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, 2017

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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer ☒	Accelerated filer ☐	Non-accelerated filer ☐ (do not check if a smaller reporting company)	Smaller reporting company ☐ Emerging growth 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, 2017, as reported by the NASDAQ Global Select Market was

approximately $4,948,421,509.

The number of shares outstanding of the issuer's common stock, par value $0.01 per share, as of February 14, 2018, was 43,239,722.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for the registrant's 2018 annual meeting of shareholders scheduled to be held on June 27, 2018, are incorporated by reference in Part III of this Form 10-K.

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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 (Remodulin); 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, formulations 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 and Unituxin were approved by the FDA in 2013 and 2015, respectively. Our sales, marketing and other commercial 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.

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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 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 all formulations of treprostinil, a prostacyclin analogue, 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. 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 Group 2, and Tyvaso to treat pulmonary hypertension in certain categories of WHO Group 3. For further details, see *Research and Development* below.

Remodulin

We sell Remodulin to specialty pharmaceutical distributors in the United States and to pharmaceutical distributors internationally. We recognized approximately $670.9 million, $602.3 million and $572.8 million in Remodulin net product sales, representing 39 percent, 38 percent and 39 percent of our total revenues for the years ended December 31, 2017, 2016 and 2015, respectively. Remodulin is indicated to treat patients with PAH, to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with functional class II-IV (moderate to severe) symptoms.

Outside of the United States, Remodulin is approved for the treatment of PAH in 38 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 prostacyclin therapies 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 four generic drug companies that filed abbreviated new drug applications (ANDAs) with the FDA to market generic versions of Remodulin in the United States. Under the terms of these settlements, Sandoz, Inc. (Sandoz) is permitted to launch its generic version of Remodulin in the United States in June 2018, and Teva Pharmaceuticals USA, Inc. (Teva), Par Sterile Products, LLC (Par) and Dr. Reddy's Laboratories, Inc. (Dr. Reddy's), are permitted to launch 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. 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 sell Tyvaso to the same specialty pharmaceutical distributors in the United States that distribute Remodulin. We recognized approximately $372.9 million, $404.6 million and $470.1 million in Tyvaso net product sales, representing 22 percent, 25 percent and 32 percent of our total revenues for the years ended December 31, 2017, 2016 and 2015, respectively.

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, and related accessories. A single ampule containing Tyvaso is emptied into the Tyvaso Inhalation System once per day, so the Tyvaso Inhalation System only needs to be cleaned once daily. Tyvaso is regulated by the FDA as a drug-device combination product, consisting of Tyvaso drug product and the Tyvaso Inhalation System.

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.

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.

Orenitram

Orenitram is the only FDA approved, orally administered prostacyclin analogue, and is the only oral PAH prostacyclin class therapy approved in the United States that is titratable to a maximum tolerated dose, without a dose ceiling. We sell Orenitram to the same specialty pharmaceutical distributors in the United States that distribute Remodulin and Tyvaso. We recognized approximately $185.8 million, $157.2 million and $118.4 million in Orenitram net product sales, representing 11 percent, ten percent and eight percent of our total revenues for the years ended December 31, 2017, 2016 and 2015, respectively. The primary study that established efficacy included predominately patients with functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75 percent) or PAH associated with connective tissue disease (19 percent). The most common side effects observed in our clinical studies were headache, nausea and diarrhea.

In February 2018, we settled patent litigation with Actavis Laboratories FL, Inc. (Actavis) relating to its ANDA seeking to market a generic version of Orenitram in the United States. Under the terms of this settlement, Actavis will be permitted to launch its generic version of Orenitram in the United States in June 2027, although Actavis may be permitted to enter the market earlier under certain circumstances. For further detail, see the section below entitled *Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity—Generic Competition*.

Adcirca

Adcirca is a PDE-5 inhibitor, the active pharmaceutical ingredient of which is tadalafil. Tadalafil is also the active pharmaceutical ingredient in Cialis®, which is marketed by Eli Lilly and Company (Lilly) for 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. We recognized approximately $419.7 million, $372.2 million and $278.8 million in Adcirca net product sales, representing 24 percent, 23 percent and 19 percent of our total revenues for the years ended December 31, 2017, 2016 and 2015, respectively.

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 new drug application (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.

A U.S. patent for Adcirca for the treatment of pulmonary hypertension expired in November 2017. Lilly has two additional patents expiring in April and November 2020, respectively, covering Adcirca and claiming pharmaceutical compositions and free drug particulate forms (the 2020 Patents). The Patent Trial and Appeal Board (PTAB) of the U.S. Patent and Trademark Office (USPTO) has issued a Final Written Decision finding these patents invalid as the result of an *inter partes* review (IPR) proceeding initiated by Actelion Pharmaceuticals Ltd. Lilly's appeal of the PTAB's decision is pending before the United States Court of Appeals for the Federal Circuit. In May 2017, we amended our license agreement with Lilly relating to Adcirca to clarify and extend the term of the agreement and to amend the economic terms of the agreement following the expiration of a patent covering Adcirca in November 2017. As a result of this amendment, beginning December 1, 2017, our royalty rate on net product sales of Adcirca increased from five percent to ten percent, and we are required to make milestone payments to Lilly equal to $325,000 for each $1,000,000 in net product sales. Adcirca's cost of product sales as a percentage of Adcirca's net product sales has increased significantly since December 1, 2017 due to these cost increases. In the event that Lilly prevails in one or both of the appeals noted above: (a) the previous five percent royalty rate will apply and the effective date of the new payment structure will be deferred until the expiration, lapse, abandonment or invalidation of the last claim of the 2020 Patents covering commercialization of Adcirca for pulmonary hypertension; and (b) to the extent we had previously paid amounts in excess of five percent, those amounts will be refunded by Lilly. The FDA has already tentatively approved ANDAs filed by at least two generic companies to market generic versions of Adcirca following the expiration of the November 2017 patent. However, the FDA granted Lilly's request for pediatric exclusivity, which provides an additional six-month exclusivity period through May 2018. As a result, following the expiration of regulatory exclusivity in May 2018, we anticipate the launch of generic versions of Adcirca resulting in decreased Adcirca sales, which will likely lead to a material adverse impact on Adcirca revenue. As amended, the term of our license agreement with Lilly expires on the latest to occur 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; (2) expiration of any government-conferred exclusivity rights to use Adcirca for the treatment of pulmonary hypertension in the United States; or (3) December 31, 2020.

Product to Treat Cancer—Unituxin

In March 2015, the FDA approved our Biologics License Application (BLA) for Unituxin, in combination with granulocyte-macrophage colony-stimulating factor (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. We recognized approximately $76.0 million, $62.5 million and $20.5 million in Unituxin net product sales, representing four percent, four percent and one percent of our total revenues for the years ended December 31, 2017, 2016 and 2015, respectively.

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Research and Development

We focus most of our research and development efforts on the following near-term pipeline programs (intended to result in product launches in the 2018-2021 timeframe) and medium-term pipeline programs (intended to result in product launches in the 2022-2025 timeframe). We are also engaged in a variety of additional medium- and long-term research and development efforts, including technologies designed to increase the supply of transplantable organs and tissues and improve outcomes for transplant recipients through regenerative medicine, xenotransplantation, biomechanical lungs and ex-vivo lung perfusion.

Near-Term Pipeline Programs (2018-2021)

Product	Mode of Delivery	Indication	Current Status STUDY NAME	Our Territory
Implantable System for Remodulin	Continuous intravenous via implantable pump	PAH	Pending regulatory approval	United States, United Kingdom, Canada, France, Germany, Italy and Japan
RemUnity™ (treprostinil)	Continuous subcutaneous via pre-filled, semi-disposable system	PAH	Pre-NDA	Worldwide
OreniPlus™ (Orenitram in combination with approved background therapy)	Oral	PAH (decrease morbidity and mortality)	Phase IV *FREEDOM-EV*	Worldwide
Tysuberprost™ (esuberaprost in combination with Tyvaso)	Oral (esuberaprost) Inhaled (Tyvaso)	PAH (decrease morbidity and mortality)	Phase III *BEAT*	North America, Europe, Mexico, South America, Egypt, India, Israel, South Africa and Australia
RemoPro™ (pain-free subcutaneous Remodulin prodrug)	Continuous subcutaneous	PAH	Pre-Clinical	Worldwide
Dinutuximab	Intravenous	Small cell lung cancer	Phase II/III *DISTINCT*	Worldwide
Tyvaso-ILD™ (treprostinil)	Inhaled	Pulmonary hypertension associated with idiopathic pulmonary fibrosis (WHO Group 3)	Phase III *INCREASE*	Worldwide

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Medium-Term Pipeline Programs (2022-2025)

Product	Mode of Delivery	Indication	Current Status STUDY NAME	Our Territory
Tyvaso (treprostinil)	Inhaled	Pulmonary hypertension associated with chronic obstructive pulmonary disease (WHO Group 3)	Phase III *PERFECT*	Worldwide
Aurora-GT™ (eNOS gene therapy)	Intravenous	PAH	Phase II/III *SAPPHIRE*	United States
OreniLeft™ (treprostinil)	Oral	Pulmonary hypertension associated with left ventricular diastolic dysfunction (WHO Group 2)	Phase III *SOUTHPAW*	Worldwide

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) 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 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 the Implantable System for Remodulin in the United States, we are pursuing parallel regulatory filings with Medtronic relating to the device and the drug, respectively. Medtronic's premarket approval application (PMA) for the device was approved by the FDA in December 2017. We resubmitted our NDA for the use of Remodulin in the implantable pump on January 30, 2018, and we anticipate a two-month review period.

Medtronic is entirely responsible for regulatory approvals and all manufacturing and quality systems related to its infusion pump and related components. Medtronic entered into 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. During the fourth quarter of 2017, Medtronic was notified by the FDA that these provisions have been satisfied, and Medtronic has therefore been permitted to recommence manufacture and sale of the systems without limitation, but certain other elements of the consent decree remain in effect, such as the requirements to comply with a remediation plan and to submit to periodic auditing of Medtronic's quality systems. Although we believe we will be permitted to launch

the Implantable System for Remodulin following FDA approval, any non-compliance by Medtronic with its consent decree could interrupt its manufacture and sale of the device.

RemUnity and RemoPro

In December 2014, we entered into an exclusive agreement with DEKA Research & Development Corp. (DEKA) to develop a pre-filled, semi-disposable 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. The RemUnity system consists of a small, lightweight, durable pump that is intended to have a service life of at least three years. The RemUnity system uses disposable cartridges pre-filled with treprostinil, which can be connected to the pump with less patient manipulation than is typically involved in filling currently-available subcutaneous pumps. Currently, we are engaged in engineering, design and development efforts to optimize the RemUnity system to deliver treprostinil in pre-filled reservoirs, and intend to complete human factor studies and functionality testing in subjects before submitting an application to the FDA to approve the pre-filled RemUnity system.

We are also engaged in pre-clinical development of a new prodrug of treprostinil called RemoPro, which is intended to enable subcutaneous delivery without the site pain currently associated with subcutaneous Remodulin. A prodrug is a metabolically inactive compound that, after administration, metabolizes into an active compound. RemoPro is intended to be inactive in the subcutaneous tissue, which should decrease or eliminate site pain. Once RemoPro is absorbed into the blood, it metabolizes into treprostinil.

Orenitram, OreniPlus and OreniLeft

In 2013, the FDA approved Orenitram for the treatment of PAH 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.

In order for Orenitram to reach its full commercial potential, we believe we need to complete successfully further studies to support an amendment to Orenitram's label to indicate that Orenitram delays morbidity and/or mortality (also known as "time to clinical worsening") in PAH patients who are on an approved oral background therapy. We refer to this initiative to amend 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. Enrollment of this study was completed in December 2017, and we anticipate full results of the study will be available during the second half of 2018.

We are also enrolling patients in a study of Orenitram (*SOUTHPAW*) to treat WHO Group 2 pulmonary hypertension (specifically associated with left ventricular diastolic dysfunction), which we refer to as OreniLeft. There are presently no FDA approved therapies indicated for treatment of WHO Group 2 pulmonary hypertension.

