Horizon Pharma plc
Form 10-K
February 27, 2017

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission File Number 001-35238

HORIZON PHARMA PUBLIC LIMITED COMPANY

(Exact name of Registrant as specified in its charter)

Ireland (State or other jurisdiction of incorporation or organization)	Not Applicable (I.R.S. Employer Identification No.)
Connaught House, 1st Floor 1 Burlington Road, Dublin 4, D04 C5Y6, Ireland (Address of principal executive offices)	Not Applicable (zip code)

011 353 1 772 2100

(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
Ordinary shares, nominal value $0.0001 per share	The NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

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 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 is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company.

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

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

The aggregate market value of the registrant's voting ordinary shares held by non-affiliates of the registrant, based upon the $16.47 per share closing sale price of the registrant's ordinary shares on June 30, 2016 (the last business day of the registrant's most recently completed second quarter), was approximately $2.2 billion. Solely for purposes of this calculation, the registrant's directors and executive officers and holders of 10% or more of the registrant's outstanding ordinary shares have been assumed to be affiliates and an aggregate of 24,135,899 ordinary shares held by such persons on June 30, 2016 are not included in this calculation.

As of February 22, 2017, the registrant had outstanding 162,334,893 ordinary shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the registrant's 2017 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

HORIZON PHARMA PLC

FORM 10-K — ANNUAL REPORT

For the Fiscal Year Ended December 31, 2016

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PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains "forward-looking statements" — that is, statements related to future, not past, events — as defined in Section 21E of the Securities Exchange Act of 1934, as amended, that reflect our current expectations regarding our future growth, results of operations, financial condition, cash flows, performance, business prospects, and opportunities, as well as assumptions made by, and information currently available to, our management. Forward-looking statements include any statement that does not directly relate to a current or historical fact. We have tried to identify forward-looking statements by using words such as "believe," "may," "could," "will," "estimate "continue," "anticipate," "intend," "seek," "plan," "expect," "should," or "would." Among the factors that could cause actual re differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation: our ability to successfully execute our sales and marketing strategy, including continuing to successfully recruit and retain sales and marketing personnel and to successfully build the market for our medicines; whether we will be able to realize the expected benefits of strategic transactions, such as our acquisitions of Hyperion Therapeutics Inc., Crealta Holdings LLC and Raptor Pharmaceutical Corp., including whether and when such transactions will be accretive to our net income; the rate and degree of market acceptance of, and our ability and our distribution and marketing partners' ability to obtain coverage and adequate reimbursement and pricing for, our medicines from government and third-party payers and risks relating to the success of our patient access programs; our ability to maintain regulatory approvals for our medicines; our ability to conduct clinical development and obtain regulatory approvals for our medicine candidates, including potential delays in initiating and completing studies and filing for and obtaining regulatory approvals and whether data from clinical studies will support regulatory approval; our need for and ability to obtain additional financing; the accuracy of our estimates regarding future financial results; our ability to successfully execute our strategy to develop or acquire additional medicines or companies, including disruption from any future acquisition or whether any acquired development programs will be successful; our ability to manage our anticipated future growth; the ability of our medicines to compete with generic medicines, especially those representing the active pharmaceutical ingredients in our medicines as well as new medicines that may be developed by our competitors; our ability and our distribution and marketing partners' ability to comply with regulatory requirements regarding the sales, marketing and manufacturing of our medicines and medicine candidates; the performance of our third-party distribution partners, licensees and manufacturers over which we have limited control; our ability to obtain and maintain intellectual property protection for our medicines; our ability to defend our intellectual property rights with respect to our medicines; our ability to operate our business without infringing the intellectual property rights of others; the loss of key commercial or management personnel; regulatory developments in the United States and other countries, including potential changes in healthcare laws and regulations; and other risks detailed below in Part I — Item 1A. "Risk Factors."

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

Item 1. Business

Unless otherwise indicated or the context otherwise requires, references to the "Company", "we", "us" and "our" refer to Horizon Pharma plc and its consolidated subsidiaries, including its predecessor Horizon Pharma, Inc., or HPI. All references to "Vidara" are references to Horizon Pharma plc (formerly known as Vidara Therapeutics International Public Limited Company) and its consolidated subsidiaries prior to the effective time of the merger of the businesses of HPI and Vidara on September 19, 2014, or the Vidara Merger. The disclosures in this report relating to the pre-Vidara Merger business of Horizon Pharma plc, unless noted as being the business of Vidara prior to the Vidara Merger, pertain to the business of HPI prior to the Vidara Merger.

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Overview

We are a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. We market eleven medicines through our orphan, rheumatology and primary care business units. Our marketed medicines are ACTIMMUNE® (interferon gamma-1b), BUPHENYL® (sodium phenylbutyrate) Tablets and Powder, DUEXIS® (ibuprofen/famotidine), KRYSTEXXA® (pegloticase), MIGERGOT® (ergotamine tartrate & caffeine suppositories), PENNSAID® (diclofenac sodium topical solution) 2% w/w, or PENNSAID 2%, PROCYSBI® (cysteamine bitartrate) delayed-release capsules, QUINSAIR™ (aerosolized form of levofloxacin), RAVICTI® (glycerol phenylbutyrate) Oral Liquid, RAYOS® (prednisone) delayed-release tablets and VIMOVO® (naproxen/esomeprazole magnesium).

Our Strategy

Our strategy is to continue to build a well-balanced, diversified, high-growth biopharmaceutical company. We are executing our strategy through the successful commercialization of our existing medicines, a strong commitment to patient access and support and business development efforts focused on transformative acquisitions to accelerate our rare disease leadership as well as on-market and development-stage medicines to fill out our pipeline.

We are building a sustainable biopharmaceutical company by helping ensure that patients have access to their medicines and support services, and by investing in the further development of medicines for patients with rare or underserved diseases. Our growing business is diversified across three business units: orphan, rheumatology and primary care, and is driven by a successful commercial model that focuses on differentiated, long-life medicines, innovative patient access programs and a disciplined business development strategy. Our key areas of focus are:

Revenue diversification – We have successfully diversified our portfolio of medicines from two in 2013 to eleven in December 2016. Our intent is to continue to generate organic growth, broaden our medicine portfolio to ensure net revenues are not dominated by any one medicine and increase the proportion of net revenues derived from our orphan medicines.

Clinical development – We work diligently to unlock the full therapeutic potential of our medicines by working closely with regulatory agencies, premier academic centers with established study consortiums, healthcare professionals and patient groups to facilitate our clinical development programs and generate data for possible new indications that may help more patients in need. We also continue to look at opportunities to augment our rare disease pipeline through development-stage acquisitions.

Business development – We have a disciplined and robust acquisition strategy, and our focus is on rapid value creation and improving the performance of each of the medicines we acquire. We have completed seven acquisitions over the past five years, including two transformative transactions in 2016 that brought us three new rare disease medicines. While we remain focused on acquiring clinically-differentiated medicines and executing transactions that are accretive and net present value positive, we have expanded our acquisition criteria to potentially include medicines in late-stage development.

Our Company

We are a public limited company formed under the laws of Ireland. Our predecessor, HPI, was originally incorporated in Delaware in March 2010 and Vidara was originally incorporated in Ireland in December 2011. We operate through a number of international and U.S. subsidiaries with principal business purposes to perform research and development or manufacturing operations, serve as distributors of our medicines, hold intellectual property assets or provide us with services and financial support.

Our principal executive offices are located at Connaught House, 1st Floor, 1 Burlington Road, Dublin 4, D04 C5Y6, Ireland and our telephone number is 011 353 1 772 2100. Our website address is www.horizonpharma.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this Annual Report on Form 10-K.

Mergers and Acquisitions

The Vidara Merger occurred on September 19, 2014 and was accounted for as a reverse acquisition under the acquisition method of accounting for business combinations, with HPI treated as the acquiring company for accounting purposes. As part of the Vidara Merger, a wholly owned subsidiary of Vidara merged with and into HPI, with HPI surviving the Vidara Merger as a wholly owned subsidiary of Vidara. Prior to the Vidara Merger, Vidara changed its name to Horizon Pharma plc. Upon the consummation of the Vidara Merger, the historical financial statements of HPI became our historical financial statements. Accordingly, the historical financial statements of HPI are included in the 2014 comparative periods.

On October 17, 2014, we acquired the U.S. rights to PENNSAID 2% from Nuvo Research Inc., or Nuvo, for $45.0 million in cash.

On May 7, 2015, we completed our acquisition of Hyperion Therapeutics Inc., or Hyperion, in which we acquired all of the issued and outstanding shares of Hyperion's common stock for $46.00 per share in cash or approximately $1.1 billion on a fully-diluted basis. Hyperion marketed RAVICTI and BUPHENYL. Following the completion of the acquisition, Hyperion became our wholly owned subsidiary and was renamed Horizon Therapeutics, Inc. (which subsequently converted to a limited liability company, Horizon Therapeutics, LLC).

On January 13, 2016, we completed our acquisition of Crealta Holdings LLC, or Crealta, for approximately $539.7 million, including cash acquired of $24.9 million. Crealta marketed KRYSTEXXA and MIGERGOT. Following the completion of the acquisition, Crealta became our wholly owned subsidiary and was renamed Horizon Pharma Rheumatology LLC.

On October 25, 2016, we completed our acquisition of Raptor Pharmaceutical Corp., or Raptor, in which we acquired all of the issued and outstanding shares of Raptor's common stock for $9.00 per share in cash. The total consideration was $860.8 million, including cash acquired of $24.9 million and $56.0 million to repay Raptor's outstanding debt. Raptor marketed PROCYSBI and QUINSAIR. Following completion of the acquisition, Raptor became our wholly owned subsidiary and converted to a limited liability company, changing its name to Horizon Pharmaceutical LLC.

The consolidated financial statements presented herein include the results of operations of the acquired Vidara, Hyperion, Crealta and Raptor businesses from the applicable dates of acquisition.

Our Medicines

We believe our medicines address unmet therapeutic needs in orphan diseases, arthritis, pain and inflammation and inflammatory diseases and provide significant advantages over existing therapies.

Our current marketed medicine portfolio consists of the following:

Medicine	Disease	Marketing Rights
ORPHAN BUSINESS UNIT MEDICINES:		
ACTIMMUNE	Chronic granulomatous disease and severe, malignant osteopetrosis	United States and selected foreign countries
BUPHENYL	Urea cycle disorders	Worldwide (1)
PROCYSBI	Nephropathic cystinosis	Worldwide
QUINSAIR	Treatment of chronic pulmonary infections due to pseudomonas aeruginosa in cystic fibrosis patients	Worldwide (2)
RAVICTI	Urea cycle disorders	Worldwide (3)
RHEUMATOLOGY BUSINESS UNIT MEDICINES:		
KRYSTEXXA	Chronic refractory gout	Worldwide
RAYOS/LODOTRA	Rheumatoid arthritis, polymyalgia rheumatic, systemic lupus erythematosus and multiple other indications	Worldwide (4)
PRIMARY CARE BUSINESS UNIT MEDICINES:		
DUEXIS	Signs and symptoms of osteoarthritis and rheumatoid arthritis	Worldwide (5)
MIGERGOT	Vascular headache	United States
PENNSAID 2%	Pain of osteoarthritis of the knee(s)	United States
VIMOVO	Signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis	United States

(1) BUPHENYL is known as AMMONAPS in certain European countries. The distribution rights for BUPHENYL in Europe, certain Asian, Latin American, Middle Eastern, North African and other countries have been granted to Swedish Orphan Biovitrum AB, or SOBI. Orphan Pacific, Inc. holds an exclusive distribution agreement for the distribution of AMMONAPS in Japan.

(2) We have not received regulatory approval to distribute QUINSAIR in the United States.

(3) RAVICTI distribution rights in the Middle East and North Africa have been granted to SOBI. In June 2016, we partnered with Clinigen Group plc's Idis managed access division to initiate a managed access program in selected European countries, which agreement terminates on April 10, 2017 and after which we will partner with SOBI to

continue our managed access program in selected European countries. We expect to commercially launch RAVICTI in Europe in 2017 through an exclusive distribution agreement with SOBI.

(4) Mundipharma International Corporation Limited, or Mundipharma, is our exclusive distributor for LODOTRA in Europe, Asia and Latin America. The majority of LODOTRA sales are in Germany and Italy where reimbursement has been approved.

(5) DUEXIS rights in Latin America have been licensed to Grünenthal S.A., or Grünenthal.

ORPHAN BUSINESS UNIT

Market

Chronic Granulomatous Disease

Chronic granulomatous disease, or CGD, is a genetic disorder of the immune system. It is described as a primary immunodeficiency disorder, which means it is not caused by another disease or disorder. In people who have CGD, a type of white blood cell, called a phagocyte, is defective. These defective phagocytes cannot generate superoxide, leading to an inability to kill harmful microorganisms such as bacteria and fungi. As a result, the immune system is weakened. People with CGD are more likely to have certain problems such as recurrent severe bacterial and fungal infections and chronic inflammatory conditions. These patients are prone to developing masses called granulomas, which can occur repeatedly in organs throughout the body and cause a variety of problems. CGD is considered to be a condition that patients can live with and manage. Studies suggest overall survival has improved over the last decade with more patients living well into adulthood. Approximately 1 out of every 100,000 to 200,000 babies in the United States is born with CGD.

Severe, Malignant Osteopetrosis

Severe, malignant osteopetrosis, or SMO, is a form of osteopetrosis and is sometimes referred to as marble bone disease or malignant infantile osteopetrosis because it occurs in very young children. While exact numbers are not known, it has been estimated that 1 out of 250,000 children is born with SMO. During normal bone development, existing bone material is constantly being replaced by new bone. Cells called osteoblasts cause new bone formation while other cells called osteoclasts remove old bone through a process called resorption. In people with osteopetrosis, this balance is not maintained because their osteoclasts do not function properly. As a result, resorption of old bone material decreases while the formation of new bone continues. This leads to an abnormal increase in bone mass, which can make the bones more brittle. Because abnormal bone development affects many different systems in the body, osteopetrosis may cause problems such as blood disorders, decreased ability to fight infection, bone fractures, problems with vision and hearing, and abnormal appearance of the face and head.

