENT REQUIRED BY SECTION 906, HAS BEEN PROVIDED TO UNITED THERAPEUTICS CORPORATION AND WILL BE RETAINED BY UNITED THERAPEUTICS CORPORATION AND FURNISHED TO THE SECURITIES AND EXCHANGE COMMISSION OR ITS STAFF UPON REQUEST.

QuickLinks

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the annual report of United Therapeutics Corporation (the "Company") on Form 10-K for the period ended December 31, 2016 as filed with the Securities and Exchange Commission (the "Report"), I, James C. Edgemond, Chief Financial Officer and Treasurer of the Company, certify, to the best of my knowledge, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ JAMES C. EDGEMOND

James C. Edgemond
Chief Financial Officer and Treasurer
(Principal Financial Officer)
United Therapeutics Corporation
February 22, 2017

THE FOREGOING CERTIFICATION IS BEING FURNISHED SOLELY PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 AND IS NOT BEING FILED AS PART OF THE FORM 10-K OR AS A SEPARATE DISCLOSURE DOCUMENT.

A SIGNED ORIGINAL OF THIS WRITTEN STATEMENT REQUIRED BY SECTION 906, OR OTHER DOCUMENT AUTHENTICATING, ACKNOWLEDGING, OR OTHERWISE ADOPTING THE SIGNATURE THAT APPEARS IN TYPED FORM WITHIN THE ELECTRONIC VERSION OF THIS WRITTEN STATEMENT REQUIRED BY SECTION 906, HAS BEEN PROVIDED TO UNITED THERAPEUTICS CORPORATION AND WILL BE RETAINED BY UNITED THERAPEUTICS CORPORATION AND FURNISHED TO THE SECURITIES AND EXCHANGE COMMISSION OR ITS STAFF UPON REQUEST.

QuickLinks