Tysuberprost

In 2012, we completed a phase I safety study of esuberaprost, a single-isomer orally bioavailable prostacyclin analogue, and the data suggested that dosing esuberaprost four times a day was tolerable. We believe that esuberaprost and treprostinil have differing prostacyclin receptor-binding profiles and are studying the potential safety and efficacy benefits for patients when used in combination. We also believe that inhaled treprostinil and oral esuberaprost have complementary pharmacokinetic and pharmacodynamic profiles, which indicate that they should provide greater efficacy in combination. In March 2017, we completed enrollment of our phase III registration study called *BEAT* (***BE***raprost 314d

Add-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 Tyvaso or have a less than optimal response to Tyvaso treatment. We refer to the resulting use of esuberaprost and Tyvaso therapies in combination with each other 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 conducting studies of Unituxin in adult patients with other forms of GD2-expressing cancers. We are currently enrolling the phase III portion of a phase II/III study called *DISTINCT*, in patients with small cell lung cancer. During the fourth quarter of 2017, we completed the phase II portion of the study, and commenced the phase III portion of the study following an interim safety review. These research and development efforts into new indications for Unituxin have been substantially outsourced to a contract research organization called Precision Oncology, LLC.

Unituxin therapy is associated with severe side effects, including infections, infusion reactions, hypokalemia, hypotension, pain, fever, and capillary leak syndrome. In post-approval use of Unituxin, the adverse reactions of prolonged urinary retention, transverse myelitis, and reversible posterior leukoencephalopathy syndrome have been observed. Unituxin's label also includes a boxed warning related to serious infusion reactions and neurotoxicity.

Finally, we are developing a fully humanized (non-chimeric) version of dinutuximab, the active ingredient in Unituxin. This new version is expected to reduce some of the side effects associated with Unituxin, which is a chimeric composed of a combination of mouse and human proteins.

Tyvaso and Tyvaso-ILD

In October 2017, we received FDA approval of a supplement to our NDA for Tyvaso, covering a new inhalation device as part of the Tyvaso Inhalation System. The new device, called the TD-300/A, was designed based on physician and prescriber feedback, and is intended to aid patient compliance and enhance ease of use. We plan to launch the TD-300/A in 2018, which we believe will help reduce the rate of Tyvaso discontinuation associated with the current device. In addition to the TD-300/A, we are engaged in research and development efforts into new devices to further optimize the delivery of inhaled treprostinil.

We are enrolling 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 combined pulmonary fibrosis and emphysema), which we refer to as Tyvaso-ILD. We are also planning a phase III registration study called *PERFECT* (***P***ulmonary hypertension ***E***n***R***ichment study ***F***or the ***E***valuation of ***C***OPD with ***T***yvaso), which is a study of Tyvaso in patients with WHO Group 3 pulmonary hypertension associated with chronic obstructive pulmonary disease. There are presently no FDA approved therapies indicated for treatment of WHO Group 3 pulmonary hypertension.

Aurora-GT

We are enrolling a phase II/III study (called *SAPPHIRE*) of a gene therapy product called Aurora-GT, in which a PAH patient's own endothelial progenitor cells are isolated, transfected with the

gene for human endothelial 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. This study is being conducted entirely in Canada, and is sponsored by Northern Therapeutics, Inc., a Canadian entity in which we have a 49.7 percent voting stake and a 71.8 percent financial stake. We have the exclusive right to pursue this technology in the United States, and plan to seek FDA approval of Aurora-GT if *SAPPHIRE* is successful.

Organ Manufacturing

Each year, end stage organ failure kills millions of people. A significant number of these patients could have benefited from an organ transplant. Unfortunately, the number of usable, donated organs available for transplantation has not grown significantly over the past half century while the need has soared. Our long-term goals are aimed at addressing this shortage. With advances in technology, we believe that creating an unlimited supply of tolerable manufactured organs is now principally an engineering challenge, and we are dedicated to finding engineering solutions. Since 2011, we have been 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, regenerative medicine, biomechanical lungs, and other technologies 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, and our manufactured lungs, kidneys and hearts have set records for viability in FDA-required animal models. Most recently, in February 2018 we reached a significant milestone by achieving 30-day survival of our genetically modified porcine lungs in FDA-required animal models. 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. While we continue to develop and commercialize therapies for rare and life-threatening conditions, we view organ manufacturing as the ultimate technology solution for a broad array of diseases, many of which (such as PAH) have proven incurable thus far through more traditional pharmaceutical and biologic therapies. For this reason, in 2015 we created a wholly-owned public benefit corporation called Lung Biotechnology PBC, chartered with the express purpose "to address the acute national shortage of transplantable lungs and other organs with a variety of technologies that either delay the need for such organs or expand the supply."

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*. During the years ended December 2017, 2016 and 2015, we incurred $264.6 million, $147.6 million and $245.1 million in research and development expenses.

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 the importance of early treatment; and (3) increase awareness of our commercial products and how they fit into the various stages of disease progression and treatment. 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. and its affiliates, including Curascript SD Specialty Distribution (collectively 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.

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

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

United States Distribution of Adcirca

Under our manufacturing and supply agreement with Lilly (see *Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity—Agreements with Lilly Related to Adcirca* below for more details), Lilly manufactures and distributes Adcirca 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. Upon shipment, Lilly sends an invoice and collects the amount due from the customer subject to customary discounts and rebates, if any. Although Lilly provides these services on our behalf, we maintain the risk of loss as it pertains to inventory, product returns and non-payment of invoices. The manufacturing and supply agreement will continue in effect until expiration or termination of our license agreement for Adcirca. Lilly retains authority under the license agreement for all regulatory activities with respect to Adcirca, as well as its retail pricing, which has been and is expected to remain at price parity with Cialis. 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 and Tyvaso

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 sell Tyvaso commercially to a distributor that has exclusive distribution rights in Israel. 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. We also maintain similar named patient programs for Tyvaso in certain countries.

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 our treprostinil-based products, Remodulin, Tyvaso and Orenitram. We have been granted three patents relating to manufacturing treprostinil that expire in 2028 and are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book (see Orange Book below), for Remodulin, Tyvaso and Orenitram. One of these patents has been held invalid by the PTAB following an IPR proceeding, as discussed below under *Generic Competition*.

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 have also been granted two patents directed to a method of treating pulmonary hypertension and a kit for treating pulmonary hypertension. These two patents expire in 2028 and are listed in the Orange Book. Counterparts to these two patents are issued in several other countries. Both are subject to an ongoing IPR proceeding, as discussed below under *Generic Competition*.

- *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 seven unexpired Orange Book-listed patents with expiration dates ranging from 2024 to 2029. Tyvaso currently has eight unexpired Orange Book listed patents with expiration dates ranging from 2018 to 2028. Orenitram currently has thirteen unexpired Orange Book listed patents with expiration dates ranging from 2024 to 2031. Additional patent applications are pending, and if granted, may be eligible for listing in the Orange Book.

Regulatory Exclusivity

Remodulin's regulatory exclusivity in the United States and Europe has expired. In 2010, the FDA granted orphan drug designation for Tyvaso, which resulted in an orphan exclusivity period that expired in July 2016. In 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, and we are currently challenging that denial in litigation pending before the United States District Court for the District of Columbia.

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, Par and Dr. Reddy's, 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 can market its generic version of Remodulin in the United States beginning in June 2018, and Teva, Par and Dr. Reddy's can each launch their generic versions in the United States beginning in December 2018, although each of these companies may be permitted to enter the market earlier under certain circumstances. We also settled litigation with Actavis relating to its ANDA seeking FDA approval to market a generic version of Orenitram before the expiration of certain of our U.S. patents. Under the terms of this settlement agreement, Actavis can market its generic version of Remodulin in the United States beginning in June 2027, although Actavis 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 seeking 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. In addition, Watson filed IPR petitions seeking to invalidate the claims of two of our patents that expire in 2028 and relate to Tyvaso, and on January 11, 2018, the PTAB issued decisions to institute IPR proceedings with respect to both patents.

Finally, SteadyMed Ltd. (SteadyMed) filed an IPR petition 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 March 2017, the PTAB issued a Final Written Decision in this matter, finding that all claims of the '393 patent are not patentable. In May 2017, we appealed this decision to the U.S. Court of Appeals for the Federal Circuit, and the Federal Circuit affirmed the PTAB's Final Written Decision. In February 2018, we submitted a petition for certiorari with the United States Supreme Court to review the Federal Circuit decision. The '393 patent remains valid and enforceable until all appeals have been exhausted. We are currently asserting the '393 patent (along with several other patents) against Watson in connection with its efforts to obtain approval to market a generic version of Tyvaso.

In January 2016, SteadyMed announced that the FDA had granted orphan drug designation for 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 June 2017, SteadyMed submitted an NDA to the FDA seeking approval of Trevyent for the treatment of PAH. In August 2017, SteadyMed announced receipt of a refuse-to-file letter from the FDA, in which the FDA refused to accept SteadyMed's NDA for review, requested further information on certain device specifications and required performance testing and additional design verification and validation testing on the final, to-be-marketed Trevyent product. SteadyMed has indicated it plans to resubmit its NDA by the end of 2018.

We intend to continue vigorously defending the '393 patent, but even if the ultimate result is unfavorable to us, we have other patents covering subject matters similar to the '393 patent and with the same expiration date (December 2028). Specifically, in March 2017, the USPTO awarded us two additional patents related to the '393 patent, U.S. Patent Nos. 9,593,066 and 9,604,901. We prosecuted the applications that resulted in these new patents in parallel with the '393 patent IPR proceedings and presented claims addressing the invalidity arguments raised by SteadyMed in the '393 patent IPR proceedings and by Watson in our ongoing litigation. The USPTO allowed the new patent claims with

full knowledge of the '393 patent IPR proceedings, the invalidity arguments presented therein, and the invalidity arguments raised by Watson in connection with the '393 patent. Thus, we anticipate that these new patents should be less susceptible to challenge than the '393 patent. We have listed both of these new patents in the Orange Book for Remodulin, Tyvaso and Orenitram and may in the future decide to assert these patents against any competitor marketing or seeking approval to market generic versions of Remodulin, Tyvaso or Orenitram. Following the Final Written Decision in the '393 patent IPR, SteadyMed asked the PTAB to invalidate the new patents because SteadyMed claimed that the new patents' claims are patentably indistinct from the '393 patent claims. The PTAB denied SteadyMed's request. Thus, SteadyMed must petition the PTAB to request new IPR proceedings if it wishes to attempt to invalidate the patents issued in March 2017. SteadyMed also asked the PTAB to assert jurisdiction over additional new patent applications we filed related to the '393 patent that are pending before the USPTO and hold that the claims are patentably indistinct over the claims of the '393 patent. The PTAB denied SteadyMed's request. As a result, the USPTO could potentially award us additional patents based on these applications.

For further details regarding the Watson, Actavis and SteadyMed matters, please see Note 16—*Litigation*, to our consolidated financial statements.

As a result of our settlements with Sandoz, Teva, Par and Dr. Reddy's, we expect to see generic competition for Remodulin from these companies in the United States beginning in June 2018 (Sandoz) and December 2018 (Teva, Par and Dr. Reddy's) (or earlier under certain circumstances). The two patents granted in March 2017 will not impact these settlements allowing generic competition for Remodulin. 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.

The U.S. patent for Adcirca for the treatment of pulmonary hypertension expired in November 2017. The FDA has granted additional regulatory exclusivity through May 2018. After this time, we expect generic competition for Adcirca and a resulting significant reduction of Adcirca sales, which would lead to a material adverse impact on Adcirca revenues. For additional information, refer to *Part I, Item 1—Business Overview—Products to Treat Pulmonary Arterial Hypertension—Adcirca.*

Patent expiration, patent litigation and generic competition for any of our commercial PAH products could have a significant, adverse impact on our revenues, profits and stock price, 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 profits*, contained in *Part I, Item 1A—Risk Factors* included in this Report.

Agreements with Lilly 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 based on our net product sales of Adcirca. Lilly retained the exclusive rights to develop, manufacture and commercialize pharmaceutical products containing tadalafil, the active pharmaceutical ingredient in Adcirca, for 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®. In May 2017, we amended our license agreement with Lilly relating to Adcirca, in order to clarify and extend the term of the agreement and to amend the economic terms of the agreement following a patent expiry in November 2017. For additional discussion, refer to our *Adcirca* product description contained in *Part I, Item 1—Business Overview—Products to Treat Pulmonary Arterial Hypertension*.

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 net 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

We have orphan drug exclusivity in the United States for Unituxin, expiring March 2022, which precludes the FDA from approving 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) 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 the Implantable System for Remodulin, 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 the Implantable System for Remodulin for the treatment of PAH in the exclusive territories. Our agreement with Medtronic expires on a country-by-country basis upon the later of ten years from first commercial sale in the relevant country, or ten years after we no longer have a valid patent claim covering the use of Remodulin to treat PAH in such country. Either party may terminate the agreement immediately for safety, quality or regulatory concerns, in the event of the other party's bankruptcy or insolvency, or in the case of a material breach by the other party that remains uncured following the relevant cure period. In addition, either party may terminate the agreement without cause on one year's notice to the other party.