Urea Cycle Disorders

Urea cycle disorders, or UCDs, are inherited metabolic diseases caused by a deficiency of one of the enzymes or transporters that constitute the urea cycle. The urea cycle involves a series of biochemical steps in which ammonia, a potent neurotoxin, is converted to urea, which is excreted in the urine. UCD patients may experience episodes where they get symptoms from the ammonia in their blood being excessively high – called hyperammonemic crises – which may result in irreversible brain damage, coma or death. UCD symptoms may first occur at any age depending on the severity of the disorder, with more severe defects presenting earlier in life. We estimate that there are approximately 2,000 patients with UCDs living in the United States.

Nephropathic Cystinosis

We estimate that there are approximately 500 patients diagnosed with cystinosis living in the United States and an estimated 2,000 patients worldwide. Nephropathic cystinosis comprises ninety-five percent of known cases of cystinosis. In these patients, elevated cystine leads to cellular dysfunction and death; without treatment, the disease is usually fatal by the end of the first decade of life. Cystinosis is progressive, eventually causing irreversible tissue damage and multi-organ failure, including kidney failure, blindness, muscle wasting and premature death. Nephropathic cystinosis is usually diagnosed in infancy after children display symptoms to physicians, including markedly increased urination, thirst, dehydration, gastrointestinal distress, failure to thrive, rickets, photophobia and kidney symptoms specific to Fanconi syndrome. Management of cystinosis requires lifelong therapy.

Pseudomonas Aeruginosa Infection in Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 70,000 people worldwide. Cystic fibrosis is caused by a mutation in the cystic fibrosis transmembrane conductance regulator, or CFTR, gene. Defective or missing CFTR protein causes poor flow of salt and water into or out of the cell in several organs, including the lungs. This leads to the buildup of abnormally thick secretions that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death.

Patients with cystic fibrosis are highly susceptible to colonization with bacterial infections of the lung, largely because their pulmonary mucous secretions are thicker, stickier, and more difficult to expectorate than those of healthy individuals. This creates an environment in the lung that favors bacterial proliferation. As of 2014, a median of approximately thirty-five percent of all patients with cystic fibrosis in the European Union, or EU, were colonized with Pseudomonas aeruginosa, a gram-negative bacterial infection. Infection rates climb as patients age.

Our Solutions

ACTIMMUNE

ACTIMMUNE is a biologically manufactured protein called interferon gamma-1b that is similar to a protein the human body makes naturally. In the body, interferon gamma is produced by cells of the immune system and helps to prevent infection in patients with CGD and enhances osteoclast function in patients with SMO. ACTIMMUNE is approved by the U.S. Food and Drug Administration, or FDA, to reduce the frequency and severity of serious infections associated with CGD and for delaying time to disease progression in patients with SMO. The precise way that ACTIMMUNE works to help prevent infection in patients with CGD and slow the worsening of SMO is not fully understood, but ACTIMMUNE is believed to work by modifying the cellular function of various cells, including those in the immune system and those that help form bones.

Efficacy in CGD

The International Chronic Granulomatous Disease Cooperative Study Group conducted a controlled clinical trial in 128 patients (ages ranging from one to forty-four years old) at thirteen medical centers across four countries. The purpose of this clinical trial was to evaluate the safety and efficacy of ACTIMMUNE in reducing the frequency and severity of serious infections in patients with CGD. Patients enrolled in the trial were randomly selected to receive either ACTIMMUNE or placebo in addition to antibiotics. The number and timing of serious infections were tracked in all patients for up to 1 year. Investigators concluded that ACTIMMUNE is an effective and safe therapy for patients with CGD, because the therapy statistically reduced the frequency of serious infections.

Efficacy in SMO

In a controlled clinical trial, sixteen patients were randomized to receive either ACTIMMUNE with calcitriol or calcitriol alone. The age of patients ranged from one month to eight years; with a mean age of one and one-half years. The median time to progression in the ACTIMMUNE plus calcitriol arm was 165 days versus a median of sixty-five days in the calcitriol only arm. In a separate analysis that combined data from a second trial, nineteen of twenty-four patients on ACTIMMUNE therapy (with or without calcitriol) for at least six months had reduced trabecular bone volume compared to baseline.

Commercial Status

ACTIMMUNE is the only drug currently approved by the FDA for the treatment for CGD and SMO. Our licenses allow us to market and sell ACTIMMUNE in the United States, Canada and Japan. We currently commercialize ACTIMMUNE in the United States and also supply ACTIMMUNE to patients in Canada, if so requested by way of a prescription from their treating physicians, through Health Canada’s, or HC, Special Access Program, which provides access to non-marketed drugs in Canada for practitioners treating patients with serious or life-threatening conditions when conventional therapies have failed, are unsuitable or are unavailable. We have not registered or sold ACTIMMUNE in Japan.

On May 18, 2016, we entered into a definitive agreement with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim International, to acquire certain rights to interferon gamma-1b, which Boehringer Ingelheim International currently commercializes under the trade names IMUKIN, IMUKINE, IMMUKIN and IMMUKINE in

an estimated thirty countries, primarily in Europe and the Middle East. The transaction is expected to close in 2017 and we are continuing to work with Boehringer Ingelheim International to enable the transfer of applicable marketing authorizations.

BUPHENYL

BUPHENYL tablets for oral administration and BUPHENYL powder for oral, nasogastric, or gastrostomy tube administration are indicated as adjunctive therapy in the chronic management of patients with UCDs involving deficiencies of carbamoyl phosphate synthetase, ornithine transcarbamylase or argininosuccinic acid synthetase.

BUPHENYL is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. It is important that the diagnosis be made early and treatment initiated immediately to improve chances of survival. BUPHENYL must be combined with dietary protein restriction and, in some cases, essential amino acid supplementation.

Commercial Status

BUPHENYL was approved by the FDA in the United States in 1996 and by the European Medicines Agency, or EMA, in Europe in 1999. We commercially market and distribute BUPHENYL in the United States. BUPHENYL is known as AMMONAPS in certain European countries, and the marketing and distribution rights are granted to SOBI through the end of 2021. We provide BUPHENYL in certain other countries through various Special Access Programs and licensed distributors.

PROCYSBI

PROCYSBI is an approved therapy for the management of nephropathic cystinosis. PROCYSBI capsules contain cysteamine bitartrate in the form of innovative microspheronized beads that are individually coated to create delayed and extended-release properties, allowing patients to maintain consistent therapeutic systemic drug levels over a twelve-hour dosing period. The enteric-coated beads are pH sensitive and bypass the stomach for dissolution and absorption in the more alkaline environment of the proximal small intestine. Randomized controlled clinical trials and extended treatment with PROCYSBI therapy demonstrated consistent cystine depletion as monitored by levels of the biomarker (and surrogate marker), white blood cell cystine.

In addition to the population of patients who have already been identified, we believe that a number of patients with atypical phenotypic presentation and end-stage renal disease have their condition as a result of undiagnosed late-onset nephropathic cystinosis, and would benefit from treatment with PROCYSBI.

Commercial Status

PROCYSBI received marketing approval from the FDA in April 2013 for the management of nephropathic cystinosis in adults and children six years and older. In August 2015, the FDA approved PROCYSBI for expanded use to treat children two to six years of age with nephropathic cystinosis. In Europe, PROCYSBI received marketing authorization in September 2013 from the European Commission, or EC, for marketing in the EU countries as an orphan medicine for the management of proven nephropathic cystinosis. The EU marketing authorization allows us to commercialize PROCYSBI in the 28 Member States of the EU plus Norway, Liechtenstein and Iceland. PROCYSBI received seven years of market exclusivity, through 2020, for patients six years of age and older as an orphan drug in the United States, and ten years of market exclusivity, through 2023, as an orphan drug in Europe. PROCYSBI received orphan drug designation in the United States for the treatment of patients aged two to six years of age, through 2022.

QUINSAIR

QUINSAIR is a formulation of the antibiotic drug levofloxacin, suitable for inhalation via a nebulizer. This route of delivery allows higher concentrations of drug in the lung sputum than can be achieved via systemic (for example, oral) administration. QUINSAIR, as approved, is administered twice daily in twenty-eight-day cycles, using a hand-held nebulizer with a disposable handset known as the Zirela® device, manufactured by our partner PARI Pharma GmbH, or PARI, and configured specifically for use with QUINSAIR.

Commercial Status

QUINSAIR is the first fluoroquinolone inhaled antibiotic to be approved in Canada and the EU for the treatment of chronic pulmonary infections due to Pseudomonas aeruginosa in cystic fibrosis patients. QUINSAIR was approved in the EU and Canada on the basis of three randomized, controlled studies, one Phase 2 and two Phase 3. In the EU, QUINSAIR is eligible for “new data” regulatory exclusivity of ten years after approval, beginning with its March 2015 marketing authorization, a period which is concurrent with, and independent from, the period of any applicable patent. QUINSAIR is not approved in the United States. Raptor launched QUINSAIR in Germany and Denmark in the first half of 2016 and we launched QUINSAIR in Canada in December 2016. We do not plan to pursue approval in the United States for QUINSAIR as a treatment of pseudomonas aeruginosa in adults with cystic fibrosis.

RAVICTI

RAVICTI is indicated for use as a nitrogen-binding agent for chronic management of adult and pediatric patients two years of age and older (two months of age and older in Europe) with UCDs that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. RAVICTI must be used with dietary protein restriction and, in some cases, dietary supplements (for example, essential amino acids, arginine, citrulline or protein-free calorie supplements).

Efficacy in the Treatment of UCDs in Adult Patients

A randomized, double-blind, active-controlled, crossover, non-inferiority study compared RAVICTI to sodium phenylbutyrate by evaluating venous ammonia levels in patients with UCDs that had been on sodium phenylbutyrate prior to enrollment for control of their UCD. Patients adhered to a low-protein diet and received amino acid supplements throughout the study. After two weeks of dosing, by which time patients had reached a steady state on each treatment, all patients had twenty-four hours of ammonia measurements.

Another study was conducted to assess monthly ammonia control and hyperammonemic crisis over a twelve-month period. A total of fifty-one adults were in the study and all but six had been converted from sodium phenylbutyrate to RAVICTI. Venous ammonia levels were monitored monthly. Of fifty-one adult patients participating in the twelve-month, open-label treatment with RAVICTI, seven patients (fourteen percent) reported a total of ten hyperammonemic crises.

The efficacy of RAVICTI in pediatric patients two to seventeen years of age was evaluated in two fixed-sequence, open-label, sodium phenylbutyrate to RAVICTI switchover studies, seven and ten days in duration. These studies compared blood ammonia levels of patients on RAVICTI to venous ammonia levels of patients on sodium phenylbutyrate in twenty-six pediatric UCD patients. Twenty-four hour blood ammonia levels of UCD patients six to seventeen years of age (Study 3) and patients two to five years of age (Study 4) were similar between treatments but trended higher with sodium phenylbutyrate.

Long-term (twelve-month), uncontrolled, open-label studies were conducted to assess monthly ammonia control and hyperammonemic crisis over a twelve-month period. Of the twenty-six pediatric patients six to seventeen years of age participating in these two trials, five patients (nineteen percent) reported a total of five hyperammonemic crises.

Commercial Status

RAVICTI was approved for marketing in the United States in 2013. Current FDA approval is for patients from two years of age and older only.

In November 2015, the EC adopted a binding decision to approve RAVICTI for use as an adjunctive therapy for chronic management of adult and pediatric patients two months of age and older with six subtypes of UCDs. This decision followed the Positive Opinion previously adopted on September 24, 2015 by the Committee for Medicinal Products for Human Use, or CHMP, of the EMA. The approval authorizes us to market RAVICTI in all twenty-eight Member States of the EU and the centralized marketing authorization will form the basis for recognition by the Member States of the European Economic Area, or EEA, namely Norway, Iceland and Liechtenstein, for the medicine to be placed on the market. In June 2016, we partnered with Clinigen Group plc’s Idis managed access division to initiate a managed access program in selected European countries, which agreement will terminate on April 10, 2017 and after which we will partner with SOBI to continue our managed access program in selected European countries. We expect to commercially launch RAVICTI in Europe in 2017 through an exclusive distribution agreement with SOBI.

We have worldwide rights to market and distribute RAVICTI. In relation to marketing and distribution rights in the Middle East and North Africa region, we have entered into a distribution agreement with SOBI through 2018. In March 2016, HC issued a Notice of Compliance for RAVICTI for use as an adjunctive therapy for chronic management of adult and pediatric patients two years of age and older with UCDs, and we launched RAVICTI in Canada in November 2016.

We are in the process of seeking approval for label expansions for RAVICTI, with assessments in progress studying the use of RAVICTI in patients both from two months to two years (on June 29, 2016 we submitted a supplemental new drug application, or sNDA, with the FDA for this indication) and from birth to two months (targeted sNDA submission in the first quarter of 2018). In patients with UCDs for which RAVICTI is an FDA-approved medicine, there is a variable age of diagnosis (from newborn to adulthood), and the severity of the disease can be associated with the age of onset and enzymatic deficit. However, a prompt diagnosis and careful management of the disease can lead to good clinical outcomes.

Competition

ACTIMMUNE presently faces limited competition. ACTIMMUNE is the only drug currently approved by the FDA specifically for the treatment for CGD and SMO. While there are additional or alternative approaches used to treat patients with CGD and SMO, including the increasing trend towards the use of bone marrow transplants in patients with CGD, there are currently no medicines on the market that compete directly with ACTIMMUNE.

In the United States, RAVICTI and BUPHENYL compete with generic forms of sodium phenylbutyrate. In Europe and certain other countries, RAVICTI and BUPHENYL compete with Pheburane, which is a sugar-coated version of sodium phenylbutyrate. Pheburane claims a taste advantage over BUPHENYL. However the volume of Pheburane that must be ingested multiple times per day is much greater than BUPHENYL, and significantly greater than RAVICTI, and is a barrier to patient compliance.