Esuberaprost 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.

Pursuant to a 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 March 2017, we amended our license agreement with Toray to further reduce the royalty rate to single digits in exchange for contingent milestone payments in the event that we do not achieve certain clinical and regulatory events by certain dates. In addition, Toray granted us sole manufacturing rights for commercial esuberaprost.

In 2011, the FDA granted orphan designation for esuberaprost for treatment of PAH. Thus, the FDA should grant orphan drug exclusivity if esuberaprost 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 system for subcutaneous delivery of Remodulin, which we refer to as RemUnity. Under the terms of the agreement, we are funding the development costs related to the semi-disposable 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 agreement with DEKA expires on the last to occur of twenty-five years from the first product launch under the agreement, or upon the expiration of the last valid claim of a patent licensed from DEKA under the agreement that covers the RemUnity system. Either party may terminate the agreement immediately upon a material breach by the other party that is uncured following the relevant cure period, or in the event of the other party's bankruptcy or insolvency.

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 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. 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 finished Unituxin drug product, and are constructing an additional facility to increase our manufacturing capacity for dinutuximab, the active ingredient in Unituxin. We have no plans to develop a redundant manufacturing source for Orenitram.

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 (which was acquired by Johnson & Johnson in 2017) 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.

We anticipate generic bosentan will be launched in the United States during the 2018-2020 timeframe. Generic bosentan 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®. In 2015, Gilead announced the positive results of the *AMBITION* study of ambrisentan and tadalafil as an up-front combination therapy for PAH, which we believe has driven increased use of Letairis and Adcirca. We expect generic ambrisentan will be launched in the United States in 2018;

- *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 2012, several companies began marketing generic formulations of sildenafil citrate;

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

- *Adempas*®. Approved in 2013 in the United States and 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. Uptravi is also marketed in Japan by Nippon Shinyaku Co., Ltd.

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 reported positive phase II results for ralinepag in patients with PAH in July 2017, and is currently planning a phase III study;

- *Trevyent*, a formulation of treprostinil being developed by SteadyMed to treat PAH using SteadyMed's pre-filled, disposable PatchPump technology. SteadyMed received a refusal to file letter from the FDA in August 2017, and has indicated it plans to resubmit its NDA by the end of 2018;

- *Bardoxolone*, an oral therapy being developed by Reata Pharmaceuticals, Inc. for treatment of PAH associated with connective tissue disease. Reata is enrolling patients in a phase III clinical trial, with data expected during the second half of 2018;

- *LIQ861*, a powder formulation of treprostinil designed for deep-lung delivery using a disposable, dry powder inhaler being developed by Liquidia Technologies Inc., which announced commencement of a phase III study in PAH patients in January 2018;

- *CAM2043*, a liquid crystal gel formulation of treprostinil being developed as a once-weekly subcutaneous depot injection for PAH by Camurus AB. Camarus announced the commencement of a phase I clinical study in December 2017;

- *Treprostinil Technosphere*®, an inhaled, dry powder formulation of treprostinil being developed for PAH by MannKind Corporation, which has announced the filing of an investigational new drug application for a phase I clinical study it plans to commence in 2018; and

- *INS1009*, an inhaled nanoparticle formulation of a treprostinil prodrug being developed by Insmed Incorporated for PAH. Insmed announced the completion of a phase I study in September 2016.

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. 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 treprostinil-based 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 four generic drug companies permitting them to launch generic versions of Remodulin in 2018. We also settled litigation with Actavis permitting it to launch a generic version of Orenitram in June 2027. We are also engaged in litigation with a generic company seeking to launch a generic version Tyvaso. 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 developed by Apeiron Biologics AG that is already approved in Europe to treat high-risk neuroblastoma. 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 2018.

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 21st Century Cures Act (Cures Act), which became law in December 2016, expanded the types of studies that qualify for orphan drug grants. Orphan drug designation also may qualify an applicant for federal tax credits 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).

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.

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 Cures Act requires the FDA to establish a program that would expedite access to devices that provide more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions, for which no approved or cleared treatment exists or which offer significant advantages over existing approved or cleared alternatives; in 2017, the FDA published draft guidance on this "breakthrough" devices pathway.

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 non-significant 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 the FDA will issue a designation letter within 60 calendar days of the filing of the RFD. Depending on the type of combination product, the FDA may require a single application for approval, clearance, or licensure of the combination product, or separate applications for the constituent parts. During the review of marketing applications, the lead Center may consult or collaborate with other FDA Centers. In 2017, the FDA released final documents addressing the application of cGMP requirements and classification issues relating to combination products.

The Cures Act sets forth a number of provisions pertaining to combination products, such as procedures for negotiating disagreements between sponsors and 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 participants who qualify based on income. 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. Remodulin and Tyvaso are reimbursed by 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. As a condition of the inclusion of 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, are subject to regulatory changes and amendments that we cannot control, 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 and prescribers, purchasers, formulary managers and others. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties, exclusion from participation in federal healthcare programs and liability under the False Claims Act. 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. In addition, although the Office of Inspector General of the Department of Health and Human Services (OIG) issues guidance and advisory opinions regarding compliance with the anti-kickback statute, and applicable exemptions and safe harbors, such guidance and opinions may change over time.

The federal False Claims Act prohibits any person from, among other things, presenting, or causing to be presented, a false or fraudulent claim for payment to the federal government, or making, or causing to be made, a false statement material to a false or fraudulent 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; for violating the anti-kickback laws; 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 treble damages, 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 the 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.

In December 2017, Congress repealed a PPACA requirement that individuals obtain healthcare insurance coverage or face a penalty, which could decrease the number of patients who have coverage under health plans that pay for patient use of our products.

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 the FDA's authority regarding drugs that target rare diseases, and broadens the type of data and information that may be used to support a drug or biologic application for a genetically targeted drug or variant protein targeted drug. The law requires the FDA to facilitate development programs for, and provides expedited review of, regenerative advanced therapies. The law further requires the FDA to establish a program to evaluate the use of real world evidence, i.e., evidence from sources other than randomized clinical trials, to support the approval of certain drug 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 800 employees as of December 31, 2017. The success of our business is highly dependent on attracting and retaining highly talented and qualified personnel.

Industry Segments and Geographic Areas

Since 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 14—*Segment Information* to our consolidated financial statements.

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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*.

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EXECUTIVE OFFICERS OF THE REGISTRANT

The following is a list, as of February 21, 2018, 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.	63	Chairman, Chief Executive Officer and Director
Michael Benkowitz	46	President and Chief Operating Officer
James C. Edgemond	50	Chief Financial Officer and Treasurer
Paul A. Mahon, J.D.	54	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 2008 through January 2013. He also served in a variety of roles at The Corporate Executive Board Company from 1998 to 2008, serving as Executive Director, Finance from 2005 to 2008. He began his career as a public accountant at KPMG Peat Marwick LLP, from 1990 through 1998, where he served in a variety of roles, including as a Senior Manager prior to his departure.

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

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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, including our expectation that revenue growth will recommence in 2019, following a temporary decline in 2018;
- 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, including from generic entries 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 (among others) those described in this Report relating to our *FREEDOM-EV* study of Orenitram, our *BEAT* study of esuberaprost, our collaboration with DEKA to develop the RemUnity system, our plan to develop a pain-free subcutaneous formulation of treprostinil called RemoPro, and our program to develop the Implantable System for Remodulin, which we are working on with Medtronic;
- The outcome of pending and potential future legal and regulatory actions, including investigations, 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 forms of Adcirca, which we expect will become available following loss of regulatory exclusivity in May 2018; generic forms of Remodulin, which we expect four 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 protection 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 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 versions of Adcirca following loss of regulatory exclusivity in May 2018, as well as generic versions of Remodulin, which could be launched in the United States by Sandoz in June 2018 and by Teva, Par and Dr. Reddy's in December 2018, and a generic version of Orenitram, which could be launched in the United States by Actavis in June 2027, 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 conducting two pivotal clinical 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 clinical study with time to clinical worsening as its primary endpoint. The timing to complete 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 to 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, canceled 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 good clinical practices (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®, Veletri®, Volibris®, 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. Trevyent has 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 delivery system), 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 mid-2018, and generic treprostinil may be launched in 2018, as described elsewhere in this Report. It is unclear what revenues, if any, we will generate from Adcirca sales after loss of regulatory exclusivity in May 2018.

Legislation such as the 21st 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. 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 October 2017, the Medicare Drug Price Negotiation Act of 2017 was proposed in Congress, with similar requirements. More recently, in November 2017, CMS announced a Final Rule that would adjust the applicable payment rate as necessary for certain separately payable drugs and biologicals acquired under the 340B Program from average sales price (ASP) plus 6 percent to ASP minus 22.5 percent.

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. In addition, third-party payers may encourage the use of less-expensive generic alternative therapies following the launch of generic forms of Remodulin (anticipated in June 2018) and Adcirca (anticipated in May 2018). 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.

Patient assistance programs for pharmaceutical products have come under increasing scrutiny by governments, legislative bodies and enforcement agencies. These activities may result in actions that have the effect of reducing prices or demand for our products, harming our business or reputation, or subjecting us to fines or penalties.

Recently, there has been enhanced scrutiny of company-sponsored patient assistance programs, including insurance premium and co-pay assistance programs and manufacturers' donations to third-party charities that provide such assistance. If we, our vendors or donation recipients, are deemed to have failed to comply with relevant laws, regulations or government guidance in any of these areas, we could be subject to criminal and civil sanctions, including significant fines, civil monetary penalties and exclusion from participation in government healthcare programs, including Medicare and Medicaid, and burdensome remediation measures. Actions could also be brought against executives overseeing our business or other employees.

In December 2017, we entered into a civil Settlement Agreement with the DOJ and the OIG. The Settlement Agreement relates to a May 2016 subpoena from the DOJ requesting documents regarding the Company's support of 501(c)(3) organizations that provide financial assistance to patients. Other companies received similar inquiries as part of a DOJ investigation regarding whether that support may violate the Federal Anti-Kickback Statute and the Federal False Claims Act. In connection with the civil settlement, we also entered into a Corporate Integrity Agreement (the CIA) with the OIG, which requires us to maintain our corporate compliance program and to undertake a set of defined corporate integrity obligations for a period of five years from the date the agreement was signed. We may be required to incur significant future costs to comply with the CIA.

It is possible that any actions taken by the DOJ as a result of this industry-wide inquiry could reduce demand for our products and/or reduce coverage of our products, including by federal health care programs such as Medicare and Medicaid and state health care programs. If any or all of these events occur, our business, prospects and stock price could be materially and adversely affected.

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, once we launch the Implantable System for Remodulin, we will rely on Medtronic as the sole manufacturer of the SynchroMed II infusion system and related components used in the Implantable System for Remodulin.

If any of our internal or 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 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. We manufacture all of our Orenitram and Unituxin ourselves, and we do not have an FDA-approved back-up manufacturing site for these products. 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 drug substance, although we are in the process of qualifying a third-party manufacturer for finished Unituxin drug product. We presently have no plans to engage a third-party contract manufacturer for Orenitram. Our long-term organ manufacturing programs will involve exceptionally complicated manufacturing processes, many of which have never been attempted on a clinical or commercial scale. It will take substantial time and resources to develop and implement such manufacturing processes, 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 current good manufacturing practices 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;

- Natural and man-made disasters (such as fires, contamination, power loss, hurricanes, earthquakes, flooding, terrorist attacks and acts of war) impacting our internal and third-party manufacturing sites could cause a supply disruption—for example, Medtronic and Lilly manufacture the Synchromed II pump and Adcirca, respectively, at their facilities in Puerto Rico, which is vulnerable to hurricanes;

- 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) manufacturing our clinical and commercial products; (2) conducting clinical trials, preclinical studies and other research and development activities; (3) obtaining regulatory approvals; (4) conducting pharmacovigilance-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 the price of Adcirca set by Lilly could adversely impact demand or reimbursement for 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). In particular, Medtronic is entirely responsible for regulatory approvals and all manufacturing and quality systems related to its infusion pump and related components. Medtronic entered into a consent decree relating to the SynchroMed II implantable infusion pump systems. Medtronic's failure to comply with the ongoing obligations under the consent decree could adversely impact Medtronic's ability to manufacture and supply the Implantable System for Remodulin.

Finally, we rely heavily on DEKA for the development of RemUnity, our pre-filled, semi-disposable 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 with these requirements 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, biomechanical lungs 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.

We are also required to comply with the corporate integrity obligations set forth in the CIA we entered into in December 2017 for a period of five years from the date the agreement was signed.

If we fail to comply with applicable regulatory requirements or the CIA, 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.

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 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 and prescribers, purchasers, formulary managers, patients, and others. The exemptions and safe harbors under this statute may be narrow, and practices that involve compensation may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices do not always qualify for safe harbor protection.

The Federal False Claims Act, as amended by the Patient Protection and Affordable Care Act of 2010 (PPACA), prohibits any person from presenting or causing to be presented a false or fraudulent claim or making or causing a false statement material to a false or fraudulent claim. Several pharmaceutical and health care companies have been investigated under this law for allegedly providing free product to customers with the expectation that the customers would bill federal health care 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 similar to the Federal Anti-Kickback Statute and the Federal False Claims Act. Sanctions under these federal and state laws may include treble civil monetary penalties, exclusion of a manufacturer's product from reimbursement under state government programs, debarment, criminal fines, and imprisonment.

Any investigation, inquiry or other legal proceeding under these laws and relating to our operations may adversely affect our business, results of operations or reputation.

The PPACA also imposed reporting requirements for pharmaceutical, biologic and device manufacturers regarding payments or other transfers of value made to physicians and teaching hospitals, including 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 healthcare 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. We may face uncertainties as a result of 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. In addition, Unituxin is associated with severe side effects, and its label contains a boxed warning relating to potential infusion reactions and neurotoxicity. 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, expired in October 2017, and three more will expire in 2028. Our patents relating to our individual treprostinil-based products expire at various times between 2018 and 2031. We settled patent litigation with Sandoz, Teva, Par and Dr. Reddy's, which will permit them to launch generic versions of Remodulin in the United States in June 2018 (Sandoz) and December 2018 (Teva, Par and Dr. Reddy's), although they may be permitted to enter the market earlier under certain circumstances. We also settled patent litigation with Actavis, which will permit Actavis to launch a generic version of Orenitram in the United States in June 2027, although Actavis may be permitted to enter the market earlier under certain circumstances. The U.S. patent for Adcirca for the treatment of pulmonary hypertension expired in November 2017, and FDA-conferred regulatory exclusivity will expire in May 2018. We have no issued patents or pending patent applications covering Unituxin. For further details, please see *Part I, Item 1.—Business—Patents and Other Proprietary Rights, Strategic Licenses and Market Exclusivity—Generic Competition.*

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, IPRs, post-grant reviews and interference proceedings, before the USPTO or other applicable patent filing office, or other means. We are currently involved in litigation challenging several of our patents related to Tyvaso as a result of an ANDA filing by Watson. If Watson receives approval to sell a generic version of Tyvaso and/or prevails in any patent litigation, Tyvaso 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 (PTAB) of the USPTO 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. In March 2017, the PTAB issued a Final Written Decision in connection with the IPR, finding that all claims of the subject patent are not patentable. The United States Court of Appeals for the Federal Circuit affirmed that decision, and in February 2018, we filed a petition for certiorari seeking review of the Federal Circuit decision by the United States Supreme Court. In June 2017, Watson filed petitions for *inter partes* review of two of our patents listed in the Orange Book for Tyvaso. On January 11, 2018, the PTAB issued decisions to institute *inter partes* review proceedings with respect to both patents. For details on the status of these matters, please see Note 16—*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, our 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, our Share Tracking Awards Plan (STAP) awards 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 2023. Our ability to make payments on or refinance our debt obligations, including any outstanding balance under the 2016 Credit Agreement, and 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 information about our products and the diseases that our therapies are designed to treat. Social media practices in our industry continue to evolve and regulations 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.

Tax legislation may materially adversely affect us.

Tax laws are dynamic and continually changing as new laws are passed and new interpretations of the law are issued or applied. In December 2017, the United States enacted significant changes with The Tax Cuts and Jobs Act (Tax Reform), and certain provisions of the new law may adversely affect us. Many aspects of the new legislation are unclear and may not be clarified for some time. As a result, our estimates of the impact of Tax Reform on our business are subject to change. In addition, governmental tax authorities are increasingly scrutinizing the tax positions of companies. If federal, state or foreign tax authorities change applicable tax laws or issue new guidance, our overall taxes could increase, and our business, financial condition or results of operations may be adversely impacted.

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, 2017 - December 31, 2017	$ 168.42	$ 114.60
January 1, 2016 - December 31, 2016	$ 155.54	$ 98.33
January 1, 2015 - December 31, 2015	$ 188.56	$ 119.57

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 ANDA filed by Watson seeking approval

for a generic version of Tyvaso and to our pending lawsuits defending our patent rights, the IPR petitions submitted by Watson related to two of our Tyvaso patents, and our pending petition for certiorari seeking review by the United States Supreme Court of the Federal Circuit decision that upheld the decision of the PTAB that all claims of one of our patents (which patent is listed in the Orange Book for Remodulin, Tyvaso and Orenitram) are unpatentable;

- 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 Industries, Inc. 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 and occupy 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 complex. We own several other buildings in Silver Spring used principally for office and laboratory space. We are constructing a 29,000 square foot facility in Silver Spring to serve as a monoclonal antibody manufacturing site, and a 121,000 square foot facility in Silver Spring to provide additional office 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 site 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—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 are also constructing a 75,000 square foot building in Jacksonville, Florida, to serve as a regional ex-vivo lung perfusion facility as part of our collaboration with the Mayo Clinic.

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 16—*Litigation*, to our consolidated financial statements, which is incorporated herein by reference.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

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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:

	2017		2016	
	High	Low	High	Low
January 1 - March 31	$ 168.42	$ 135.38	$ 155.54	$ 108.47
April 1 - June 30	$ 133.12	$ 118.34	$ 121.03	$ 98.33
July 1 - September 30	$ 136.81	$ 114.60	$ 129.64	$ 107.73
October 1 - December 31	$ 151.28	$ 118.58	$ 145.38	$ 111.68

Number of Holders

As of February 14, 2018, 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

We did not repurchase any of our outstanding equity securities during the three months ended December 31, 2017, as our most recent share repurchase program was completed in September 2017.

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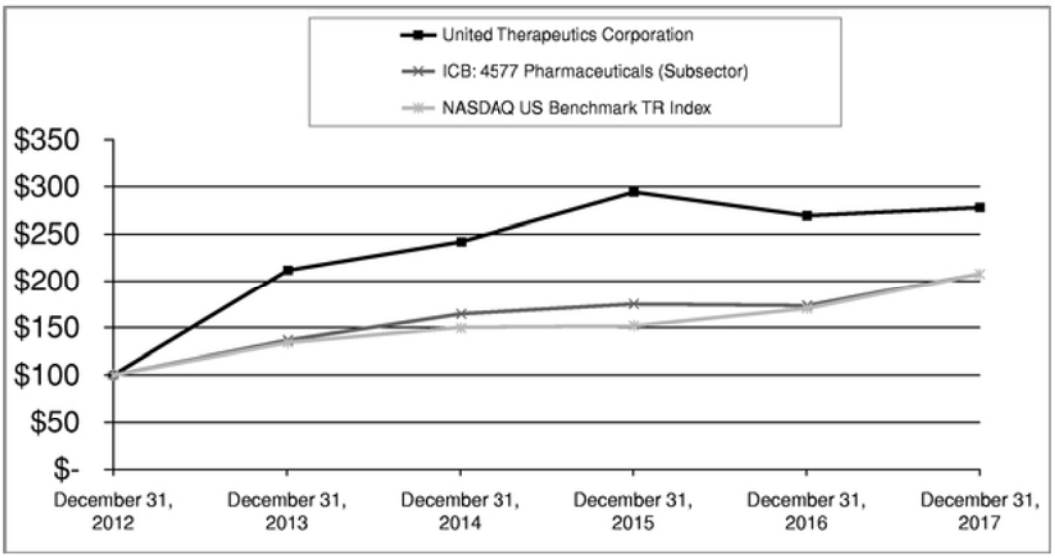
Comparison of Five-Year Total Cumulative Shareholder Return

The following chart shows the performance from December 31, 2012 through December 31, 2017 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.



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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,				
	2017	2016	2015	2014	2013
Consolidated Statements of Operations Data:					
Revenues	$ 1,725.3	$ 1,598.8	$ 1,465.8	$ 1,288.5	$ 1,117.0
Operating income	$ 814.9	$ 1,061.7	$ 699.0	$ 538.8	$ 292.5
Net income	$ 417.9	$ 713.7	$ 651.6	$ 340.1	$ 174.6
Net income per common share:					
Basic[(1)]	$ 9.50	$ 16.29	$ 14.17	$ 7.06	$ 3.49
Diluted[(1)]	$ 9.31	$ 15.25	$ 12.72	$ 6.28	$ 3.28

	As of December 31,				
	2017	2016	2015	2014	2013
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable investments	$ 1,430.1	$ 1,053.1	$ 991.8	$ 818.2	$ 1,142.0
Total assets	$ 2,879.4	$ 2,325.6	$ 2,184.4	$ 1,884.4	$ 2,087.6
Total non-current liabilities	$ 313.7	$ 130.9	$ 144.0	$ 114.5	$ 95.6
Total stockholders' equity	$ 2,101.8	$ 1,851.3	$ 1,588.6	$ 1,242.4	$ 1,259.3

(1) Refer to Note 10—*Stockholders' Equity—Earnings Per Common Share* to our consolidated financial statements 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 our consolidated financial statements.

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*, a monoclonal antibody approved by the FDA for the treatment of high-risk neuroblastoma.

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 Implantable System for Remodulin and the RemUnity system for delivery of intravenous and subcutaneous Remodulin, respectively. 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 Group 2 pulmonary hypertension (which we refer to as OreniLeft). We are also studying dinutuximab in patients with small cell lung cancer. 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, RemoPro 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, biomechanical lungs 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 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 and Tyvaso to distributors internationally. We sell Adcirca through Lilly's pharmaceutical wholesale network. To the extent we have increased the price of any of these products, increases have typically been in the single-digit percentages per year, except for Adcirca, the price of which is set solely by Lilly. In 2018, we anticipate revenues will decrease as compared to 2017, given the impact of anticipated generic competition for Adcirca beginning mid-2018, as well as reimbursement challenges for our oral therapies leading to increased utilization of our patient assistance programs. We are investing in the development of new products and label expansions for existing products, which we expect to result in a return to revenue growth beginning in 2019.

We require our specialty pharmaceutical distributors to maintain reasonable levels of inventory reserves because the interruption of Remodulin, Tyvaso or Orenitram therapy 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 do not precisely reflect changes in patient demand.

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 and milestone 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 also include share-based compensation and salary-related expenses for direct manufacturing and indirect support personnel, quality review and release for commercial distribution, direct materials and supplies, depreciation, facilities-related expenses and other overhead costs. Our cost of product sales for Adcirca increased significantly as a percentage of Adcirca revenues beginning December 1, 2017, from five percent to an effective rate of approximately 42.5 percent, as a result of the increased royalty and milestone payments contained in our amended license agreement with Lilly.

Research and Development

Our research and development expenses primarily include costs associated with the research and development of products and post-marketing research commitments. These costs also include share-based compensation and salary-related expenses for research and development functions, professional fees for preclinical and clinical studies, costs associated with clinical manufacturing, facilities-related expenses, regulatory costs and costs associated with 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 have incurred, and expect to continue to incur, increased clinical trial-related expenses, driven by the recent expansion of our pipeline programs, which we expect will result in the enrollment of several large clinical 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 also include share-based compensation, salary-related expenses, product marketing and sales operations costs, and other costs incurred to support our sales efforts. General and administrative expenses also include our core corporate support functions such as human resources, finance and legal, external costs such as insurance premiums, legal fees, grants to non-affiliated, non-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 our non-employee directors. In October 2017, we also began issuing restricted stock units to employees under the 2015 Plan. Over time, we expect to increase the percentage of our equity awards made to employees in the form of restricted stock units, instead of stock options. The grant date fair values of stock options and restricted stock units are recognized as share-based compensation expense ratably over their vesting periods.

The fair values of STAP awards and stock option grants are measured using inputs and assumptions under the Black-Scholes-Merton model. The fair value of restricted stock units is measured using our stock price on the date of grant.

Although we have ceased granting STAP awards, we still have a significant number of STAP awards outstanding. 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 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 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 grow the revenues of our existing commercial products, including through approval of new and/or improved indications, formulations and delivery devices. These and other research and development efforts are designed to provide revenue growth in the near and medium term, while efforts are under way to develop technologies in organ manufacturing 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, including competition from generic companies; (6) our ability to effectively manage our business in an increasingly complex legal and regulatory environment; (7) our ability to defend against challenges to our patents; and (8) the risks identified in *Part I, Item 1A—Risk Factors*, included in this Report.