Other than PROCYSBI, we are aware of two pharmaceutical products currently approved to treat cystinosis. Cystagon® (immediate-release cysteamine bitartrate capsules), is a systemic cystine-depleting therapy for cystinosis in the United States manufactured by Mylan N.V., and by Orphan Europe SARL in markets outside of the United States. Cystagon was approved by the FDA in 1994 and by the EC in 1997. Cystaran® (cysteamine ophthalmic solution) was approved by FDA in 2012 for treatment of corneal crystal accumulation in patients with cystinosis and is marketed by Sigma Tau Pharmaceuticals, Inc.

While we believe that PROCYSBI will continue to be well received in the market, Cystagon remains on the market and we expect it will compete with PROCYSBI for the foreseeable future. We are not aware of any pharmaceutical company with an active program to develop an alternative therapy for cystinosis. Academic researchers in the United States and Europe are pursuing gene therapy and stem cell therapy, as well as pro-drug and PEGylated drug approaches as alternatives to cysteamine bitartrate. We believe that the development timeline to an approved product for these approaches is many years with substantial uncertainty.

In relation to QUINSAIR, chronic pulmonary infections due to Pseudomonas aeruginosa are currently treated primarily with inhaled antibiotics, including tobramycin, an aminoglycoside-class antibiotic sold by Novartis Pharmaceuticals Corporation as TOBI® or in dry-powder-inhalation format as TOBI Podhaler® and sold by others in generic form, aztreonam, a monobacter-class antibiotic which is marketed in an inhaled formulation by Gilead Sciences, Inc. under the tradename Cayston®, and colistimethate sodium, a polymixin-class antibiotic which is approved and marketed in inhaled formulations in Europe. Tobramycin, aztreonam and colistimethane are primarily effective against gram-negative bacteria such as Pseudomonas aeruginosa. However, the prevalence of multi-drug-resistant Pseudomonas aeruginosa is growing. Thus, we believe there is an unmet need that might be addressed with a new class of inhaled antibiotic such as the fluoruquinolone class that levofloxacin represents.

RHEUMATOLOGY BUSINESS UNIT

Market

Chronic Refractory Gout

Chronic refractory gout, or CRG, is a type of arthritis that occurs when uric acid build-up in the blood remains high and inflammation persists even after treatment with conventional therapies. Gout is one of the most common forms of inflammatory arthritis, estimated to affect 8.3 million in the United States, with CRG impacting 40,000 to 50,000 people in the United States. CRG frequently causes crippling disabilities and significant joint damage.

Rheumatoid Arthritis

Rheumatoid arthritis, or RA, is a chronic disease that causes pain, stiffness and swelling, primarily in the joints. According to a 2006 DataMonitor report, 2.9 million people in the United States suffer from RA, of which 1.8 million are diagnosed and treated with various drugs. RA has no known cause, but unlike osteoarthritis, or OA, RA is not associated with factors such as aging. RA occurs when the body's immune system malfunctions, attacking healthy tissue and causing inflammation, which leads to pain and swelling in the joints and may eventually cause permanent joint damage and painful disability. The primary symptoms of RA include progressive immobility and pain, especially in the morning, with long-term sufferers experiencing continual joint destruction for the remainder of their lives. There is no known cure for RA. Once the disease is diagnosed, treatment is prescribed for life to alleviate symptoms and/or to slow or stop disease progression. RA treatments include medications, physical therapy, exercise, education and sometimes surgery. Early, aggressive treatment of RA can delay joint destruction. Treatment of RA usually includes multiple drug therapies taken concurrently. Disease-modifying anti-rheumatic drugs, or DMARDs, are the current standard of care for the treatment of RA, in addition to rest, exercise and anti-inflammatory drugs such as nonsteroidal anti-inflammatory drugs, or NSAIDs.

Polymyalgia Rheumatica

Polymyalgia rheumatica, or PMR, is an inflammatory disorder that causes significant muscle pain and stiffness. The pain and stiffness often occur in the shoulders, neck, upper arms and hip with pronounced morning stiffness lasting at least one hour. Most people who develop PMR are older than sixty-five years of age. It rarely affects people younger than fifty. There are approximately 1.1 million patients with PMR in the United States and it afflicts one in every 133 people over the age of fifty. Prednisone is the standard of care for treating PMR and treatment is generally initiated at a relatively high dose (for example, 10-20 mg per day) and reduced as clinical improvement is seen. Treatment usually lasts eighteen to twenty-four months. Similar to RA, PMR is associated with circadian patterns of Interleukin 6, or IL-6, elevation in early morning hours.

Systemic Lupus Erythematosus

Systemic lupus erythematosus, or SLE, is a chronic autoimmune disease that causes inflammation and pain in the joints and muscles as well as overall fatigue. SLE affects from 161,000 to 322,000 adults in the United States. More than 90 percent of cases of SLE occur in women, frequently starting at childbearing age. In addition to affecting the muscles and joints, it can affect other organs in the body such as the kidneys, tissue lining the lungs (pleura), heart (pericardium), and brain. Most patients feel fatigue and have rashes, arthritis (painful and swollen joints) and fever. SLE flares vary from mild to serious.

In November 2015, we announced our collaboration with the Alliance for Lupus Research, or ALR, to study the effect of RAYOS on the fatigue experienced by SLE patients. SLE is a chronic autoimmune disease that causes inflammation and pain in the joints and muscles, as well as overall fatigue. RAYOS is currently indicated for patients with SLE. The first study planned as part of the collaboration is an investigator-initiated, randomized, double-blind, active comparator, cross-over study in which patients will be randomized to receive either prednisone for three months or RAYOS at 10 p.m. for three months, and then switched to the alternative medication for an additional three months. Approximately sixty-two patients across twenty-five sites will be enrolled in the United States. Fatigue will be measured by the Functional Assessment of Chronic Illness Therapy-Fatigue and the Fatigue Severity Scale, as well as the Vitality scale of the Medical Outcome Study thirty-six-item short form health survey.

Market Opportunity and Limitations of Existing Treatments

Morning Stiffness, Pain and Immobility

A Medical Marketing Economics May 2008 study of 150 RA patients in the United States, which we sponsored, showed that despite the use of a combination of currently available treatments for RA, more than ninety percent of the patients reported suffering from morning stiffness, pain and immobility, which is linked to peak IL-6 levels in the early morning hours. We believe an optimal treatment would reduce IL-6 levels in the early morning hours.

Side Effects of Current High-Dose Corticosteroid Treatments

According to the 2006 DataMonitor report, approximately 50 percent of RA patients in the United States, Japan, France, Italy, Spain, Germany and the United Kingdom are prescribed combination therapy which often includes corticosteroids, with prednisone being one of the most common. Corticosteroids, including prednisone, are used to suppress various autoimmune, inflammatory and allergic disorders by inhibiting the production of various pro-inflammatory cytokines. Joint inflammation in RA is driven by excessive production of inflammatory mediators and cytokines, such as IL-6 and TNF-alpha. While corticosteroids are potent and effective agents to treat patients with RA, they are often used at high doses to treat RA flares or significant inflammation. High-dose oral corticosteroid treatment is not a viable long-term treatment option due to adverse side effects such as osteoporosis, cardiovascular disease and weight gain. However, clinical studies have shown that the long-term use of low-dose prednisone (<10 mg per day) does not dramatically increase total adverse events. In addition, low doses, typically less than 10 mg daily, of corticosteroids such as prednisone have been shown to treat the symptoms of RA while slowing the overall progression of the disease.

Our Solutions

KRYSTEXXA

KRYSTEXXA is an orphan biologic medicine which is the first and only FDA-approved medicine for the treatment of CRG. KRYSTEXXA is a PEGylated uric acid specific enzyme (uricase) indicated for the treatment of CRG in adult patients that are refractory to conventional therapy. Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated. KRYSTEXXA has a unique mechanism of action which rapidly reverses disease progression. A PEGylated uric acid specific enzyme catalyzes the conversion of serum uric acid to allantoin, which is then excreted in urine. This PEGylated uric acid specific enzyme is given via an intravenous infusion to patients every two weeks.

Commercial Status

KRYSTEXXA was launched in the United States in January 2011.

RAYOS/LODOTRA

The medicine sold and marketed as RAYOS in the United States is known as LODOTRA outside the United States. While the FDA has approved RAYOS for the treatment of RA, ankylosing spondylitis, or AS, PMR, primary systemic amyloidosis, asthma, chronic obstructive pulmonary disease, SLE and a number of other conditions, we have focused our promotion of RAYOS/LODOTRA on rheumatology indications, including RA and PMR.

The proprietary formulation technology of RAYOS/LODOTRA enables a delayed-release of prednisone approximately four hours after administration. The RAYOS/LODOTRA proprietary delivery system synchronizes the prednisone delivery time with the patient's elevated cytokine levels, thereby taking effect at a physiologically optimal point to inhibit cytokine production, and thus significantly reduces the signs and symptoms of RA and PMR.

RAYOS/LODOTRA was developed using Vectura Group plc's (as successor in interest to SkyePharma AG, or SkyePharma), or Vectura, proprietary GeoClock™ and GeoMatrix™ technologies, for which we hold an exclusive worldwide license for the delivery of glucocorticoid, a class of corticosteroid. RAYOS/LODOTRA is composed of an active core containing prednisone, which is encapsulated by an inactive porous shell. The inactive shell acts as a barrier between the medicine's active core and a patient's gastrointestinal, or GI, fluids. RAYOS/LODOTRA is intended to be administered at bedtime. At approximately four hours following bedtime administration of RAYOS/LODOTRA, water in the digestive tract diffuses through the shell, causing the active core to expand, which

leads to a weakening and breakage of the shell and allows the release of prednisone from the active core. Our pharmacokinetic studies have shown that the blood concentration of prednisone from RAYOS/LODOTRA is similar to immediate release prednisone except for the intended time delay of medicine release after administration.

Commercial Status

We began marketing RAYOS to U.S. rheumatologists in December 2012. LODOTRA received its first approval in Europe in March 2009. Mundipharma is our exclusive distributor for LODOTRA in Europe, Asia and Latin America. The majority of LODOTRA sales are in Germany and Italy where reimbursement has been approved.

Competition

As the only FDA approved medication for the treatment of CRG, KRYSTEXXA faces limited direct competition. We believe that the complexity of manufacturing KRYSTEXXA provides a barrier to potential generic competition. However, a number of competitors have medicines in Phase 1 or Phase 2 trials. On December 22, 2015, AstraZeneca AB, or AstraZeneca, secured approval from the FDA for Zurampic® (lesinurad) 200mg tablets in combination with a xanthine oxidase inhibitor, or XOI, for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with an XOI alone. In April 2016, the U.S. rights to Zurampic were licensed to Ironwood Pharmaceuticals Inc. Although Zurampic is not a direct competitor because it has not been approved for CRG, this therapy could be used prior to use of KRYSTEXXA, and if effective, could reduce the target patient population for KRYSTEXXA.

RAYOS/LODOTRA competes with a number of medicines in the market to treat RA, including corticosteroids, such as prednisone, traditional DMARDs, such as methotrexate, and biologic agents, such as Humira and Enbrel. The majority of RA patients are treated with DMARDs, which are typically used as initial therapy in patients with RA. Biologic agents are typically added to DMARDs as combination therapy. It is common for an RA patient to take a combination of a DMARD, an oral corticosteroid, an NSAID, and/or a biologic agent. We are not currently aware of any other delayed-release prednisone medicine in development.

PRIMARY CARE BUSINESS UNIT

Market

Pain is a serious and costly public health concern. In 2010, the U.S. National Center for Health Statistics reported that approximately 30 percent of U.S. adults 18 years of age and over reported recent symptoms of pain, aching or swelling around a joint within the past 30 days.

Some of the most common and debilitating chronic inflammation and pain-related diseases are OA, RA and acute and chronic pain. According to National Health Interview Survey data analyzed by the U.S. Centers for Disease Control and Prevention, from 2010-2012, 52.5 million U.S. adults eighteen years of age and over had reported being diagnosed with some form of arthritis. With the aging of the U.S. population, the prevalence of arthritis is expected to rise by approximately forty percent by 2030, impacting sixty-seven million people in the United States.

Osteoarthritis

OA is a type of arthritis that is caused by the breakdown and eventual loss of the cartilage of one or more joints. Cartilage is a protein substance that serves as a cushion between the bones of the joints. Among the over 100 different types of arthritis conditions, OA is the most common and occurs more frequently with age. OA commonly affects the hands, feet, spine and large weight-bearing joints, such as the hips and knees. Symptoms of OA manifest in patients as joint pain, tenderness, stiffness, limited joint movement, joint cracking or creaking (crepitation), locking of joints and local inflammation. OA can also lead to joint deformity in later stages of the disease. Many drugs are used to treat the inflammation and pain associated with OA, including aspirin and other NSAIDs, such as ibuprofen, naproxen and diclofenac that have a rapid analgesic and anti-inflammatory response.

Rheumatoid Arthritis

The market for RA has been discussed above in the Rheumatology Business Unit section (refer to Page 10).

Ankylosing Spondylitis

AS is a type of arthritis that affects the spine. AS symptoms include pain and stiffness from the neck down to the lower back. The spine’s bones (vertebrae) may grow or fuse together, resulting in a rigid spine. These changes may be mild or severe, and may lead to a stooped-over posture. Early diagnosis and treatment helps control pain and stiffness and may reduce or prevent significant deformity.

Market Opportunity and Limitations of Existing Treatments

GI-Associated Adverse Events

NSAIDs are very effective at providing pain relief, including pain associated with OA and RA; however, there are significant upper GI-associated adverse events that can result from the use of NSAIDs. According to a 2004 article published in Alimentary Pharmacology & Therapeutics, significant GI side effects, including serious ulcers, afflict up to approximately twenty-five percent of all chronic arthritis patients treated with NSAIDs for three months, and OA and RA patients are two to five times more likely than the general population to be hospitalized for NSAID-related GI complications. It is estimated that NSAID-induced GI toxicity causes over 16,500 related deaths in OA and RA patients alone and over 107,000 hospitalizations for serious GI complications each year. In more than seventy percent of patients with these serious GI complications, there are no prior symptoms.