We believe the increased use of dual-upfront oral therapy (tadalafil and ambrisentan) following positive results of the *AMBITION* study, combined with the launch of Uptravi, an oral IP-receptor agonist, has delayed many patients' initiation of inhaled or infused prostacyclin therapies, which we believe has depressed our sales of Tyvaso and Remodulin. In addition, Uptravi competes directly with our oral prostacyclin therapy, Orenitram, which we believe has depressed our sales of Orenitram. Given the progressive nature of PAH, we believe many patients will begin taking Orenitram, Tyvaso or Remodulin after their disease progresses while on these or other oral therapies, leading to increased revenue from these three products.

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

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Results of Operations

Revenues

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

	Year Ended December 31,			Percentage Change	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Net product sales:					
Remodulin	$ 670.9	$ 602.3	$ 572.8	11.4%	5.2%
Tyvaso	372.9	404.6	470.1	(7.8)%	(13.9)%
Adcirca	419.7	372.2	278.8	12.8%	33.5%
Orenitram	185.8	157.2	118.4	18.2%	32.8%
Unituxin	76.0	62.5	20.5	21.6%	204.9%
Other	—	—	5.2	—%	(100.0)%
Total revenues	$ 1,725.3	$ 1,598.8	$ 1,465.8	7.9%	9.1%

Revenues for the year ended December 31, 2017 increased by $126.5 million as compared to the same period in 2016. Remodulin net product sales increased by $68.6 million, with $47.4 million related to the one-time purchase of Remodulin inventory by an international distributor, due to an expansion of the distributor's commercial responsibilities during the third quarter. The remaining increase in Remodulin net product sales was due to an increase in the number of patients being treated with Remodulin. Adcirca net product sales increased by $47.5 million primarily due to price increases, which were determined by Lilly. Additional revenue growth resulted from a $28.6 million increase in Orenitram net product sales due to an increase in the number of patients being treated with Orenitram and a $13.5 million increase in Unituxin net product sales due to an increase in the number of vials sold and price increases. These revenue increases were partially offset by a $31.7 million decrease in Tyvaso net product sales, with $11.1 million of the decrease due to an additional one-time liability for estimated Medicaid rebates that we recorded during 2017 related to Tyvaso sales prior to January 1, 2017. The remaining decrease in Tyvaso net product sales resulted from a net decrease in the number of patients being treated with Tyvaso, which we believe was driven by the availability of oral prostacyclin-class therapies and the increased propensity to treat patients with multiple oral therapies earlier in their disease progression, which can delay the need to prescribe inhaled therapies such as Tyvaso.

Revenues for the year ended December 31, 2016 increased by $133.0 million as compared to the same period in 2015. Adcirca net product sales increased by $93.4 million due to an increase in the number of Adcirca bottles sold and Lilly-determined price increases. Unituxin net product sales increased by $42.0 million due to the launch of Unituxin in the third quarter of 2015. Orenitram net product sales increased by $38.8 million due to an increase in the number of patients being treated with Orenitram. Remodulin net product sales increased by $29.5 million due to an increase in the number of patients being treated with Remodulin. These increases were partially offset by a $65.5 million decrease in Tyvaso net product sales due to a decrease in the number of patients being treated with Tyvaso and 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.

For the years ended December 31, 2017, 2016 and 2015 approximately 60 percent, 64 percent and 72 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, 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) rebates and chargebacks; (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, 2017				
	Rebates and Chargebacks	Prompt Pay Discounts	Allowance for Sales Returns	Distributor Fees	Total
Balance, January 1, 2017	$ 46.0	$ 4.3	$ 7.7	$ 2.8	$ 60.8
Provisions attributed to sales in:					
Current period	228.2	37.9	0.9	14.5	281.5
Prior periods	13.3	—	—	(0.2)	13.1
Payments or credits attributed to sales in:					
Current period	(163.1)	(33.3)	—	(10.9)	(207.3)
Prior periods	(50.4)	(4.2)	(1.4)	(2.8)	(58.8)
Balance, December 31, 2017	$ 74.0	$ 4.7	$ 7.2	$ 3.4	$ 89.3

	Year Ended December 31, 2016				
	Rebates and Chargebacks	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 and Chargebacks	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

Cost of Product Sales

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

	Year Ended December 31,			Percentage Change	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Category:					
Cost of product sales	$ 103.1	$ 72.1	$ 60.2	43.0%	19.8%
Share-based compensation expense[(1)]	2.6	0.6	8.8	333.3%	(93.2)%
Total cost of product sales	$ 105.7	$ 72.7	$ 69.0	45.4%	5.4%

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

Cost of Product Sales. The increase in cost of product sales of $31.0 million for the year ended December 31, 2017 as compared to the same period in 2016, was primarily attributable to a $21.9 million increase in royalty expense for Adcirca. As a result of an amendment to our license agreement with Lilly, our royalty rate on net product sales of Adcirca increased from five percent to an effective rate of approximately 42.5 percent effective December 1, 2017. The remaining increase in cost of product sales was primarily attributable to an increase in 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.

Research and Development Expense

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

	Year Ended December 31,			Percentage Change	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Category:					
Research and development projects	$ 256.4	$ 157.6	$ 157.4	62.7%	0.1%
Share-based compensation expense (benefit)[(1)]	8.2	(10.0)	87.7	182.0%	(111.4)%
Total research and development expense	$ 264.6	$ 147.6	$ 245.1	79.3%	(39.8)%

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

Research and development projects. The increase in research and development projects of $98.8 million for the twelve months ended December 31, 2017, as compared to the same period in 2016, was driven by the expansion of our pipeline programs to treat cardiopulmonary disease and cancer and to develop technologies in organ manufacturing. Research and development expense for the treatment of cardiopulmonary diseases increased by $38.4 million for the twelve months ended December 31, 2017, as compared to the same period in 2016, due to increased spending on several clinical and non-clinical studies, including *FREEDOM-EV*, *INCREASE* and *SOUTHPAW*, on the development of new drug products, including RemoPro, and drug delivery device developments, including the Implantable System for Remodulin and the RemUnity system. The increases in research and development expenses were partially offset by a decrease in expenses for esuberaprost formulation and the related *BEAT* study, as the clinical trial is fully enrolled. Research and development expense for cancer-related projects increased by $21.3 million for the twelve months ended December 31, 2017, as compared to the same period in 2016, due to an increase in spending on the *DISTINCT* study. Research and development expenses for organ manufacturing projects increased by $36.3 million for

the twelve months ended December 31, 2017, as compared to the same period in 2016, due to increased preclinical work on technologies designed to increase the supply and distribution of transplantable organs and tissues.

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	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Category:					
General and administrative	$ 203.1	$ 210.7	$ 174.6	(3.6)%	20.7%
Sales and marketing	64.3	84.6	94.3	(24.0)%	(10.3)%
Share-based compensation expense[1]	62.7	21.5	183.8	191.6%	(88.3)%
Total selling, general and administrative expense	$ 330.1	$ 316.8	$ 452.7	4.2%	(30.0)%

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

General and administrative. The decrease in general and administrative expenses of $7.6 million for the year ended December 31, 2017, as compared to the same period in 2016, primarily resulted from: (1) a $32.0 million decrease in grants to non-affiliated, non-profit organizations that provide financial assistance to patients with PAH; and (2) a $9.3 million decrease of expenses in connection with the disposition and write down of various properties in 2016. The decrease was partially offset by: (1) a $9.4 million increase in legal fees incurred in connection with intellectual property litigation and the DOJ investigation of our support of 501(c)(3) organizations that provide financial assistance to patients; (2) a $9.2 million increase in compensation due to an increase in staffing; and (3) a $6.5 million increase in consulting expenses.

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 a $20.0 million increase in grants to non-affiliated, non-profit organizations that provide financial assistance to patients with PAH; and $9.3 million increase of expenses in connection for disposition and write down of various properties.

Sales and marketing. The decrease in sales and marketing expenses of $20.3 million for the year ended December 31, 2017, as compared to the same period in 2016, primarily resulted from a $11.3 million decrease in compensation and related costs associated with the 2016 consolidation of our sales and marketing staff.

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 as we consolidated our sales and marketing staff in the last half of 2016.

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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	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Category:					
Stock options	$ 43.0	$ 24.8	$ 4.9	73.4%	406.1%
Restricted stock units	2.2	1.1	—	100.0%	100.0%
Share tracking awards plan	27.1	(15.2)	274.2	278.3%	(105.5)%
Employee stock purchase plan	1.2	1.4	1.2	(14.3)%	16.7%
Total share-based compensation expense	$ 73.5	$ 12.1	$ 280.3	507.4%	(95.7)%

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

	Year Ended December 31,			Percentage Change	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Cost of product sales	$ 2.6	$ 0.6	$ 8.8	333.3%	(93.2)%
Research and development	8.2	(10.0)	87.7	182.0%	(111.4)%
Selling, general and administrative	62.7	21.5	183.8	191.6%	(88.3)%
Total share-based compensation expense	$ 73.5	$ 12.1	$ 280.3	507.4%	(95.7)%

Share-based compensation. The increase in share-based compensation of $61.4 million for the year ended December 31, 2017, as compared to the same period in 2016, was primarily due to: (1) a $42.3 million increase in STAP expense related to an increase in our stock price during 2017 and the continued vesting of outstanding awards; and (2) an $18.2 million increase in stock option expense due to additional awards granted and outstanding in 2017. We expect the share-based compensation for restricted stock units to increase in the future as additional restricted stock units are granted. Refer to Note 9—*Share-Based Compensation* for more information.

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, was primarily due to a $289.4 million decrease in STAP expense related to a decrease in our stock price during 2016, partially offset by a $19.9 million increase in stock option expense due to additional awards granted and outstanding in 2016.

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.

Settlement of Loss Contingency

In December 2017, we entered into a civil Settlement Agreement with the U.S. Government to resolve a DOJ investigation related to our support of 501(c)(3) organizations that provide financial assistance to patients. During the second quarter of 2017, we recorded a $210.0 million accrual relating to this matter, and ultimately paid this amount, plus interest, to the U.S. Government upon settlement. This matter is described in more detail in Note 16—*Litigation —Department of Justice Subpoena*, to our consolidated financial statements.

Impairment of Cost Method Investments

During the year ended December 31, 2017, we recorded $49.6 million of impairment charges related to our cost method investments in privately-held companies. There were no such impairment charges in the years ended December 31, 2015 and 2016.

Income Tax Expense

The provision for income taxes was $351.6 million for the year ended December 31, 2017, compared to $346.5 million for the same period in 2016. The change in the provision for income taxes was primarily due to a charge for the revaluation of deferred taxes due to the lower future corporate tax rate enacted by Tax Reform, and increases in nondeductible items, partially offset by a decrease in net income before taxes. The provision for income taxes was $346.5 million for the year ended December 31, 2016 compared to $392.8 million for the year ended 2015. The decrease in the provision for income taxes between those years resulted primarily from a decrease in non-deductible compensation related to the STAP awards resulting from a decrease in our stock price from December 31, 2015 to December 31, 2016. For the years ended December 31, 2017, 2016 and 2015, the effective tax rates were approximately 46 percent, 33 percent and 38 percent, respectively. For additional details, refer to Note 11—*Income Taxes* to our consolidated financial statements.

Tax Reform has multiple provisions that impact our tax expense. The significant impacts of Tax Reform include a reduction in the U.S. federal corporate tax rate from 35 percent to 21 percent, a requirement for companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred, additional limitations on deductions for executive compensation, the opportunity to fully expense (take 100 percent bonus depreciation) qualified property, reduction of the Orphan Drug Credit, repeal of the Section 199 deduction for domestic manufacturing activities, and creation of new taxes on certain foreign-sourced earnings.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed in reasonable detail to complete the accounting for certain income tax effects of Tax Reform. As a result of changes under Tax Reform, we have recognized a provisional amount of $71.0 million of additional tax expense in our consolidated financial statements for the year ended December 31, 2017. The additional tax expense is primarily due to the revaluing of our ending net deferred tax assets at December 31, 2017 because of the reduction in the U.S. corporate income tax rate under Tax Reform. While we have substantially completed our provisional analysis of the income tax effects of Tax Reform, and recorded a reasonable estimate of such effects, the ultimate impact may differ from these provisional amounts, possibly materially, due to, among other things, further refinement of our calculations, additional analysis, changes in assumptions, and actions we may take as a result of Tax Reform.

Going forward, we expect to see a decrease in our effective tax rate as a result of Tax Reform, principally driven by the reduced federal corporate tax rate, partially offset by added limitations on deductions for executive compensation, reduction of the Orphan Drug Credit and repeal of the Section 199 deduction.

Share Repurchase

In April 2017, our Board of Directors approved a share repurchase program authorizing up to $250.0 million in aggregate repurchases of our common stock. Pursuant to this authorization, in May 2017, we paid $250.0 million upon entering into an accelerated share repurchase agreement (ASR) with Citibank, N.A. (Citibank). Pursuant to the terms of the ASR, in June 2017, Citibank delivered to us approximately 1.7 million shares of our common stock, representing the minimum number of shares we

were entitled to receive under the ASR. Upon termination of the ASR in September 2017, Citibank delivered to us approximately 0.3 million additional shares of our common stock.

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 long-term demand for our commercial products other than Adcirca 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, with a current maturity date of January 2023, of which $250.0 million was drawn and outstanding as of December 31, 2017. See *Unsecured Revolving Credit Facility* below for further details.

Cash and Cash Equivalents and Marketable Investments

	Year Ended December 31,		Percentage Change
	2017	2016	2017 v. 2016
Cash and cash equivalents	$ 705.1	$ 1,023.0	(31.1)%
Marketable investments—current	222.3	27.8	699.6%
Marketable investments—non-current	502.7	2.3	NM(1)
Total cash and cash equivalents and marketable investments	$ 1,430.1	$ 1,053.1	35.8%

(1) Calculation is not meaningful.

The net increase in our cash and cash equivalents and marketable investments was primarily due to: (1) $474.2 million in cash generated from operations; and (2) $39.9 million of proceeds from the exercise of stock options, partially offset by: (1) $86.3 million in cash paid to purchase property, plant and equipment; and (2) $60.4 million in cash used to purchase investments in privately-held companies,

Cash Flows

	Year Ended December 31,			Percentage Change	
	2017	2016	2015	2017 v. 2016	2016 v. 2015
Net cash provided by operating activities	$ 474.2	$ 643.6	$ 382.8	(26.3)%	68.1%
Net cash (used in) provided by investing activities	$ (835.6)	$ 48.3	$ 503.6	NM(1)	(90.4)%
Net cash provided by (used in) financing activities	$ 43.3	$ (497.7)	$ (447.0)	108.7%	(11.3)%

(1) Calculation is not meaningful.

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 decrease of $169.4 million in net cash provided by operating activities for the year ended December 31, 2017 compared to the year ended December 31, 2016 was primarily due to:

(1) $210.0 million paid to settle a loss contingency; and (2) a $78.4 million net cash outflow due to changes in other operating assets and liabilities. The decrease was partially offset by: (1) a $126.5 million increase in revenues during the year, which resulted in higher cash collections; and (2) a $15.5 million decrease in cash paid for income taxes due to timing of payments.

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, partially offset by a $69.1 million increase in cash paid for income taxes.

Investing Activities

The increase of $883.9 million in net cash used in investing activities for the year ended December 31, 2017 compared to the year ended December 31, 2016 was primarily due to: (1) a $826.9 million increase in cash used for net purchases of available-for-sale, held-to-maturity and other investments; (2) a $48.3 million increase in cash paid to purchase property, plant and equipment; and (3) a $24.4 million increase in cash paid to purchase investments held at cost. The increase in cash used was partially offset by $8.3 million in proceeds from the sale of property, plant and equipment.

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: (1) a $350.0 million decrease in cash due to the sale of our PPRV in September 2015, which did not recur in 2016; and (2) a $128.0 million decrease in cash provided by the net maturities of held-to-maturity and other investments. The decrease in cash used was partially offset by: (1) a $16.1 million decrease in cash paid to purchase investments held at cost; and (2) a $11.8 million decrease in cash paid to purchase property, plant and equipment.

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 $250.0 million over the next three years.

Financing Activities

The increase of $541.0 million in net cash provided by financing activities for the year ended December 31, 2017 compared to the year ended December 31, 2016 was primarily due to: (1) $250.0 million in proceeds from borrowing under our line of credit used to fund the ASR described in Note 7 *—Debt—Unsecured Revolving Credit Facility*, to our consolidated financial statements; (2) a $250.0 million decrease in repurchases of our common stock; and (3) a $32.2 million increase in proceeds from stock option exercises.

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: (1) a $105.5 million increase in repurchases of our common stock; and (2) a $63.1 million decrease in proceeds from stock option exercises including excess tax benefits from share based compensation. The increase in cash used was partially offset by a $117.6 million decrease 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.

In June 2014, our Board of Directors authorized the repurchase of up to $500.0 million of our common stock. In the aggregate, we repurchased approximately 3.3 million shares of common stock under this program for $500.0 million during 2014 and 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. In accordance with the terms of the 2016 Credit Agreement, in January 2017 and in January 2018, we extended the maturity date of the 2016 Credit Agreement by one year to January 2022 and January 2023, respectively. On June 1, 2017, we borrowed $250.0 million under this facility and used the funds to initiate the accelerated share repurchase program noted above. As we no longer intend to repay the full outstanding balance within one year, the balance has been reclassified from short-term to long-term within the consolidated balance sheets. Refer to Note 7—*Debt—Unsecured Revolving Credit Facility,* to our consolidated financial statements.

Secured Line of Credit

In 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, 2017, 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	$ 6.7	$ 3.4	$ 1.6	$ 1.3	$ 0.4
Long-term debt obligations[1]	295.8	9.2	18.3	268.3	—
Obligations under the STAP[2]	231.7	231.3	0.4	—	—
Obligations under the SERP[3]	93.2	16.4	5.8	—	71.0
Purchase obligations[4]	550.4	463.9	76.0	6.5	4.0
Total[5]	$ 1,177.8	$ 724.2	$ 102.1	$ 276.1	$ 75.4

(1) Long-term debt obligations include future interest payments on our LIBOR-based variable rate obligations under the 2016 Credit Agreement. We extended the maturity date of the 2016 Credit Agreement by one year in January 2018 to extend its maturity to January 2023. Refer to Note 7—*Debt* to our consolidated financial statements for further details.

(2) 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 9—*Share-based Compensation* to our consolidated financial statements for further details.

(3) Consists of actuarially derived, estimated future payouts of benefits. Refer to Note 12—*Employee Benefit Plans—Supplemental Executive Retirement Plan* to our consolidated financial statements for further details.

(4) Purchase obligations primarily include: (i) commitments related to research and development (including clinical trials) for new and existing products; (ii) open purchase orders for capital

expenditures; and (iii) 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.

(5) In addition to amounts in the table above, we are contractually obligated to pay additional amounts upon the achievement of various development, regulatory and commercial milestones for agreements we have entered into with third parties. These payments are contingent upon the occurrence of various future events, some of which have a high degree of uncertainty of occurring. These contingent payments have not been included in the table above, and, except with respect to the fair value of the contingent consideration obligations, are not recorded on our consolidated balance sheets.

Toray License Obligations

In 2000, we entered into a license 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 2007 amendment to this agreement, we issued Toray 200,000 shares of our common stock. 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 this agreement 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. In March 2017, we amended our license agreement with Toray to further reduce the royalty rate to single digits in exchange for a commitment to make milestone payments to Toray in the event that we do not achieve certain clinical and regulatory events by certain dates.

Obligations Under License and Assignment Agreements

Historically, we paid Lilly a five percent royalty on net product sales of Adcirca. In May 2017, we amended our license agreement with Lilly relating to Adcirca. As a result of this amendment, beginning December 1, 2017, our royalty rate on net product sales of Adcirca increased from five percent to ten percent and we are required to make milestone payments to Lilly equal to $325,000 for each $1,000,000 in net product sales. We pay a single-digit percentage royalty based on net product sales of Orenitram under our license agreement with Supernus. We also pay The Scripps Research Institute a one percent royalty on sales of Unituxin. We have entered into other license 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

We generate revenues from the sale of our five commercial products: Remodulin, Tyvaso, Orenitram, Unituxin and Adcirca. Revenue is recognized when title and the risks and rewards of ownership have transferred to our distributors, which is generally when our product is delivered to the distributor's location. These revenues are subject to various product sales allowances, referred to as gross-to-net deductions, which are deducted from revenues to determine net product sales. For a description of our related accounting policies, refer to Note 2—*Summary of Significant Accounting Policies—Revenue Recognition* in the consolidated financial statements.

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

Rebates and Chargebacks

Our most significant rebates relate to our participation in state Medicaid programs and contractual rebates offered to managed care organizations covering Medicare Part D and commercial plans. Chargebacks relate to our participation in programs with the U.S. Department of Veterans Affairs and 340B covered entities. Although we accrue for our allowance for rebates and chargebacks in the same period that we recognize revenue, the actual rebate or chargeback on the sale of our product to a distributor is not invoiced to us until a future period, generally within six months from the date of sale. Due to this time lag, we must estimate the amount of rebates and chargebacks to accrue. As of December 31, 2017, we had a $74.0 million liability related to rebates and chargebacks.

Estimates associated with our participation in state Medicaid programs are particularly susceptible to adjustment given the extensive time lag that may occur between our recording of an accrual and its ultimate invoicing by individual state Medicaid programs, which can occur up to several years after the sale of our product. Because of the time lag for Medicaid and other rebates, in any particular quarter, our adjustments may incorporate revisions of accruals for prior quarters. Historically, adjustments to our estimates to reflect actual results or updated expectations have not been material to our overall financial results. Provisions attributed to sales in prior periods have been less than one percent of our net product sales for each of the years ended December 31, 2017, 2016 and 2015.

Allowance for Sales Returns

The sales terms for Adcirca and Unituxin include return rights; however, we have not recorded an allowance for returns of Unituxin because our historical returns have been insignificant. For our sales of Adcirca, we record an allowance for returns in the same period that we recognize revenue. Return rights extend throughout the distribution channel and allow for returns of expired product for up to 12 months past the product's expiration date. As there are generally 24 to 36 months from the initial sale of Adcirca to its expiration date, we must estimate the amount of product that will be returned. Historically, actual returns have not differed materially from our estimates, and have been less than one percent of our net product sales for each of the years ended December 31, 2017, 2016 and 2015.

Following the loss of exclusivity for Adcirca in the second quarter of 2018, we may experience an elevated level of product returns as product inventory remaining in the distribution channel expires.

For a roll-forward of the liability accounts associated with our gross-to-net deductions, see *Part II—Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations—Revenues.*

Share-Based Compensation

Our share-based awards are classified as either liabilities (STAP awards) or as equity (stock options, restricted stock units and rights to purchase stock under our employee stock purchase plan). We recognize related share-based compensation expense based on the fair value of outstanding STAP awards on the grant date and at the end of each reporting period, and based on the grant date fair value of stock options and restricted stock units. With the exception of restricted stock units, we estimate the fair value of all share-based awards using the Black-Scholes-Merton valuation model. We measure the fair value of restricted stock units using the stock price on the grant date. Valuation models, like the Black-Scholes-Merton model, require the use of subjective assumptions that could materially impact the estimation of fair value and related compensation expense to be recognized. These assumptions include the expected volatility of our stock price and the expected term of awards. Developing these assumptions requires the use of judgment. For additional information on the assumptions used in the Black-Scholes-Merton valuation model, see Note 9—*Share-Based Compensation,* to our consolidated financial statements.

Effective January 1, 2017, we adopted the provisions of ASU 2016-09, *Compensation—Stock Compensation.* As part of the adoption, we established an accounting policy election to account for forfeitures of share-based awards when they occur. Upon adoption, we recognized a cumulative-effect adjustment for the removal of the forfeiture estimate with respect to awards that were continuing to vest as of January 1, 2017. The adjustment resulted in a decrease to retained earnings of $5.8 million, which is net of a $3.2 million tax benefit. Refer to Note 3—*Recently Issued Accounting Standards—Accounting Standards Adopted During 2017*, to our consolidated financial statements.

Performance-Based Stock Options

In March 2017, we began issuing stock options with performance conditions under the 2015 Plan. The awards have vesting conditions tied to the achievement of specified performance conditions. The performance conditions have target performance levels that span from one to three years. Throughout the performance period, we re-assess the estimated performance and update the number of performance-based awards that we believe will ultimately vest. Upon the conclusion of the performance period, the performance level achieved will be measured and the ultimate number of shares that may vest will be determined. The estimation of future performance requires the use of judgment. Share-based compensation expense for these awards is recorded ratably over their vesting period, depending on the specific terms of the award and achievement of the specified performance conditions. During 2017, we granted 0.9 million stock options with performance vesting conditions with a total grant date fair value of $53.9 million assuming achievement of target performance levels.