Despite the fact that GI ulcers are one of the most prevalent adverse events resulting from the use of NSAIDs in the United States, according to a 2006 article published in BMC Muskoskeletal Disorders, eleven observational studies indicated that physicians do not commonly co-prescribe GI protective agents to high-risk patients. Physicians prescribe concomitant therapy to only twenty-four percent of NSAID users, and studies show sub-optimal patient compliance with concomitant prophylaxis therapy. According to a 2003 article published in Alimentary Pharmacology & Therapeutics, in a study of 784 patients, thirty-seven percent of patients were non-compliant, a rate increasing to sixty-one percent in patients treated with three or more drugs. This noncompliance results in a substantial unmet clinical need, which we believe can be appropriately addressed with DUEXIS or VIMOVO, creating smarter solutions for both patients and physicians.

Topical NSAIDs

Within the NSAID market there exists a significant niche for topical NSAIDs, which are prescribed more than five million times per year. Topical NSAID treatment may be appropriate for some patients, such as patients who may benefit from the lower systemic exposure in a topical NSAID, patients with OA in just one joint such as the knee, patients who have trouble taking oral medications, or patients who are older. However, applying the correct dosage of the topical NSAID amount can often be a barrier to patient compliance, and there exists a market for a more convenient and more accurate application technique.

Our Solutions

DUEXIS

DUEXIS tablets are a proprietary, single-tablet combination containing a fixed-dose combination of ibuprofen, the most widely prescribed NSAID, and famotidine, a well-established GI agent used to treat dyspepsia, gastroesophageal reflux disease and active ulcers, in one pill. Based on clinical study results, DUEXIS has been proven to reduce the risk of ibuprofen-induced upper GI ulcers in patients taking ibuprofen for OA or RA.

Ibuprofen: One of the World’s Most Widely Prescribed NSAIDs

Ibuprofen continues to be one of the most widely prescribed NSAIDs worldwide. According to Intercontinental Marketing Services, or IMS, in the United States alone, there were over 42 million prescriptions written for ibuprofen in 2015. Ibuprofen’s flexible three times daily dosing allows it to be used for both chronic conditions such as arthritis and chronic back pain, and acute conditions such as sprains and strains.

Famotidine: A Safe and Effective GI Agent

Famotidine is the most potent marketed drug in the class of histamine-2 receptor antagonists, or H2RA. H2RAs are a class of drugs used to block the action of histamine on the cells in the stomach that secrete gastric acid. Famotidine was chosen as the ideal GI protectant to be combined with ibuprofen as it is a well-studied compound with an estimated 18.8 million patients treated worldwide that provides distinct advantages including:

- rapid onset of action; and
- well-tolerated with a low incidence of adverse drug reactions and a demonstrated safety margin of up to eight times the approved prescription dose for an extended period of greater than twelve months.

Although famotidine as a standalone product is not indicated for risk reduction of GI ulcers, two well-controlled clinical trials of famotidine formulated in DUEXIS found a significant decrease in the risk of developing upper GI ulcers, which in the clinical trials was defined as a gastric and/or duodenal ulcer in patients who are taking ibuprofen for those indications. Additionally, over-the-counter dosages of famotidine have been shown to be ineffective.

Benefits of a Fixed-Dose Combination Therapy

Numerous studies have demonstrated that fixed-dose combination therapy provides significant advantages over taking multiple pills. Specifically, fixed-dose combinations can reduce the number of pills, ensure that the correct dosage of each component is taken at the correct time and improve compliance, often associated with better treatment outcomes. DUEXIS has been formulated to provide an optimal dosing regimen of ibuprofen and famotidine together in the convenience of a single pill. Data shows that physicians co-prescribe GI protective agents less than twenty-five percent of the time when prescribing an NSAID. On occasions where a patient is co-prescribed a GI protective agent, data shows that after three prescriptions, sixty-one percent of patients no longer take a GI protective agent.

Commercial Status

DUEXIS is indicated for the relief of signs and symptoms of RA and OA and to decrease the risk of developing upper-GI ulcers (which in the clinical trials was defined as a gastric and/or duodenal ulcer) in patients who are taking ibuprofen for these indications. We began marketing DUEXIS to U.S. physicians in December 2011.

In June 2012, we licensed DUEXIS rights in Latin America to Grünenthal, a private company focused on the promotion of pain medicines.

PENNSAID 2%

PENNSAID 2% is a topical NSAID that is applied directly to the knee and is indicated for the treatment of pain of OA of the knee(s). PENNSAID 2% contains diclofenac sodium, a commonly prescribed NSAID to treat OA pain. PENNSAID 2% also includes dimethyl sulfoxide, or DMSO, a penetrating agent that helps ensure that diclofenac sodium is absorbed through the skin to the site of inflammation and pain. Topical NSAIDs such as PENNSAID 2% are an alternative to oral NSAID treatment because they reduce systemic exposure to a fraction of that provided by an oral NSAID. PENNSAID 2% is the only topical NSAID offered with the convenience of a metered-dose pump, which ensures that the patient will get the correct amount of PENNSAID 2% solution each time. PENNSAID 2% is easy to apply for patients because PENNSAID 2% is applied in two pumps, twice daily, delivering relief right to the site of OA knee pain.

Commercial Status

On January 16, 2014, the FDA approved PENNSAID 2% for the treatment of the pain of OA of the knee(s). We acquired the U.S. rights to PENNSAID 2% in October 2014, and began marketing PENNSAID 2% with our primary care sales force in early January 2015.

VIMOVO

VIMOVO is a proprietary, fixed-dose, delayed-release tablet. VIMOVO combines enteric-coated naproxen, an NSAID, surrounded by a layer of immediate-release esomeprazole magnesium surrounding the core. Naproxen has proven anti-inflammatory and analgesic properties and esomeprazole magnesium reduces the stomach acid secretions that can cause upper GI ulcers. Both naproxen and esomeprazole magnesium have well-documented and excellent long-term safety profiles and both medicines have been used by millions of patients worldwide. Based on clinical trial results, VIMOVO has been shown to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID associated gastric ulcers.

Naproxen: One of the World’s Most Widely Prescribed NSAIDs

Naproxen is another of the most widely prescribed NSAIDs worldwide. According to IMS, in the United States alone, there were more than seventeen million prescriptions written for naproxen in 2015. In addition, naproxen’s twice daily dosing allows it to be used for chronic conditions such as arthritis and AS.

Esomeprazole Magnesium: A Safe and Effective GI Agent

Esomeprazole magnesium, a gastroprotective agent, is a proton pump inhibitor, or PPI, that works by inhibiting the secretion of gastric acid thus decreasing the amount of acid in the stomach. PPIs are considered to be very potent inhibitors of acid secretion. Esomeprazole magnesium is indicated for reducing the risk of NSAID-induced gastric ulcers.

Benefits of a Fixed-Dose Combination Therapy

VIMOVO is specifically formulated to allow esomeprazole magnesium to achieve its gastroprotective impact before naproxen is released into the system. VIMOVO's design is intended to produce a sequential delivery of gastroprotective esomeprazole before exposure to naproxen. Data shows that physicians co-prescribe GI protective agents less than 25 percent of the time when prescribing an NSAID. On occasions where a patient is co-prescribed a GI protective agent, data shows that after three prescriptions, 61 percent of patients no longer take a GI protective agent.

Commercial Status

Following our acquisition of the U.S. rights to VIMOVO in November 2013, we began marketing VIMOVO in early January 2014. VIMOVO is indicated for the relief of signs and symptoms of OA, RA and AS and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers. VIMOVO is not interchangeable with the individual components of naproxen and esomeprazole magnesium.

MIGERGOT

MIGERGOT is indicated as therapy to abort or prevent vascular headaches, such as migraines, migraine variants or so-called "histaminic cephalalgia". MIGERGOT is not promoted by our sales representatives.

Competition

Our competitors in our primary care markets include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies and generic drug companies, although we are not currently aware of any other ibuprofen/famotidine combination medicine or naproxen/esomeprazole magnesium combination medicine in development.

DUEXIS and VIMOVO compete with other NSAIDs, including Celebrex® which was marketed by Pfizer Inc., and is also a generic medicine known as celecoxib and supplied by other pharmaceutical companies. Celecoxib is an NSAID that selectively inhibits the COX-2 enzyme and is an effective anti-arthritic agent that reduces the risk of ulceration compared to traditional NSAIDs such as ibuprofen. DUEXIS and VIMOVO also compete with TIVORBEX™ (indomethacin) capsules, marketed by Iroko Pharmaceuticals, LLC.

In general, DUEXIS and VIMOVO also face competition from the separate use of NSAIDs for pain relief and GI medications to address the risk of NSAID-induced ulcers. Use of these therapies separately in generic form may be less expensive than DUEXIS and VIMOVO. We expect to compete with the separate use of NSAIDs and ulcer medications primarily through DUEXIS' and VIMOVO's advantages in dosing convenience and patient compliance, and by educating physicians about such advantages. DUEXIS is the only NSAID medicine containing a histamine-2 receptor antagonist with an indication to reduce the risk of NSAID-induced upper GI ulcers and VIMOVO is the only NSAID medicine containing a PPI with an indication to reduce the risk of NSAID-induced ulcers. Data shows that physicians co-prescribe GI protective agents less than twenty-five percent of the time when prescribing an NSAID. On occasions where a patient is co-prescribed a GI protective agent, data shows that after three prescriptions, sixty-one percent of patients no longer take a GI protective agent.

PENNSAID 2% faces competition from generic versions of diclofenac sodium topical solutions which are priced significantly lower than the price we charge for PENNSAID 2%. PENNSAID 2% competes primarily with Diclofenac, a market leader in the topical NSAID category. We expect to compete with these other medicines primarily through PENNSAID 2%'s dosing convenience and patient compliance. Unlike the other two medicines that are dosed four times per day and require the patient to measure out the correct dose, only PENNSAID 2% is easy to apply with the convenience of twice-daily dosing and a metered-dose pump, which ensures that the patient will get the correct amount of PENNSAID 2% solution each time.

Distribution

Finished tablets of DUEXIS, VIMOVO, RAYOS, MIGERGOT, BUPHENYL and PROCYSBI, vials of ACTIMMUNE and KRYSTEXXA, bottles of RAVICTI, PENNSAID 2% and QUINSAIR and powder of BUPHENYL are shipped to central third-party logistics FDA-compliant warehouses for storage and distribution into the supply chain. Our third-party logistics providers specialize in integrated operations that include warehousing and transportation services that can be scaled and customized to our needs based on market conditions and the demands and delivery service requirements for our medicines and materials. Their services eliminate the need to build dedicated internal infrastructures that would be difficult to scale without significant capital investment. Our third-party logistics providers warehouse all medicines in controlled FDA-registered facilities. Incoming orders are prepared and shipped through an order entry system to ensure just in time delivery of the medicines.

Sales and Marketing

As of December 31, 2016, our sales force was composed of approximately 480 sales representatives consisting of approximately 20 orphan disease sales representatives, 100 rheumatology sales specialists and 360 primary care sales representatives.

Our orphan disease representatives focus on marketing our orphan medicines to a limited number of healthcare practitioners who specialize in fields such as pediatric immunology, allergy, infectious diseases and metabolic disorders to help them understand the potential benefits of our medicines. We have entered into, and may continue to enter into, agreements with third parties for commercialization of our medicines outside the United States.

Part of our commercial strategy for RAYOS and our primary care medicines is to offer physicians the opportunity to have their patients fill prescriptions through pharmacies participating in our HorizonCares patient access program. For commercial patients who are prescribed our primary care medicines or RAYOS, the HorizonCares program offers co-pay assistance when a third-party commercial payer covers a prescription but requires an eligible patient to pay a co-pay or deductible, and offers full subsidization when a third-party commercial payer rejects coverage for an eligible patient. During 2016, we entered into business arrangements with pharmacy benefit managers, or PBMs, and other payers to secure formulary status and reimbursement of our medicines, such as our arrangements with Express Scripts, Inc., CVS Caremark and Prime Therapeutics LLC. While we believe that this strategy will result in broader inclusion of certain of our primary care medicines on healthcare plan formularies, and therefore increase payer reimbursement and lower our cost of providing patient access programs, these arrangements generally require us to pay administrative and rebate payments to the PBMs and/or other payers and regardless of our agreements with the PBMs, the extent of formulary status and reimbursement will ultimately depend to a large extent upon individual healthcare plan formulary decisions.

We have a comprehensive compliance program in place to address adherence with various laws and regulations relating to our sales, marketing, and manufacturing of our medicines, as well as certain third-party relationships, including pharmacies. Specifically with respect to pharmacies, the compliance program utilizes a variety of methods and tools to monitor and audit pharmacies, including those that participate in our patient access programs, to confirm their activities, adjudication and practices are consistent with our compliance policies and guidance.

Manufacturing, Commercial and Supply Agreements

We have agreements with third parties for active pharmaceutical ingredients, or APIs, and manufacturing of our medicines, formulation and development services, fill, finish and packaging services, transportation, and distribution and logistics services for certain medicines. In most cases, we retain certain levels of safety stock or maintain alternate supply relationships that we can utilize without undue disruption of our manufacturing processes if a third party fails to perform its contractual obligations.

ACTIMMUNE

ACTIMMUNE is a recombinant protein that is produced by fermentation of a genetically engineered Escherichia coli bacterium containing the DNA which encodes for the human protein. Purification of the active drug substance is achieved by conventional column chromatography. The resulting active drug substance is then formulated as a highly purified sterile solution and filled in a single-use vial for subcutaneous injection, which is the ACTIMMUNE finished drug medicine. In support of its manufacturing process, we and Boehringer Ingelheim RCV GmbH & Co KG, or Boehringer Ingelheim, store multiple vials of the Escherichia coli bacterium master cell bank and working cell bank in order to ensure that it will have adequate backup should any cell bank be lost in a catastrophic event.

Boehringer Ingelheim Supply Agreement

In July 2013, Vidara and Boehringer Ingelheim entered into an exclusive supply agreement, which we assumed as a result of the Vidara Merger and amended effective as of June 1, 2015. Pursuant to the agreement, Boehringer Ingelheim manufactures the ACTIMMUNE active drug substance and commercial quantities of the ACTIMMUNE finished drug medicine. Boehringer Ingelheim is our sole source supplier for ACTIMMUNE active drug substance and finished drug medicine. Under the terms of this agreement, we are required to purchase minimum quantities of finished drug medicine of 75,000 vials per annum. Boehringer Ingelheim manufactures our commercial requirements of ACTIMMUNE on an annual basis, and based on our forecasts and the annual contractual minimum purchase quantity. The supply agreement has a term that runs until July 31, 2020 and which can be further renewed by agreement between parties. Under this supply agreement, either we or Boehringer Ingelheim may terminate the agreement for an uncured material breach by the other party or upon the other party's bankruptcy or insolvency.

In October 2016, we committed to purchase additional units of ACTIMMUNE from Boehringer Ingelheim in 2017. These additional units of ACTIMMUNE were intended to cover anticipated demand should the results of the Phase 3 trial, Safety, Tolerability and Efficacy of ACTIMMUNE Dose Escalation in Friedreich's Ataxia study, or STEADFAST, evaluating ACTIMMUNE for the treatment of Friedreich's ataxia, or FA, be successful and U.S. marketing approval for FA subsequently be received. In December 2016, we announced topline results from the study, and, based on the trial results, the decision to discontinue the STEADFAST program.

License Agreements

As a result of the Vidara Merger, we acquired a license agreement, as amended, with Genentech, Inc., or Genentech, who was the original developer of ACTIMMUNE. Under such agreement, we are or were obligated to pay royalties to Genentech on our net sales of ACTIMMUNE as follows:

- For the period from November 26, 2014 through May 5, 2018, a royalty in the twenty percent to thirty percent range for the first $3.7 million in net sales achieved in any calendar year, and in the one percent to nine percent range for all additional net sales in any year; and
- From May 6, 2018 and for so long as we continue to commercially sell ACTIMMUNE, an annual royalty in the low-single digits as a percentage of annual net sales.

Either Genentech or we may terminate the agreement if the other party becomes bankrupt or defaults, however, in the case of a default, the defaulting party has thirty days to cure the default before the license agreement may be terminated.

Under the terms of an assignment and option agreement with Connetics Corporation (which was the predecessor parent company to InterMune Pharmaceuticals Inc. and is now part of GlaxoSmithKline), or Connetics, we are obligated to pay royalties to Connetics on our net sales of ACTIMMUNE as follows:

- Low-single digits as a percentage of net sales of ACTIMMUNE in the United States.

RAVICTI

We have clinical and commercial supplies of glycerol phenylbutyrate API manufactured for us by two alternate suppliers, Helsinn Advanced Synthesis SA (Switzerland) and DSM Fine Chemicals Austria (now Patheon Austria GmbH & Co KG) on a purchase order basis. We have finished RAVICTI drug medicine manufactured by Lyne Laboratories, Inc. under a manufacturing agreement and we have an agreement in place for a fill/finish supplier, Halo Pharmaceuticals, Inc., for European supplies.

Ucyclyd Asset Purchase Agreement

As a result of the Hyperion acquisition, we acquired an asset purchase agreement with Ucyclyd Pharma, Inc., or Ucyclyd, pursuant to which we are obligated to pay to Ucyclyd tiered mid- to high- single digit royalties on our global net sales of RAVICTI. The asset purchase agreement cannot be terminated for convenience by either party. However, we have a license to certain Ucyclyd manufacturing technology, and Ucyclyd may have a license to certain of our technology, and the party granting a license is permitted to terminate the license if the other party fails to comply with any payment obligations relating to the license and does not cure such failure within a defined time period.

Brusilow License Agreement

As a result of the Hyperion acquisition, we acquired a license agreement with Saul W. Brusilow, M.D. and Brusilow Enterprises, Inc., or Brusilow, pursuant to which we license patented technology related to RAVICTI from Brusilow. Under such agreement, we are obligated to pay low-single digit royalties to Brusilow on net sales of RAVICTI that are covered by a valid claim of a licensed patent. The license agreement may be terminated for any uncured breach as well as bankruptcy. We may also terminate the agreement at any time by giving Brusilow prior written notice, in which case all rights granted to us would revert to Brusilow.

BUPHENYL

When Hyperion purchased BUPHENYL, Hyperion assumed all of Ucyclyd's rights and obligations under its manufacturing agreements for the medicine. We assumed these agreements when we acquired Hyperion. We purchase API for BUPHENYL from CU Chemie Uetikon GmbH and final manufacturing, testing and packaging of the medicine is provided by Pharmaceutics International Inc.

Amended and Restated Collaboration Agreement

Under the terms of an amended and restated collaboration agreement with Ucyclyd, we are obligated to pay to Ucyclyd tiered mid to high single-digit royalties on our net sales in the United States of BUPHENYL to UCD patients outside of the FDA approved labeled age range for RAVICTI.

PROCYSBI

PROCYSBI drug product is comprised of enteric coated beads of cysteamine bitartrate encapsulated in gelatin capsules. PROCYSBI drug product and API, cysteamine bitartrate, are manufactured on a contract basis by third parties.

Patheon Manufacturing Services Agreement

As a result of the Raptor acquisition, we assumed a manufacturing services agreement, as amended, with Patheon Pharmaceuticals Inc., or Patheon. Pursuant to the agreement, we must provide a rolling, non-binding forecast of PROCYSBI, with a portion of the forecast being a firm written order. The agreement has an initial term that runs until December 31, 2017 and which automatically renews for successive two year terms if not terminated at least eighteen months in advance. Notice of termination of the agreement was not given by any party by June 30, 2016, therefore the agreement will be in force until at least December 31, 2019.

Cambrex Profarmaco Milano Supply Agreement

As a result of the Raptor acquisition, we assumed an API supply agreement, as amended, with Cambrex Profarmaco Milano, or Cambrex. Pursuant to the agreement, we must provide rolling, non-binding forecasts, with a portion of the forecast being the minimum floor of the firm order that must be placed. The Cambrex supply agreement has an initial term that runs until November 30, 2020 and which automatically renews for successive two-year terms if not terminated at least one year in advance.

UCSD License Agreement

As a result of the Raptor acquisition, we assumed a license agreement, as amended, with The Regents of the University of California, San Diego, or UCSD. We must pay UCSD a royalty in the mid-single digits on net sales of PROCYSBI in countries where PROCYSBI is covered by a patent right, and a royalty in the low-single digits on net sales of PROCYSBI in countries where PROCYSBI is not covered by a patent right. We must pay UCSD a minimum

annual royalty in an amount less than $0.1 million. Royalties terminate upon the later of (a) the expiration date of the longest-lived patent rights on a country-by-country basis; and (b) ten years after first commercial sale of PROCYSBI. We may also be obligated to pay UCSD milestone payments for each orphan indication and for each non-orphan indication. We are also subject to diligence obligations relating to performing activities for specified indications, marketing licensed medicines in the United States, filling market demand for licensed medicines following commencement of marketing at any time during the agreement and obtaining all necessary governmental approvals for the manufacture, use and sale of licensed medicines.

QUINSAIR

QUINSAIR drug product, its API, levofloxacin hemihydrate, and the Zirela nebulizer device are all manufactured on a contract basis by third parties.

Teva Supply Agreement

The API is exclusively supplied by TEVA API Inc.. We must provide a twelve-month rolling forecast, and the first three months of this forecast is binding. The term of the TEVA supply agreement runs until April 11, 2021 with automatic one-year renewal periods unless notice is provided six months before termination.

Catalent Supply Agreement

QUINSAIR drug product is manufactured by Catalent Pharma Solutions, LLC. The term of the Catalent supply agreement runs until March 10, 2019. We must provide a twelve-month rolling forecast, and the first four months of this forecast is binding.

PARI Supply Agreement

Nebulizers are supplied by PARI in Starnberg, Germany. We are obligated to provide a twelve-month rolling forecast, and the first three months of this forecast is binding. The supply agreement runs until at least April 12, 2026.

RAYOS/LODOTRA

We rely on well-established third-party manufacturers for the manufacture of RAYOS/LODOTRA. We purchase the API for RAYOS/LODOTRA from Tianjin Tianyao Pharmaceuticals Co., Ltd. in China and from Sanofi Chimie SA in France. We have contracted with Jagotec AG, or Jagotec, for the production of RAYOS/LODOTRA tablets through its affiliate Vectura, and we entered into an agreement with Patheon for the packaging and assembling of RAYOS/LODOTRA.

Vectura and Jagotec Agreements

Development and License Agreement

In August 2004, we entered into a development and license agreement with Vectura, as successor in interest to SkyePharma, and Jagotec, a wholly owned subsidiary of Vectura, regarding certain proprietary technology and know-how owned by Vectura for the delayed-release of corticosteroids. Under the agreement, which was amended in August 2007, we received an exclusive, sub-licensable worldwide license to the oral formulation of any glucocorticoid, including prednisone, prednisolone, methylprednisolone and/or cortisone, with delayed-release technology covered by intellectual property rights and know-how owned by Vectura. We were also granted an option to acquire a royalty-free, exclusive and sub-licensable right to license and manufacture RAYOS/LODOTRA which we could exercise any time upon specified prior written notice, expiring no earlier than five years after the first launch of RAYOS/LODOTRA. We have exercised the option to acquire the manufacturing license, which became effective in April 2014.

In return for the grant of the license, Jagotec has the right to manufacture, package and supply RAYOS/LODOTRA to us in accordance with terms and conditions of a separate manufacturing and supply agreement we entered into with Jagotec. In addition, Jagotec is entitled to receive a single-digit percentage royalty on net sales of RAYOS/LODOTRA and on any sub-licensing income, which includes any payments not calculated based on the net sales of RAYOS/LODOTRA, such as license fees, and lump sum and milestone payments.

The agreement expires on a country-by-country basis, upon the expiration of the last patent rights for RAYOS/LODOTRA, which will occur between 2024 and 2028. In the event of expiration, the licenses under the agreement will be perpetual, fully paid-up and royalty-free. Either party may also terminate the agreement in the event of a liquidation or bankruptcy of the other party or upon an uncured breach by the other party.

Manufacturing and Supply Agreement

In August 2007, we entered into a manufacturing and supply agreement with Jagotec for RAYOS/LODOTRA. Under the agreement, which was amended in March 2011 and in January 2017, Jagotec or its affiliates manufacture and supply RAYOS/LODOTRA to us in bulk. The term of the agreement is to December 31, 2023, and the minimum purchase commitment is in force until that date. As of December 31, 2016, our total remaining minimum purchase commitment was approximately $6.9 million based on tablet pricing under the agreement as of that date, which amount is subject to volume and price adjustments due to, among other things, inflation, order quantities and launch and approval in certain EU countries. We also supply the prednisone API to Jagotec at our expense for use in the manufacture of RAYOS/LODOTRA.

We pay Jagotec, exclusive of any value added tax or similar governmental charges, a price for RAYOS/LODOTRA representing a negotiated mark-up over manufacturing costs. The price is adjusted annually to reflect changes in both manufacturing and materials costs as measured by the Ensemble price index. If Jagotec makes a major capital expenditure during the contract term to fulfill increased orders forecast by us, the price per unit will increase if the actual order falls short of the forecast.

KRYSTEXXA

KRYSTEXXA is a pegylated, recombinant protein that is produced by fermentation of a genetically engineered Escherichia coli bacterium containing the DNA which encodes for uricase. The cDNA coding for the uricase is based on mammalian sequences. Uricase is purified and is then PEGylated with a PEGylation agent to produce the bulk medicine, pegloticase. Pegylation and purification of the active drug substance is achieved by conventional column chromatography. The resulting highly purified sterile solution is filled in a single-use vial for intravenous infusion following dilution. In support of its manufacturing process, we store multiple vials of the Escherichia coli bacterium master cell bank and working cell bank at multiple locations in order to ensure that it will have adequate backup should any cell bank be lost in a catastrophic event.

NOF Supply Agreement

In August 2015, Crealta and NOF Corporation, or NOF, in Japan, entered into an exclusive supply agreement for the PEGylation agent used in the manufacture of KRYSTEXXA. Under the terms of this agreement, we are required to issue NOF forecasts of our requirements for the PEGylation agent, a portion of which are binding. The agreement expires in August 2020, however, either we or NOF may terminate the agreement for any reason upon 24 months' prior notice. Either we or NOF may also terminate the agreement upon a material breach, if not cured within a specified period of time, or in the event of the other party's insolvency. While there are no minimum purchase obligations under the agreement, we are required to use NOF as our exclusive supplier for the PEGylation agent, subject to certain exceptions if NOF is unable to supply the PEGylation agent.

Bio-Technology General (Israel) Supply Agreement

In March 2007, Savient Pharmaceuticals, Inc. (as predecessor in interest to Crealta), entered into a commercial supply agreement with Bio-Technology General (Israel) Ltd, or BTG Israel, for the production of the bulk KRYSTEXXA medicine, or bulk product. We assumed this agreement as part of the Crealta acquisition and amended the agreement in September 2016. Under this agreement, we have agreed to purchase certain minimum annual order quantities and are obligated to purchase at least 80 percent of our annual world-wide bulk product requirements from BTG Israel. The term of the agreement runs until December 31, 2030, and will automatically renew for successive three year periods unless earlier terminated by either party upon three years prior written notice. The agreement may be terminated earlier by either party in the event of a force majeure, liquidation, dissolution, bankruptcy or insolvency of the other party, uncured material breach by the other party or after January 1, 2024, upon three years prior written notice. Under the agreement if the manufacture of the bulk product is moved out of Israel, we may be required to obtain the approval of the Israeli Office of the Chief Scientist, or OCS, because certain KRYSTEXXA intellectual property was initially developed with a grant funded by the OCS and we may be required to pay the OCS additional amounts as a repayment for the OCS grant funding. We issue eighteen-month forecasts of the volume of KRYSTEXXA that we expect to order. The first six months of the forecast are considered binding firm orders.

Exelead PharmaSource Supply Agreement

In October 2008, Savient and Exelead, Inc. (formerly known as Sigma Tau PharmaSource, Inc. (as successor in interest to Enzon Pharmaceuticals, Inc.)), or Exelead, entered into a commercial supply agreement for the packaging and supply of the final drug medicine KRYSTEXXA, which we acquired as part of the Crealta acquisition. This agreement remains in effect until terminated, and either we or Exelead may terminate the agreement with three years notice, given thirty days prior to the agreement anniversary date. Either we or Exelead may also terminate the agreement upon a material default, if not cured within a specified period of time, or in the event of the other party’s insolvency or bankruptcy.