Investments Held at Cost

We have investments in several privately-held companies that have a strategic connection to our business, most of them in the form of preferred stock investments. We account for most of these investments in privately-held companies under the cost method of accounting because we own less than 20 percent of the companies' outstanding voting shares and do not have significant influence over their operations. Realization of our equity position in these companies is uncertain. We review these investments individually for impairment by evaluating if events or circumstances have occurred that may

have a significant adverse effect on their fair value. If such events or circumstances have occurred, we will estimate the fair value of the investment and determine if any decline in the fair value of the investment below its carrying value is other-than-temporary. In such cases, the estimated fair value of the investment is determined using unobservable inputs including assumptions by the company's management. Because several of these companies are in the early startup or development stages, these entities are subject to potential changes in cash flows, valuation, and inability to attract new investors which may be necessary for the liquidity needed to support their operations. If we determine that a decline in value in an investment is other-than-temporary, we recognize an impairment loss in the period in which the other-than-temporary decline occurs. If facts and circumstances change, we could be required to account for one or more of these investments under the equity method of accounting or consolidate the company's operations for financial accounting purposes.

Income Taxes

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

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

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, 2017, we have invested $766.7 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 typically hold these investments to maturity so that they can be redeemed at their stated or face value. Many of our investments may be called by their respective issuers prior to maturity. The following table summarizes the expected maturities and weighted average interest rates as of December 31, 2017 (dollars in millions):

	Expected Maturity		
	2018	2019	2020
Held-to-maturity investments	$ 27.7	$ 1.6	$ —
Available-for-sale investments	236.3	384.3	116.8
Weighted average interest rate	1.4%	1.9%	2.0%

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.

As of December 31, 2017, we had $250.0 million outstanding on our unsecured revolving credit facility which includes a variable interest rate component. As a result, we are subject to interest rate risk with respect to such floating-rate debt. A 100 basis point increase in the variable interest rate component of our borrowings would increase our annual interest expense by approximately $2.5 million or 28 percent.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

UNITED THERAPEUTICS CORPORATION
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of United Therapeutics Corporation (the Company) as of December 31, 2017 and 2016, 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, 2017, and the related notes and financial statement schedule listed in the Index at Item 15(a)(2) (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2017, 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 21, 2018, expressed an unqualified opinion thereon.

Basis for Opinion

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

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

/s/ Ernst & Young LLP
We have served as the Company's auditor since 2003.
Tysons, Virginia
February 21, 2018

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control over Financial Reporting

We have audited United Therapeutics Corporation's internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, United Therapeutics Corporation (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2017 and 2016, 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, 2017, and the related notes and financial statement schedule listed in the Index at Item 15(a)(2) and our report dated February 21, 2018, expressed an unqualified opinion thereon.

Basis for Opinion

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP
Tysons, Virginia
February 21, 2018

UNITED THERAPEUTICS CORPORATION

Consolidated Balance Sheets

(In millions, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 705.1	$ 1,023.0
Marketable investments	222.3	27.8
Accounts receivable, no allowance for 2017 and 2016	297.1	214.5
Inventories, net	107.9	100.0
Other current assets	115.5	59.5
Total current assets	1,447.9	1,424.8
Marketable investments	502.7	2.3
Goodwill and other intangible assets, net	45.6	33.8
Property, plant and equipment, net	545.7	489.3
Deferred tax assets, net	113.4	178.3
Other non-current assets	224.1	197.1
Total assets	$ 2,879.4	$ 2,325.6
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 171.1	$ 104.2
Share tracking awards plan	240.1	194.8
Other current liabilities	33.5	33.5
Total current liabilities	444.7	332.5
Line of credit	250.0	—
Other non-current liabilities	63.7	130.9
Total liabilities	758.4	463.4
Commitments and contingencies—Note 13		
Temporary equity	19.2	10.9
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, 69,858,840 and 69,340,985 shares issued, and 43,239,624 and 42,965,856 shares outstanding at December 31, 2017 and 2016, respectively	0.7	0.7
Additional paid-in capital	1,854.3	1,813.5
Accumulated other comprehensive loss	(19.6)	(16.8)
Treasury stock, 26,619,216 and 26,375,129 shares at December 31, 2017 and 2016, respectively	(2,579.2)	(2,379.6)
Retained earnings	2,845.6	2,433.5
Total stockholders' equity	2,101.8	1,851.3
Total liabilities and stockholders' equity	$ 2,879.4	$ 2,325.6

See accompanying notes to consolidated financial statements.

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UNITED THERAPEUTICS CORPORATION

Consolidated Statements of Operations

(In millions, except per share data)

	Year Ended December 31,		
	2017	2016	2015
Revenues:			
Net product sales	$ 1,725.3	$ 1,598.8	$ 1,460.6
Other	—	—	5.2
Total revenues	1,725.3	1,598.8	1,465.8
Operating expenses:			
Cost of product sales	105.7	72.7	69.0
Research and development	264.6	147.6	245.1
Selling, general and administrative	330.1	316.8	452.7
Settlement of loss contingency	210.0	—	—
Total operating expenses	910.4	537.1	766.8
Operating income	814.9	1,061.7	699.0
Other (expense) income:			
Interest expense	(9.0)	(3.9)	(4.7)
Gain on sale of intangible asset	—	—	350.0
Other, net	13.2	2.4	0.1
Impairment of cost method investment	(49.6)	—	—
Total other (expense) income, net	(45.4)	(1.5)	345.4
Income before income taxes	769.5	1,060.2	1,044.4
Income tax expense	(351.6)	(346.5)	(392.8)
Net income	$ 417.9	$ 713.7	$ 651.6
Net income per common share:			
Basic	$ 9.50	$ 16.29	$ 14.17
Diluted	$ 9.31	$ 15.25	$ 12.72
Weighted average number of common shares outstanding:			
Basic	44.0	43.8	46.0
Diluted	44.9	46.8	51.2

See accompanying notes to consolidated financial statements.

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UNITED THERAPEUTICS CORPORATION

Consolidated Statements of Comprehensive Income

(In millions)

	Year Ended December 31,		
	2017	2016	2015
Net income	$ 417.9	$ 713.7	$ 651.6
Other comprehensive income (loss):			
Foreign currency translation gains (losses)	0.2	(3.0)	(5.3)
Defined benefit pension plan:			
Actuarial (loss) gain arising during period, net of tax	(1.7)	6.0	0.7
Amortization of actuarial gain and prior service cost included in net periodic pension cost, net of tax	0.6	0.6	0.9
Total defined benefit pension plan, net of tax	(1.1)	6.6	1.6
Unrealized loss on available-for-sale securities, net of tax	(1.9)	—	—
Other comprehensive (loss) income, net of tax	(2.8)	3.6	(3.7)
Comprehensive income	$ 415.1	$ 717.3	$ 647.9

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, 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
Net income	—	—	—	—	—	417.9	417.9
Foreign currency translation adjustments	—	—	—	0.2	—	—	0.2
Unrealized loss on available-for-sale securities	—	—	—	(1.9)	—	—	(1.9)
Defined benefit pension plan	—	—	—	(1.1)	—	—	(1.1)
Shares issued under employee stock purchase plan	0.1	—	4.1	—	—	—	4.1
Shares issued upon expiration of warrants	—	—	(53.2)	—	53.2	—	—
Repurchase of shares	—	—	2.8	—	(252.8)	—	(250.0)
Exercise of stock options	0.5	—	39.9	—	—	—	39.9
Share-based compensation	—	—	46.4	—	—	—	46.4
Cumulative effect of accounting change	—	—	0.7	—	—	(5.8)	(5.1)
Consolidation of variable interest entity	—	—	0.1	—	—	—	0.1
Balance, December 31, 2017	69.9	$ 0.7	$ 1,854.3	$ (19.6)	$(2,579.2)	$ 2,845.6	$ 2,101.8

See accompanying notes to consolidated financial statements.

UNITED THERAPEUTICS CORPORATION

Consolidated Statements of Cash Flows

(In millions)

	Year Ended December 31,		
	2017	2016	2015
Cash flows from operating activities:			
Net income	$ 417.9	$ 713.7	$ 651.6
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation and amortization	31.0	31.6	32.9
Share-based compensation expense	73.5	12.1	280.3
Impairment of cost method investments	49.6	—	—
Gain on sale of intangible asset	—	—	(350.0)
Other	(19.4)	9.5	7.5
Excess tax benefits from share-based compensation	—	(5.9)	(37.4)
Changes in operating assets and liabilities:			
Accounts receivable	(82.7)	(21.7)	(30.5)
Inventories	(0.5)	(24.5)	(6.8)
Accounts payable and accrued expenses	66.2	0.6	17.0
Other assets and liabilities	(61.4)	(71.8)	(181.8)
Net cash provided by operating activities	474.2	643.6	382.8
Cash flows from investing activities:			
Purchases of property, plant and equipment	(86.3)	(38.0)	(49.8)
Proceeds from sale of property, plant and equipment	8.3	—	—
Purchases of held-to-maturity and other investments	(51.8)	(0.8)	(62.8)
Maturities of held-to-maturity investments	52.9	130.4	320.4
Purchases of available-for-sale investments	(718.4)	—	—
Maturities of available-for-sale investments	20.0	—	—
Purchase of investments held at cost	(60.4)	(36.0)	(54.2)
Purchase of investments under the equity method	—	(2.1)	—
Consolidation of variable interest entity	0.1	—	—
Gain on sale of intangible asset	—	—	350.0
Intangible assets acquired, net	—	(5.2)	—
Net cash (used in) provided by investing activities	(835.6)	48.3	503.6
Cash flows from financing activities:			
Proceeds from line of credit	250.0	—	—
Principal payments of debt	—	(8.8)	(133.2)
Payments of debt issuance costs	(0.7)	(6.8)	—
Payments to repurchase common stock	(250.0)	(500.0)	(394.5)
Proceeds from exercise of stock options	39.9	7.7	39.3
Issuance of stock under employee stock purchase plan	4.1	4.3	4.0
Excess tax benefits from share-based compensation	—	5.9	37.4
Net cash provided by (used in) financing activities	43.3	(497.7)	(447.0)
Effect of exchange rate changes on cash and cash equivalents	0.2	(3.0)	(5.3)
Net (decrease) increase in cash and cash equivalents	(317.9)	191.2	434.1
Cash and cash equivalents, beginning of year	1,023.0	831.8	397.7
Cash and cash equivalents, end of year	$ 705.1	$ 1,023.0	$ 831.8
Supplemental cash flow information:			
Cash paid for interest	$ 7.5	$ 1.5	$ 1.0
Cash paid for income taxes	$ 346.9	$ 362.4	$ 293.3
Cash paid for settlement of loss contingency	$ 210.0	$ —	$ —
Non-cash investing and financing activities:			
Non-cash additions to property, plant and equipment	$ 11.5	$ 2.9	$ 1.1
Issuance of common stock upon conversion of convertible notes	$ —	$ 7.5	$ 321.8

See accompanying notes to consolidated financial statements.

UNITED THERAPEUTICS CORPORATION

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 Unituxin during the third quarter of 2015.

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.

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. Estimates are used for, but not limited to, revenue recognition, share-based compensation, marketable investments, fair value measurements (including those relating to contingent consideration), investments in privately-held companies, 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 and contingent consideration are reported in Note 4—*Investments* and Note 5—*Fair Value Measurements*, respectively.

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

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

transaction between market participants at the measurement date under current market conditions. Such transactions to sell an asset or transfer a liability are assumed to occur in the principal market for that asset or liability, or in the absence of the principal market, the most advantageous market for the asset or liability.

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

Cash Equivalents

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

Marketable Investments

Our marketable investments are primarily debt securities that we classify as available-for-sale or held-to-maturity. If we have both the positive intent and the ability to hold the securities until maturity, the securities are classified as held-to-maturity. We determine the appropriate classification of the securities at the time they are acquired and evaluate the appropriateness of such classifications at each balance sheet date. Available-for-sale securities are recorded at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive income (loss) in stockholders' equity, until realized. Held-to-maturity securities are recorded at amortized cost, adjusted for the amortization of discounts or premiums. Related discounts and premiums are amortized over the term of these securities as an adjustment to the yield using the effective interest method. Marketable investments are classified as either current or non-current assets on our consolidated balance sheets based on their contractual maturity dates.

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.

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Inventories

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

	As of December 31,	
	2017	2016
Raw materials	$ 27.9	$ 25.4
Work-in-progress	24.1	24.9
Finished goods	55.9	49.7
Total inventories	$ 107.9	$ 100.0

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 2017 and 2016. Our evaluation of goodwill completed during the years ended December 31, 2017 and 2016, 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, 2017 and 2016, 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, 2017 and 2016.