Duke University and Mountain View Pharmaceutical License Agreement

In August 1998, Savient entered into an exclusive, worldwide license agreement with Duke University, or Duke, and Mountain View Pharmaceuticals Inc., or MVP. Duke developed the recombinant uricase enzyme used in KRYSTEXXA and MVP developed the PEGylation technology used in the manufacture of KRYSTEXXA. Duke and MVP may terminate the agreement if we commit fraud or for our willful misconduct or illegal conduct; upon our material breach of the agreement, if not cured within a specified period of time; upon written notice if we have committed two or more material breaches under the agreement; or in the event of our bankruptcy or insolvency. Under the terms of the agreement, we are obligated to pay Duke a mid-single digit percentage royalty on our global net sales of KRYSTEXXA and a low-double digit percentage royalty on any global sublicense revenue. We are also obligated to pay MVP a mid-single digit percentage royalty on our net sales of KRYSTEXXA outside of the United States and a low-double digit percentage royalty on any sublicense revenue outside of the United States. Royalties terminate upon last to expire of licensed patents on a country-by-country basis, and royalties are reduced by a mid-double digit percentage in countries that never had patents.

DUEXIS

We purchase DUEXIS in final, packaged form exclusively from Sanofi-Aventis U.S. LLC, or Sanofi, for our commercial requirements in North America. The first API in DUEXIS is ibuprofen in a direct compression blend called DC85 and is supplied to Sanofi by BASF Corporation, or BASF, in Bishop, Texas. The second API in DUEXIS is famotidine, which is available from a number of international suppliers. Famotidine is currently sourced from two manufacturers, Dr. Reddy’s in India and also from Quimica Syntetica (Chemo) in Spain. We currently receive both APIs in powder form and each is blended with a number of U.S. Pharmacopeia inactive ingredients.

BASF Contract

In July 2010, we entered into a contract with BASF for the purchase of DC85, which was subsequently amended effective as of January 2016. Pursuant to the agreement, we are obligated to source a significant majority of our commercial demand for DC85 from BASF. The contract expires in December 2018. Thereafter, the agreement automatically renews for successive renewal terms of three years each until terminated by either party giving specified prior written notice to the other party. Either party may also terminate the agreement in the event of uncured breach by the other party.

Manufacturing and Supply Agreement with Sanofi

In May 2011, we entered into a manufacturing and supply agreement with Sanofi, which was amended in September 2013. Pursuant to the agreement, Sanofi is obligated to manufacture and supply DUEXIS to us in final, packaged form, and we are obligated to purchase DUEXIS exclusively from Sanofi for our commercial requirements in North America and certain countries and territories in Europe, including the EU member states and Scandinavia, and South America. Sanofi must acquire the components necessary to manufacture DUEXIS, including the APIs, and is obligated to acquire all DC85 under the terms of our agreements with suppliers, including the current BASF contract. In order to allow Sanofi to perform its obligations under the agreement, we granted Sanofi a non-exclusive license to our related intellectual property. The price for DUEXIS under the agreement varies depending on the volume of DUEXIS we purchase and is subject to annual adjustments to reflect changes in costs as measured by the Producer Price Index published by the U.S. Department of Labor, Bureau of Labor Statistics, and certain other changes and events set forth in the agreement. We have paid for the purchase and installation of equipment necessary to manufacture DUEXIS tablets, and Sanofi is obligated to pay the costs of routine maintenance of the equipment. Upon expiration or termination of the agreement we may also be obligated to reimburse Sanofi for the depreciated net book value of any other equipment purchased by Sanofi in order to fulfill its obligations under the agreement.

The agreement term extends until May 2019, and automatically extends for successive two-year terms unless terminated by either party upon two years prior written notice. Either party may terminate the agreement upon thirty days prior written notice to the other party in the event of breach by the other party that is not cured within thirty days of notice (which notice period may be longer in certain, limited situations) or in the event we lose regulatory approval to market DUEXIS in all countries worldwide, and either party may terminate the agreement without cause upon two years prior written notice to the other party at any time after the third anniversary of the first commercial sale of DUEXIS in any country worldwide.

VIMOVO

AstraZeneca License Agreement

In November 2013, we entered into a license agreement with AstraZeneca, or the AstraZeneca license agreement, pursuant to which AstraZeneca granted us an exclusive license under certain intellectual property (including patents, know-how, trademarks, copyrights and domain names) of AstraZeneca and its affiliates to develop, manufacture and commercialize VIMOVO in the United States. AstraZeneca also granted us a non-exclusive license under certain intellectual property of AstraZeneca and its affiliates to manufacture, import, export and perform research and development activities with respect to VIMOVO outside the United States but solely for purposes of commercializing VIMOVO in the United States. In addition, AstraZeneca granted us a non-exclusive right of reference and use under certain regulatory documentation controlled by AstraZeneca and its affiliates to develop, manufacture and commercialize VIMOVO in the United States and to manufacture, import, export and perform research and development activities with respect to VIMOVO outside the United States but solely for purposes of commercializing VIMOVO in the United States.

Under the AstraZeneca license agreement, we granted AstraZeneca a non-exclusive sublicense under such licensed intellectual property and a non-exclusive right of reference under certain regulatory documentation controlled by us to manufacture, import, export and perform research and development activities with respect to VIMOVO in the United States but solely for purposes of commercializing VIMOVO outside the United States.

Under the AstraZeneca license agreement, we and our affiliates are subject to certain limitations and restrictions on our ability to develop, commercialize and seek regulatory approval with respect to VIMOVO or other medicines that contain gastroprotective agents in a single fixed combination oral solid dosage form with NSAIDs (excluding DUEXIS). These limitations and restrictions include, among other things, restrictions on indications for which we may commercialize VIMOVO or any such other medicines, restrictions on our ability to develop or seek regulatory

approval with respect to such other medicines that contain esomeprazole, restrictions on our ability to develop or seek regulatory approval for VIMOVO for any indications other than the indications for which NSAIDs are indicated, and restrictions on our marketing activities with respect to VIMOVO and any such other medicines.

The AstraZeneca license agreement continues in full force and effect until terminated in accordance with its terms. Under the AstraZeneca license agreement, the parties may terminate upon mutual written agreement by the parties, or either party may terminate rights granted to us with respect to licensed trademarks and licensed domain names under the AstraZeneca license agreement upon uncured material breach by the other party of certain specified provisions of the AstraZeneca license agreement.

Amended and Restated Collaboration and License Agreement with Aralez; Letter Agreement with AstraZeneca and Aralez

We entered into a license agreement with Pozen Inc., who subsequently entered into a business combination with Tribute Pharmaceuticals Canada Inc. to become known as Aralez Pharmaceuticals Inc., or Aralez. Under this agreement, we were granted an exclusive, royalty-bearing license under certain of Aralez's intellectual property in the United States to manufacture, develop and commercialize VIMOVO and other medicines controlled by us that contain gastroprotective agents in a single fixed combination oral solid dosage form with NSAIDs, excluding DUEXIS, in the United States.

Under the Aralez license agreement, we are required to pay Aralez a flat ten percent royalty based on net sales of VIMOVO and such other medicines sold by us, our affiliates or sublicensees during the royalty term, subject to minimum annual royalty obligations of $7.5 million, which minimum royalty obligations will continue for each year during which one of Aralez's patents covers such medicines in the United States and there are no competing medicines in the United States. The royalty rate may be reduced to a mid-single digit royalty rate as a result of loss of market share to competing medicines. Our obligation to pay royalties to Aralez will expire upon the later of (a) expiration of the last-to-expire of certain patents covering such medicines in the United States, and (b) ten years after the first commercial sale of such medicines in the United States. In addition, we will be obligated to reimburse Aralez for costs, including attorneys' fees, incurred by Aralez in connection with VIMOVO patent litigation moving forward, subject to agreed caps.

We are responsible for, and are required to use diligent and reasonable efforts directed to commercializing VIMOVO or another qualified medicine in the United States. We also own and maintain all regulatory filings and marketing approvals in the United States for any such medicines, including all investigational new drugs, or INDs, and new drug applications, or NDAs, for VIMOVO. Aralez covenanted that it will not at any time prior to the expiration of the royalty term, and will ensure that its affiliates do not, directly or indirectly, develop or commercialize or license any third party to develop or commercialize certain competing medicines in the United States.

The Aralez license agreement, unless earlier terminated, will expire upon expiration of the royalty term for all such medicines in the United States. Either party has the right to terminate the agreement upon uncured material breach by the other party or upon the bankruptcy or similar proceeding of the other party. We also have the right to terminate the Aralez license agreement for cause upon certain defined medicine failures.

In November 2013, we, AstraZeneca and Aralez entered into a letter agreement in which Aralez consented to AstraZeneca's assignment of the Aralez license agreement to us and that addresses the rights and responsibilities of the parties in relation to the Aralez license agreement and the amended and restated collaboration and license agreement between Aralez and AstraZeneca for territories outside the United States, or the Aralez-AstraZeneca license agreement. Under the letter agreement, we and AstraZeneca agreed to pay Aralez milestone payments upon the achievement by us and AstraZeneca, collectively, of certain annual aggregate global net sales thresholds ranging from $550.0 million to $1.25 billion with respect to medicines licensed by Aralez to us under the Aralez license agreement and to AstraZeneca under the Aralez-AstraZeneca license agreement. The aggregate milestone payment amount that may be owed by AstraZeneca and us, collectively, under the letter agreement is $260.0 million, with the amount payable by each of us and AstraZeneca with respect to each milestone to be based upon the proportional sales achieved by each of us and AstraZeneca, respectively, in the applicable year.

The letter agreement will terminate with respect to Aralez and us upon the termination of the Aralez license agreement.

Patheon Agreement

In November 2013, we entered into a master manufacturing services agreement and product agreement, or, collectively, the Patheon manufacturing agreement, with Patheon who was AstraZeneca's contract manufacturer of VIMOVO, for the manufacture and supply of VIMOVO. Under the Patheon manufacturing agreement, we agreed to purchase a specified percentage of our VIMOVO requirements for the United States from Patheon or its affiliates. In addition, under the terms of the Patheon manufacturing agreement, we are able to enter into individual product agreements with Patheon for the manufacture of specific medicines in addition to VIMOVO if agreed by us and Patheon.

Pursuant to the Patheon manufacturing agreement, we are required to supply Patheon with any active materials for VIMOVO. We must pay an agreed price for final, packaged VIMOVO supplied by Patheon subject to adjustments, including certain unilateral adjustments by Patheon, such as annual adjustments for inflation and adjustments to account for certain increases in the cost of components of VIMOVO other than active materials.

The Patheon manufacturing agreement will be effective until December 31, 2019 and will automatically renew for successive terms of three years each if there is any product agreement in effect, unless either party gives written notice to the other party of its intention to terminate the agreement at least twenty-four months prior to the end of the then current term. Either party may terminate the Patheon manufacturing agreement or any product agreement early for uncured material breach by the other party or upon the other party's bankruptcy or insolvency. We may terminate any product agreement if any regulatory authority takes any action or raises any objection that prevents us from commercializing the medicines. Additionally, Patheon may terminate the Patheon manufacturing agreement or any product agreement early if we assign our rights or obligations under the Patheon manufacturing agreement or such product agreement to a competitor of Patheon or to a party that, in the reasonable opinion of Patheon, is not a credit worthy substitute for us, or in certain other circumstances where we assign the Patheon manufacturing agreement or product agreement without Patheon's consent.

Divis Agreement

In March 2014, we entered into a manufacturing and supply agreement with Divis Laboratories Limited, or Divis, in India for the supply of naproxen. Our contract term with Divis runs through December 2018, with provisions for a three-year extension at our sole option upon written notice at least six months prior to expiration of the then current term.

Minakem Agreement

In March 2014, we entered into a manufacturing and supply agreement with Minakem Holding SAS, or Minakem, in France for the supply of esomeprazole magnesium trihydrate. Our contract term with Minakem runs through December 2018, with provisions for a three-year extension at our sole option upon written notice at least six months prior to expiration of the then current term.

PENNSAID 2%

Nuvo Supply Agreement

In October 2014, in connection with the acquisition of the U.S. rights to PENNSAID 2% from Nuvo, we entered into an exclusive supply agreement with Nuvo, which was amended in February 2016, under which Nuvo will manufacture and supply PENNSAID 2% to us. We have committed to a binding purchase order to Nuvo for delivery of PENNSAID 2%. In addition, at least ninety days prior to the first day of each calendar month during the term of the supply agreement, we are required to submit a binding written purchase order to Nuvo for PENNSAID 2% in minimum batch quantities. The term of our supply agreement is through December 31, 2029, but the agreement may be terminated earlier by either party for any uncured material breach by the other party of its obligations under the supply agreement or upon the bankruptcy or similar proceeding of the other party.

A key excipient used in PENNSAID 2% as a penetration enhancer is DMSO. We and Nuvo rely on a sole proprietary form of DMSO for which we maintain a substantial safety stock. However, should this supply become inadequate, damaged, destroyed or unusable, we and Nuvo may not be able to qualify a second source.

MIGERGOT

MIGERGOT drug product is ergotamine tartrate and caffeine-containing suppositories. The APIs, ergotamine tartrate and caffeine, are sourced from Teva in Czech Republic and from BASF in Germany, respectively. G&W Laboratories Inc., or G&W, performs the sourcing and procurement of the APIs. MIGERGOT drug product is manufactured by G&W in South Plainfield, New Jersey under a supply agreement that expires on December 31, 2023.

Customers and Information About Geographic Areas

Information regarding our total revenues attributed to United States and non-United States sources in the years ended December 31, 2016, 2015 and 2014, as well as the location of our long-lived assets, is included in Note 13 to our consolidated financial statements included in Item 15 in this Annual Report on Form 10-K.

Research and Development

We devote significant resources to research and development activities associated with our current branded medicines. For the years ended December 31, 2016, 2015 and 2014, we incurred $60.7 million, $41.9 million and $17.5 million, respectively, in research and development expenses.

ACTIMMUNE

In July 2015, we announced our collaboration with Fox Chase Cancer Center to study ACTIMMUNE in combination with PD-1/PD-L1 inhibitors in various forms of cancer including advanced urothelial carcinoma (bladder cancer) and renal cell carcinoma (kidney cancer). Pre-clinical cell line research has indicated that interferon gamma enhances cellular PD-L1 expression on endothelial cells (inner lining of the blood vessel) and on some tumor cells. By enhancing cellular PD-L1 expression on tumor cells, interferon gamma may promote or enhance the effect of the PD-1 or PD-L1 inhibitors. In December 2015, we announced that an investigator-initiated Phase 1 clinical study had been initiated to evaluate ACTIMMUNE in combination with OPDIVO® (nivolumab), marketed by Bristol-Meyers Squibb, in advanced solid tumors. The Phase 1 open label study will evaluate the combination of ACTIMMUNE and nivolumab in patients with advanced solid tumors who have progressed on at least one prior systemic therapy, which may include prior immunotherapy. Patients will be treated with a one week induction phase of ACTIMMUNE (starting dose 50 mcg/m^2 subcutaneously every other day), followed by a combination phase with ACTIMMUNE and nivolumab (3 mg/kg intravenously) for three cycles, followed by a single-agent phase of nivolumab alone for up to one year. The study will primarily assess the safety and tolerability of the combination of ACTIMMUNE and nivolumab. Secondary objectives, including overall response rate, progression free survival and overall survival, will also be assessed, as will various correlative analyses. Initial subject enrollment will occur using a modified 3+3 design, and if endpoints for safety (using dose-limiting toxicity criteria) are met, expansion cohorts in renal cell carcinoma and urothelial carcinoma are planned for up to fifteen patients per cohort. On February 23, 2017, at the American Society for Clinical Oncology - Society for Immunotherapy of Cancer meeting, investigators from Fox Chase Cancer Center presented safety data from the first two cohorts of the Phase 1 dose escalation trial evaluating ACTIMMUNE as part of a combination therapy in solid tumors for certain cancers. The preliminary data showed that combination therapy of ACTIMMUNE with nivolumab, a PD-1 inhibitor, was safe and well-tolerated in the first two cohorts. The third cohort of patients receiving ACTIMMUNE is still under study.

We are supporting Indiana University to study ACTIMMUNE in the treatment of type 2 osteopetrosis, autosomal dominant osteopetrosis, or ADO2. ADO2 is a genetic condition characterized by generalized osteosclerosis predominating in some skeletal sites such as the spine and pelvis. The short term, open label treatment trial in ADO2 patients aims to determine if administration of ACTIMMUNE increases biochemical markers of bone turnover, and thus determine if the medicine can completely or partially reverse the defective osteoclastic bone resorption in ADO2 patients. The clinical study is expected to run over a period of three years, and commenced in July 2016.

On December 8, 2016, we announced that the STEADFAST study evaluating ACTIMMUNE for the treatment of FA, did not meet its primary endpoint of a statistically significant change from baseline in the modified Friedreich's Ataxia Rating Scale at twenty-six weeks versus treatment with placebo. In addition, the secondary endpoints did not meet statistical significance. No new safety findings were identified on initial review of data other than those already noted in the ACTIMMUNE prescribing information for approved indications. We, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and the Friedreich's Ataxia Research Alliance Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study.

RAVICTI

We are in the process of seeking approval for label expansions for RAVICTI, with assessments in progress studying the use of RAVICTI in patients both from two months to two years (sNDA submitted on June 29, 2016) and from

birth to two months (targeted sNDA submission in the first quarter of 2018). Current FDA approval is for patients from two years of age and older only. In patients with UCDs for which RAVICTI is an FDA-approved medicine, there is a variable age of diagnosis (from newborn to adulthood), and the severity of the disease can be associated with the age of onset and enzymatic deficit. However, a prompt diagnosis and careful management of the disease can lead to good clinical outcomes.

RAYOS

In November 2015, we announced our collaboration with the ALR to study the effect of RAYOS on the fatigue experienced by SLE patients. SLE is a chronic autoimmune disease that causes inflammation and pain in the joints and muscles, as well as overall fatigue. RAYOS is currently indicated for patients with SLE. The first study planned as part of the collaboration is an investigator-initiated, randomized, double-blind, active comparator, cross-over study in which patients will be randomized to receive either prednisone for three months or RAYOS at 10 p.m. for three months, and then switched to the alternative medication for an additional three months. Approximately sixty-two patients across twenty-five sites will be enrolled in the United States. Fatigue will be measured by the Functional Assessment of Chronic Illness Therapy-Fatigue and the Fatigue Severity Scale, as well as the Vitality scale of the Medical Outcome Study thirty-six-item short form health survey. The study is expected to start in the first quarter of 2017.

KRYSTEXXA

In January 2016, following our acquisition of Crealta, we assumed responsibility for a study designed to test the potential reduction of immunogenicity in KRYSTEXXA patients, known as the Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect, or TRIPLE, study. The TRIPLE study is an investigator-initiated, post-market interventional, exploratory open-label, multicenter adaptive design study of approximately fifty-three patients to evaluate the effectiveness of a sixteen-week high zone tolerance regimen of KRYSTEXXA on response to therapy (serum uric acid <6 mg/dL) in adult hyperuricemic patients, < 120 kg and ≥ 120 kg in weight, with gout refractory to conventional therapy. We are also developing a potential registration study to expand the label should the TRIPLE study show positive results. Success in the TRIPLE study and the subsequent registration study would have the potential to significantly expand the patient population and usage of KRYSTEXXA.

As part of the TRIPLE study, initial, more frequent dosing is being examined to determine if this reduces antibody formation by inducing antigen specific non-responsiveness. This would prevent the formation of anti-pegloticase antibodies and prevent the loss of drug response. This involves evaluating the drug’s lowest trough level, which pharmacokinetically occurs between the first and second doses. Increasing this trough level should suppress the high titer antibody formation. Current labelling states that KRYSTEXXA should be given every two weeks. This study adds one extra dose that occurs one week after the initial dose.

Intellectual Property

Our objective is to aggressively patent the technology, inventions and improvements that we consider important to the development of our business. We have a portfolio of patents and applications based on clinical and pharmacokinetic/pharmacodynamic modeling discoveries, and our novel formulations. We intend to continue filing patent applications seeking intellectual property protection as we generate anticipated formulation refinements, new methods of manufacturing and clinical trial results.

We will only be able to protect our technologies and medicines from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them. As such, our commercial success will depend in part on receiving and maintaining patent protection and trade secret protection of our technologies and medicines as well as successfully defending these patents against third-party challenges.

We have licenses to U.S. patents covering ACTIMMUNE. If not otherwise invalidated, those patents expire in 2022. We continue to prosecute and pursue patent protection to obtain additional patent coverage on ACTIMMUNE and its uses.

We have U.S. and foreign patents and patent applications covering PROCYSBI, as well as licenses from the University of California, San Diego to U.S. and foreign patents and patent applications covering PROCYSBI. If not

otherwise invalidated, those patents expire between 2027 and 2034. We continue to prosecute and pursue patent protection to obtain additional patent coverage on PROCYSBI and its uses.

PROCYSBI received marketing authorization in September 2013 from the EC for marketing in the EU as an orphan medicinal product for the management of proven nephropathic cystinosis.

PROCYSBI received seven years of market exclusivity, through 2020, for patients six years and older as an orphan drug in the United States, and ten years of market exclusivity, through 2023, as an orphan drug in Europe.

We also have U.S. and foreign patents and patent applications covering QUINSAIR, as well as licenses from PARI to U.S. and foreign patents and patent applications covering QUINSAIR. If not otherwise invalidated, those patents expire between 2020 and 2037. We continue to prosecute and pursue patent protection to obtain additional patent coverage on QUINSAIR and its uses.

QUINSAIR received ten years of market exclusivity in the EU, beginning with its March 2015 marketing authorization.

We also have an exclusive license to U.S. and foreign patents from Brusilow Enterprises LLC covering RAVICTI which expire in the United States in 2018 and if extended, in certain countries in Europe in 2021. We also have ownership of U.S. and foreign patents and patent applications covering RAVICTI. If not otherwise invalidated, those patents expire between 2030 and 2032. We continue to prosecute and pursue patent protection to obtain additional patent coverage on RAVICTI and its uses.

In the United States, RAVICTI has been granted seven years of orphan drug exclusivity, which will expire in 2020. In the EU, RAVICTI received ten years of marketing exclusivity protection, beginning with its December 2015 marketing authorization.

We also have licenses to U.S. and foreign patents and applications covering KRYSTEXXA. If not otherwise invalidated, those patents expire between 2019 and 2030. We continue to prosecute and pursue patent protection to obtain additional patent coverage on KRYSTEXXA and its uses.

In the United States, KRYSTEXXA has received twelve years of biologic exclusivity, expiring in 2022, and seven years of orphan drug exclusivity, expiring in September 2017.

We have an exclusive license to U.S. and foreign patents and patent applications from Vectura covering RAYOS/LODOTRA. If not otherwise invalidated, those in-licensed patents expire between 2024 and 2028. We continue to prosecute and pursue additional patent coverage on RAYOS/LODOTRA and its uses. However, under the Settlement Agreement with Actavis Laboratories FL, Inc. (formerly known as Watson Laboratories, Inc. – Florida), or Actavis, Actavis may enter the market on December 23, 2022, or earlier under certain circumstances.

In the EU, LODOTRA has received ten years of marketing exclusivity protection, beginning with its March 2009 marketing authorization in Germany.

We have multiple patents and patent applications related to DUEXIS. Unless otherwise invalidated, those patents expire in 2026. However, under the license agreement with Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc., or collectively Par, Par may enter the market on January 1, 2023, or earlier under certain circumstances.

We also have ownership of U.S. patents and patent applications covering PENNSAID 2% from Nuvo. We also co-own other U.S. patent applications with Mallinckrodt LLC. If not otherwise invalidated, those patents expire between 2027 and 2030. However, under the settlement agreements with Perrigo Company plc, or Perrigo, Taro Pharmaceuticals USA, Inc. and Taro Pharmaceutical Industries, Ltd., or collectively Taro, Amneal Pharmaceuticals LLC, or Amneal, and Teligent, Inc., or Teligent, Perrigo, Taro, Amneal, and/or Teligent may enter the market on January 10, 2029, or earlier under certain circumstances. We continue to prosecute and pursue patent protection in the United States to obtain additional patent coverage on PENNSAID 2% and its uses.

We also have licenses to U.S. patents and patent applications and trademarks covering VIMOVO from Aralez and AstraZeneca. We co-own other U.S. patents and patent applications with Aralez. If not otherwise invalidated, those in-licensed patents expire between 2018 and 2031. We continue to prosecute and pursue patent protection in the United States to obtain additional patent coverage on VIMOVO and its uses.

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The patent positions of life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States or other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- we or our licensors might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that none of our pending patent applications or the pending patent applications of our licensors will result in issued patents;
- our issued patents and the issued patents of our licensors may not provide a basis for commercially viable drugs, or may not provide us with any competitive advantages, or may be challenged and invalidated by third parties;
- we may not be successful in any patent litigation to enforce our patent rights, including our pending patent litigation regarding, PENNSAID 2%, RAVICTI and/or VIMOVO;
- we may not develop additional proprietary technologies or medicine candidates that are patentable; or
- the patents of others may have an adverse effect on our business.

For a description of our legal proceedings, see Note 16 of the Notes to Consolidated Financial Statements, included in Item 15 of this Annual Report on Form 10-K.

Third-Party Coverage and Reimbursement

In both U.S. and foreign markets, our ability to commercialize our medicines successfully depends in significant part on the availability of coverage and adequate reimbursement to healthcare providers from third-party payers, including, in the United States, government payers such as the Medicare and Medicaid programs, managed care organizations and private health insurers. Third-party payers are increasingly challenging the prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. This is especially true in markets where over-the-counter and generic options exist. Even if coverage is made available by a third-party payer, the reimbursement rates paid for covered medicines might not be adequate. For example, third-party payers may use tiered coverage and may adversely affect demand for our medicines by not covering our medicines or by placing them in a more expensive formulary tier relative to competitive medicines (where patients have to pay relatively more out of pocket than for medicines in a lower tier). We cannot be certain that our medicines will be covered by third-party payers or that such coverage, where available, will be adequate, or that our medicines will successfully be placed on the list of drugs covered by particular health plan formularies. Many states have also created preferred drug lists and include drugs on those lists only when the manufacturers agree to pay a supplemental rebate. The industry competition to be included on such formularies and preferred drug lists often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payers may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other therapeutic alternative is available. In addition, because each third-party payer individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming and costly process. We may be required to provide scientific and clinical support for the use of any medicine to each third-party payer separately with no assurance that approval would be obtained, and we may need to conduct pharmacoeconomic studies to demonstrate the cost effectiveness of our medicines for formulary coverage and reimbursement. Even with studies, our medicines may be considered less safe, less effective or less cost-effective than competitive medicines, and third-party payers may not provide coverage and adequate reimbursement for our medicines or our medicine candidates. These pricing and reimbursement pressures may create negative perceptions to any medicine price increases, or limit the amount we may be able to increase our medicine prices, which may adversely affect our medicine sales and results of operations. Where coverage and reimbursement are not adequate, physicians may limit how much or under what circumstances they will prescribe or administer such medicines, and patients may decline to

purchase them. This, in turn, could affect our ability to successfully commercialize our medicines and impact our profitability, results of operations, financial condition, and future success.

The U.S. market has seen a trend in which retail pharmacies have become increasingly involved in determining which prescriptions will be filled with the requested medicine or a substitute medicine, based on a number of factors, including potentially perceived medicine costs and benefits, as well as payer medicine substitution policies. Many states have in place requirements for prescribers to indicate “dispense as written” on their prescriptions if they do not want pharmacies to make medicine substitutions; these requirements are varied and not consistent across states. We may need to increasingly spend time and resources to ensure the prescriptions written for our medicines are filled as written, where appropriate.

Coverage policies, third-party reimbursement rates and medicine pricing regulation have been subject to significant change, and may change further at any time, particularly given recent political focus on the pharmaceutical industry. Even if favorable coverage and adequate reimbursement status is attained for one or more medicines, less favorable coverage policies and reimbursement rates may be implemented in the future.