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

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

	As of December 31, 2017			As of December 31, 2016		
	Gross	Accumulated Amortization	Net	Gross	Accumulated Amortization	Net
Goodwill	$ 13.7	$ —	$ 13.7	$ 10.3	$ —	$ 10.3
Other intangible assets:						
Technology, patents and trade names	6.5	(5.0)	1.5	6.5	(4.8)	1.7
In-process research and development	30.4	—	30.4	21.5	—	21.5
Customer relationships and non-compete agreements	4.3	(4.3)	—	4.3	(4.0)	0.3
Total	$ 54.9	$ (9.3)	$ 45.6	$ 42.6	$ (8.8)	$ 33.8

Related amortization expense for the years ended December 31, 2017, 2016 and 2015, was $0.5 million, $0.6 million and $1.1 million, respectively. As of December 31, 2017, 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

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

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

	As of December 31,	
	2017	2016
Land and land improvements	$ 60.5	$ 60.1
Buildings, building improvements and leasehold improvements	408.0	409.9
Buildings under construction	119.8	44.6
Furniture, equipment and vehicles	159.9	149.7
	748.2	664.3
Less—accumulated depreciation	(202.5)	(175.0)
Property, plant and equipment, net	$ 545.7	$ 489.3

Depreciation expense for the years ended December 31, 2017, 2016 and 2015, was $30.5 million, $31.0 million and $31.8 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. 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

Our revenues are generated from the sale of our five commercially approved products: Remodulin, Tyvaso, Orenitram, Unituxin and Adcirca. Revenue is recognized 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. As is customary in the pharmaceutical industry, our revenues are subject to various product sales allowances in calculating reported net product sales. These sales allowances include: (1) rebates and chargebacks; (2) prompt pay discounts: (3) product returns; and (4) distributor fees and other allowances. We estimate sales allowances in the same period that we recognize revenue for product sales to distributors. Except for product returns, our liabilities for sales allowances are recorded in accounts payable and accrued expenses on our consolidated balance sheets. We record our allowance for product returns in other current and non-current liabilities on our consolidated balance sheets. Calculating these sales allowances involves the use of significant estimates and judgments and information obtained from external sources.

Rebates and Chargebacks. Allowances for rebates include mandated discounts due to our participation in various government health care programs and contracted discounts with commercial payers. We estimate our rebate liability on a product-by-product basis, considering actual revenue, contractual discount rates, expected utilization under each contract and historical payment experience. We also consider changes in our product pricing and information regarding changes in program regulations and guidelines. Our chargebacks represent contractual discounts payable to distributors for the difference between the invoice price paid to us by the distributor for a particular product and the contracted price that the distributor's customer pays for that product. Our chargebacks primarily relate

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

to sales of Adcirca. We estimate our chargeback liability on a product-by-product basis, primarily considering historical payment experience. Although we accrue a liability for rebates and chargebacks in the same period the product is sold, third-party reporting and payment of the rebate or chargeback amount occur on a time lag, with the majority of rebates and chargebacks paid within six months from date of sale.

Prompt pay discounts. We offer prompt pay discounts to many of our distributors, typically for payments made within 30 days. Prompt pay discounts are estimated in the period of sale based on our experience with sales to eligible distributors. Our distributors have routinely taken advantage of these discounts and we expect them to continue to do so.

Product returns. The sales terms for Adcirca and Unituxin include return rights that extend throughout the distribution channel. For Adcirca, customers have the right to return expired product for up to 12 months past the product's expiration date. Once the product is returned, it is destroyed. We recognize an allowance for returns based on historical returns experience and considering expiration dates of product shipped (generally 24 to 36 months after the initial sale). To date, actual returns have not differed materially from our estimates. For Unituxin, our historical returns have not been material and we do not record a returns allowance. For sales of our other commercial products, we do not offer our customers a general right of return.

Distributor fees and other allowances. Distributor fees include distribution and other service fees paid to certain distributors. These fees are based on contractual amounts or rates applied to purchases of our product or units of service provided in a given period. Other allowances include payments in support of patient assistance programs and are based on the actual amount of financial support provided to patients.

Trade Receivables

We invoice our customers subsequent to revenue recognition, resulting in receivables from our customers, which are presented as accounts receivable on our consolidated balance sheets. Accounts receivable consist of short-term amounts due from distributors (generally 30 to 90 days) and are stated at the amount we expect to collect. We establish an allowance for doubtful accounts based on our assessment of the collectability of specific distributor accounts. No allowance for doubtful accounts was recognized for each of the years ending December 31, 2017 and 2016. Changes in accounts receivable are primarily due to the timing and magnitude of orders of our products, the timing of delivery of our products to distributors and the timing of cash collections.

Adcirca

Adcirca is manufactured for us by Eli Lilly and Company (Lilly) and distributed through their 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. 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

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

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.

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.

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

Awards under 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. Additionally, certain executives have stock options with performance conditions that have vesting rights tied to achievement of specific targeted criteria. Share-based compensation expense for all awards is recorded ratably over their vesting period, depending on the specific terms of the award and achievement of the specified performance conditions. Refer to Note 9 —*Share-Based Compensation*.

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

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.

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Income Taxes

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

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

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

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

3. Recently Issued Accounting Standards

Accounting Standards Adopted During 2017

In July 2015, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (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 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, with no material impact 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 began to recognize excess tax benefits as income tax benefits on our consolidated statements of operations. Previously, we recognized such amounts in additional paid-in capital on our consolidated balance sheets. Additionally, on January 1, 2017, we established an accounting policy election to account for forfeitures of share-based awards when they occur. Upon adoption, we recognized a cumulative-effect adjustment for the removal of the forfeiture estimate with respect to awards that were continuing to vest as of January 1, 2017. The adjustment resulted in a decrease to retained earnings of $5.8 million, which is net of a $3.2 million tax benefit. The guidance also requires that we classify excess tax benefits as an operating activity in our consolidated statements of cash flows, whereas we previously classified such amounts as a financing activity. These amounts are now classified as "other" in our cash flows from operating activities. We have adopted ASU 2016-09 on a prospective basis and, as such, prior periods have not been adjusted, with the exception of the cumulative-effect adjustment to retained earnings for the removal of the forfeiture estimate, which was adopted on a modified retrospective basis. Refer to Note 9—*Share-Based Compensation*.

Accounting Standards Not Yet Adopted

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* (ASU 2014-09), and subsequent clarifying guidance. The new standard supersedes the revenue recognition requirements in Topic 605, *Revenue Recognition (Topic 605)*, and requires entities to recognize revenue when control of the promised goods or services is transferred to customers at an amount that reflects the consideration to which the entity expects to be entitled to, in exchange for those goods or services. We adopted the new standard on January 1, 2018, using the modified retrospective approach, applied only to contracts that were not completed as of January 1, 2018. Upon adoption, we changed the timing of revenue recognition for sales of Adcirca to recognize revenue at the time Adcirca is shipped, i.e., when control of Adcirca is transferred to a distributor upon shipment from a Lilly distribution center. Previously, we recognized sales of Adcirca when Adcirca was delivered to distributors. This change did not result in an adjustment to amounts previously recognized as revenue under Topic 605 as all shipments had reached the distributor as of December 31, 2017. Overall, the adoption did not impact the amounts reported in our financial statements and there were no other significant changes impacting the timing or measurement of our revenue or our business processes and controls.

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

3. Recently Issued Accounting Standards (Continued)

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 using a simplified impairment assessment that utilizes 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. We adopted the new standard on January 1, 2018, with no material impact to our financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (ASU 2016-02), which requires that lease assets and lease liabilities be recognized 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 currently evaluating the effect of adoption 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 is effective for fiscal years beginning after December 15, 2017, and for interim periods within those fiscal years. We adopted the new standard on January 1, 2018, with no material impact to 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 to retained earnings as of the beginning of the period of adoption. We adopted the new standard on January 1, 2018, with no material impact to our financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations-Clarifying the Definition of a Business* (ASU 2017-01). This update narrows the definition of a business by providing a screen to determine when an integrated set of assets and activities is not a business. The screen specifies that an integrated set of assets and activities is not a business if substantially all of the fair value of the gross assets acquired or disposed of is concentrated in a single asset or a group of similar identifiable assets. ASU 2017-01 should be applied prospectively and is effective for annual reporting periods beginning after December 15, 2017, and for interim periods within those fiscal years. We adopted the new standard on January 1, 2018, with no material impact to our financial statements.

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

3. Recently Issued Accounting Standards (Continued)

In January 2017, the FASB issued ASU No. 2017-04, *Intangibles-Goodwill and Other: Simplifying the Test for Goodwill Impairment* (ASU 2017-04), which simplifies how an entity is required to test goodwill for impairment. Goodwill impairment will be measured by the amount by which a reporting unit's carrying value exceeds its fair value, with the amount of impairment not to exceed the carrying amount of goodwill. ASU 2017-04 is effective for goodwill impairment tests in fiscal years beginning after December 15, 2019, and for interim periods within those fiscal years, and must be adopted on a prospective basis. Early adoption is permitted. We are currently evaluating the effect of adoption on our financial statements.

In March 2017, the FASB issued ASU No. 2017-07, *Compensation-Retirement Benefits* (ASU 2017-07), which improves the presentation of net periodic pension cost and net periodic post-retirement benefit cost. ASU 2017-07 requires employers that present a measure of operating income in their statement of income to include only the service cost component of net periodic pension cost and net periodic post-retirement benefit cost in operating expense along with other employee compensation costs. Under ASU 2017-07, the service cost component of net benefit cost is eligible for capitalization. Additionally, this update further requires other components of net benefit cost to be included in non-operating expenses. ASU 2017-07 is effective for fiscal years beginning after December 15, 2017, and for interim periods within those fiscal years. An entity is to apply the change in income statement presentation retrospectively, and the change in capitalized benefit cost prospectively. We adopted the new standard on January 1, 2018, with no material impact to our financial statements.

4. Investments

Marketable Investments

Available-for-Sale Investments

Marketable investments classified as available-for-sale consisted of the following (in millions):

As of December 31, 2017	Amortized Cost	Gross Unrealized Losses	Fair Value
U.S. government and agency securities	$ 726.5	$ (3.0)	$ 723.5
Corporate notes and bonds	13.9	—	13.9
Total	$ 740.4	$ (3.0)	$ 737.4
Reported under the following captions on the consolidated balance sheet:			
Cash and cash equivalents			$ 41.7
Current marketable investments			194.6
Non-current marketable investments			501.1
Total			$ 737.4

We had no available-for-sale investments as of December 31, 2016.

UNITED THERAPEUTICS CORPORATION

Notes to Consolidated Financial Statements (Continued)

4. Investments (Continued)

The following table summarizes the contractual maturities of available-for-sale marketable investments (in millions):

	December 31, 2017	
	Amortized Cost	Fair Value
Due within one year	$ 236.7	$ 236.3
Due in two to three years	503.7	501.1
Total	$ 740.4	$ 737.4

Held-to-Maturity Investments

Our current and long-term marketable investments included $29.3 million and $30.1 million of investments classified as held-to-maturity as of December 31, 2017 and 2016, respectively. Marketable investments classified as held-to-maturity are comprised of government-sponsored enterprises and corporate notes and bonds. We do not intend to sell these securities, nor is it more likely than not that we will be required to sell them prior to the recovery of their amortized cost basis. Furthermore, we do not believe that these securities expose us to undue market risk or counterparty credit risk. As such, we do 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, 2017	
	Amortized Cost	Fair Value
Due within one year	$ 27.7	$ 27.7
Due in two to three years	1.6	1.6
Total	$ 29.3	$ 29.3

Investments Held at Cost

As of December 31, 2017, we maintained non-controlling equity investments of approximately $184.0 million in the aggregate. These investments are initially held at cost because we do not have the ability to exercise significant influence over the companies in which these investments were made and the fair values of these investments are not readily determinable. During the year ended December 31, 2017, we made payments of $60.4 million for investments held at cost. We include our investments held at cost within other non-current assets on our consolidated balance sheets. These investments are subject to a periodic impairment review and if they are deemed to be other-than-temporarily impaired, the investment is measured and recorded at fair value. During the year ended December 31, 2017, we recorded $49.6 million of impairment charges related to our cost method investments in privately-held companies.

Variable Interest Entity

In April 2017, we made a $7.5 million minority investment in a privately-held company. In addition to our investment, we entered into an exclusive license, development and commercialization agreement