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose extensive requirements upon the clinical development, pre-market approval, manufacture, labeling, marketing, promotion, pricing, import, export, storage and distribution of medicines. These agencies and other regulatory agencies regulate research and development activities and the testing, approval, manufacture, quality control, safety, effectiveness, labeling, storage, recordkeeping, advertising and promotion of drugs and biologics. Failure to comply with applicable FDA or foreign regulatory agency requirements may result in Warning Letters, fines, civil or criminal penalties, additional reporting obligations and/or agency oversight, suspension or delays in clinical development, recall or seizure of medicines, partial or total suspension of production or withdrawal of a medicine from the market.

In the United States, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act and its implementing regulations and biologics additionally under the Public Health Service Act. The process required by the FDA before medicine candidates may be marketed in the United States generally involves the following:

- submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated annually;
- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with the FDA’s Good Laboratory Practice, or GLP, regulations;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the medicine candidate for each proposed indication;
- submission to the FDA of an NDA or biologics license application, or BLA, as appropriate, after completion of all pivotal clinical trials to demonstrate the safety, purity and potency of the medicine candidate for the indication for use;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities to assess compliance with the FDA’s current good manufacturing practices regulations for pharmaceuticals, or cGMPs; and
- FDA review and approval of an NDA or BLA prior to any commercial marketing or sale of the medicine in the United States.

The development and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our medicine candidates will be granted on a timely basis, if at all.

The results of preclinical tests (which include laboratory evaluation as well as GLP studies to evaluate toxicity in animals) for a particular medicine candidate, together with related manufacturing information and analytical data, are submitted as part of an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. IND submissions may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during medicine development. Further, an independent institutional review board, or IRB, for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the study until completed. The FDA, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive good clinical practice regulations and regulations for informed consent and privacy of individually identifiable information. Similar requirements to the U.S. IND are required in the EEA and other jurisdictions in which we may conduct clinical trials.

Clinical Trials. For purposes of NDA or BLA submission and approval, clinical trials are typically conducted in the following sequential phases, which may overlap:

- Phase 1. Studies are initially conducted in a limited population to test the medicine candidate for safety, dose tolerance, absorption, distribution, metabolism, and excretion, typically in healthy humans, but in some cases in patients.
- Phase 2. Studies are generally conducted in a limited patient population to identify possible adverse effects and safety risks, explore the initial efficacy of the medicine for specific targeted indications and to determine dose range or pharmacodynamics. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3. These are commonly referred to as pivotal studies. When Phase 2 evaluations demonstrate that a dose range of the medicine is effective and has an acceptable safety profile, Phase 3 clinical trials are undertaken in large patient populations to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial centers.
- Phase 4. The FDA may approve an NDA or BLA for a medicine candidate, but require that the sponsor conduct additional clinical trials to further assess the medicine after approval under a post marketing commitment or post marketing requirement. In addition, a sponsor may decide to conduct additional clinical trials after the FDA has approved a medicine. Post-approval trials are typically referred to as Phase 4 clinical trials.

The results of drug development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA or BLA, as appropriate. Applications also must contain extensive chemistry, manufacturing and control information. Applications must be accompanied by a significant user fee. Once the submission has been accepted for filing, the FDA's goal is to review applications within 12 months of submission or, if the application relates to an unmet medical need in a serious or life-threatening indication, eight months from submission. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA will typically conduct a pre-approval inspection of the manufacturer to ensure that the medicine can be reliably produced in compliance with cGMPs and will typically inspect certain clinical trial sites for compliance with good clinical practice, or GCP. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. The FDA may deny approval of an application by issuing a Complete Response Letter if the applicable regulatory criteria are not satisfied. A Complete Response Letter may require additional clinical data and/or trial(s), and/or other significant, expensive and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we or our collaborators interpret data. Approval may occur with boxed warnings on medicine labeling or Risk Evaluation and Mitigation Strategies, or REMS, which limit the labeling, distribution or promotion of a medicine. Once issued, the FDA may withdraw medicine approval if ongoing regulatory requirements

are not met or if safety problems occur after the medicine reaches the market. In addition, the FDA may require testing, including Phase 4 clinical trials, and surveillance programs to monitor the safety effects of approved medicines which have been commercialized and the FDA has the power to prevent or limit further marketing of a medicine based on the results of these post-marketing programs or other information.

Orphan Medicines. Under the Orphan Drug Act, the FDA may designate a medicine as an "orphan drug" if it is intended to treat a rare disease or condition, meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a medicine available in the United States for treatment of the disease or condition will be recovered from sales of the medicine. A company must request orphan drug designation before submitting an NDA for the drug and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the Prescription Drug User Fee Act, or PDUFA, goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a medicine with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the medicine generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another medicine under certain circumstances, including if a subsequent medicine with the same drug for the same indication is shown to be clinically superior to the approved medicine on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

In the EU, Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a medicine can be designated as an orphan medicinal product by the EC if its sponsor can establish: that the medicine is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States (extendable to twelve years for medicines that have complied with an agreed pediatric investigation plan pursuant to Regulation 1901/2006) and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this medicine is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if, at the end of the fifth year, it can be demonstrated on the basis of available evidence that the criteria for its designation as an orphan medicine are no longer satisfied, for example if the original orphan medicinal product has become sufficiently profitable not to justify maintenance of market exclusivity.

Other Regulatory Requirements. Medicines manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including recordkeeping, annual medicine quality review, payment of medicine and manufacturing establishment fees and reporting requirements. Adverse event experience with the medicine must be reported to the FDA in a timely fashion and pharmacovigilance programs to proactively look for these adverse events are mandated by the FDA. Our medicines may be subject to REMS requirements that affect labeling, distribution or post market reporting. Drug manufacturers and their subcontractors are required to register their establishments with

the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Following such inspections, the FDA may issue notices on Form 483 and Untitled Letters or Warning Letters that could cause us or our third-party manufacturers to modify certain activities. A Form 483 notice, if issued at the conclusion of an FDA inspection, can list conditions the FDA investigators believe may have violated cGMP or other FDA regulations or guidelines. In addition to Form 483 notices and Untitled Letters or Warning Letters, failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as suspension of manufacturing, seizure of medicine, injunctive action, additional reporting requirements and/or oversight by the agency, import alert or possible civil penalties. The FDA may also require us to recall a drug from distribution or withdraw approval for that medicine.

The FDA closely regulates the post-approval marketing and promotion of pharmaceuticals, including standards and regulations for direct-to-consumer advertising, dissemination of off-label information, industry-sponsored scientific and educational activities and promotional activities involving the Internet, including certain social media activities. Medicines may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to the medicine, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental application, which may require us to develop additional data or conduct additional preclinical studies and clinical trials. Failure to comply with these requirements can result in adverse publicity, Warning Letters or "untitled letters", corrective advertising and potential administrative, civil and criminal penalties, as well as damages, fines, withdrawal of regulatory approval, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs, additional reporting requirements and/or oversight by the agency, and imprisonment, any of which could adversely affect our ability to sell our medicines or operate our business and also adversely affect our financial results.

Physicians may, in their independent medical judgment, prescribe legally available pharmaceuticals for uses that are not described in the medicine's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use. Additionally, a significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of medicines for off-label uses and other sales practices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, false claims laws, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of medicines for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If our promotional activities, including any promotional activities that a contracted sales force may perform on our behalf, fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, suspend or withdraw an approved medicine from the market, require corrective advertising or a recall or institute fines or civil fines, additional reporting requirements and/or oversight or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution, any of which could harm our business. In addition, the distribution of prescription medicines is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription medicine samples and impose requirements to ensure accountability in distribution, including a drug pedigree which tracks the distribution of prescription drugs. Further, under the Drug Quality and Security Act, drug manufacturers are subject to a number of requirements, including, medicine identification, tracing and verification, among others, that are designed to detect and remove counterfeit, stolen, contaminated or otherwise potentially harmful drugs from the U.S. drug supply chain. These requirements will be phased in over several years and compliance will likely increase the costs of the manufacture and distribution of drug medicines.

Outside the United States, the ability of our partners and us to market a medicine is contingent upon obtaining marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from country to country and region to region.

The EU and the EEA consist of the 28 Member States of the EU, plus Norway, Iceland and Liechtenstein which are Member States of the EEA. These Member States have all acceded to the single market rules governing the supervision of medicinal products. Under the prevailing rules, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are three procedures for an MA to be obtained:

- the Centralized MA, which is issued by the EC through the Centralized Procedure, based on the scientific opinion of the CHMP of the EMA, and which is valid throughout the entire territory of the EU/EEA. When decisions on granting of a Centralized MA are taken by the EU, the EEA Member States will take corresponding decisions on the basis the relevant acts to permit marketing of medicinal products. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EU/EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- Decentralized Procedure MAs are available for products not falling within the mandatory scope of the Centralized Procedure. An identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS, to lead the evaluation of the regulatory submission. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet as distilled from the preliminary evaluation, which are sent to the other Member States (referred to as the Concerned Member States, or CMS) for their approval. If the CMS raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the RMS records the agreement, closes the procedure and informs the applicant accordingly. Each Member State concerned by the procedure is required to adopt a national decision to grant a national MA in conformity with the approved assessment report, SmPC and the labeling and package leaflet as approved. Where a product has already been authorized for marketing in a Member State of the EEA, the granted national MA can be used for mutual recognition in other Member States through the Mutual Recognition Procedure, or MRP, resulting in progressive national approval of the product in the EU/EEA.
- National MAs, which are issued by a single competent authority of the Member States of the EEA and only covers their respective territory, are also available for products not falling within the mandatory scope of the Centralized Procedure. Once a product has been authorized for marketing in a Member State of the EEA through the National Procedure, this National MA can also be recognized in other Member States through the MRP.

Under the procedures described above, before granting the MA, the EMA or the competent authority(ies) of the Member State(s) of the EEA prepare an assessment of the risk-benefit balance of the product against the scientific criteria concerning its quality, safety and efficacy.

Under Regulation (EC) No 726/2004/EC and Directive 2001/83/EC (each as amended), the EU has adopted a harmonized approach to data and market protection or exclusivity (known as the 8 + 2 + 1 formula). The data exclusivity period begins to run on the date when the first MA is granted in the EU. It confers on the MA holder of the reference medicinal product eight years of data protection and ten years of market protection. A reference medicinal product is defined to mean a medicinal product authorized based on a full dossier consisting of pharmaceutical and preclinical testing results and clinical trial data, such as a medicinal product containing a new active substance. The ten-year market protection can be extended cumulatively to a maximum period of eleven years if during the first eight years of those ten years of protection period, the MA holder obtains an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies.

The protection period means that an applicant for a generic medicinal product is not permitted to rely on preclinical pharmacological, toxicological, and clinical data contained in the file of the reference medicinal product of the originator until the first eight years of data protection have expired. Thereafter, a generic product application may be submitted and generic companies may rely on the preclinical and clinical data relating to the reference medicinal product to support approval of the generic product. However, a generic cannot market until ten years have elapsed from the initial authorization of the reference medicinal product or eleven years if the protection period is extended, based on the formula of 8+2+1.

In addition to the above, where an application is made for a new indication for a well-established substance, a non-cumulative period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication. Finally, where a change of classification of a medicinal product has been authorized on the basis of significant pre-clinical tests or clinical trials, the competent authority shall not refer to the results of those tests or trials when examining an application by another applicant for or holder of marketing authorization for a change of classification of the same substance for one year after the initial change was authorized.

The 8 + 2 + 1 exclusivity scheme applies to products that have been authorized in the EU by either the EMA through the Centralized Procedure or the competent authorities of the Member States of the EEA nationally, including through the Decentralized and Mutual Recognition procedures.

For a medicinal product which is designated as orphan under Regulation 141/2000, it will benefit from a period of ten years of orphan market exclusivity which essentially constitutes a period of market monopoly. During this period of orphan market exclusivity, no EU regulatory authority is permitted to accept or approve an application for marketing authorization for a similar medicinal product or an extension application for the same therapeutic indication. This period can be extended cumulatively to a total of twelve years if the marketing authorization holder or applicant complies with the requirements for an agreed pediatric investigation plan pursuant to Regulation 1901/2006.

The holder of a Centralized MA or National MA is subject to various obligations under the applicable EU laws, such as pharmacovigilance obligations, requiring it to, among other things, report and maintain detailed records of adverse reactions, and to submit periodic safety update reports to the competent authorities. The holder must also ensure that the manufacturing and batch release of its product is in compliance with the applicable requirements. The MA holder is further obligated to ensure that the advertising and promotion of its products complies with applicable EU laws and industry code of practice as implemented in the domestic laws of the Member States of the EU/EEA. The advertising and promotional rules are enforced nationally by the EU/EEA Member States.

Healthcare Fraud and Abuse Laws. As a pharmaceutical company, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. For example, in the United States, there are federal and state anti-kickback laws that prohibit the payment or receipt of kickbacks, bribes or other remuneration intended to induce the purchase or recommendation of healthcare products and services or reward past purchases or recommendations. Violations of these laws can lead to civil and criminal penalties, including fines, imprisonment, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement, and exclusion from participation in federal healthcare programs. These laws are applicable to manufacturers of products regulated by the FDA, such as us, and pharmacies, hospitals, physicians and other potential purchasers of such products.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" is defined as any remuneration, direct or indirect, overt or covert, in cash or in kind, and has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute may have been violated, and enforcement will depend on the relevant facts and circumstances. The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute to state that a person or entity need not have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that 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 civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent, or to have offered improper inducements to federal health care program beneficiaries to select a particular provider or supplier. The federal Anti-Kickback Statute is broad, and despite a series of narrow safe harbors, prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs, and do not contain identical safe harbors. In addition, where such activities involve foreign government officials, they may also potentially be subject to the Foreign Corrupt Practices Act. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities, including our activities with physician customers, pharmacies, and patients, as well as our activities pursuant to partnerships with other companies and pursuant to contracts with contract research organizations, could be subject to challenge under one or more of such laws.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. In addition, the ACA specified 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 civil False Claims Act. The federal False Claims Act has been the basis for numerous enforcement actions and settlements by pharmaceutical and other healthcare companies in connection with various alleged financial relationships with customers. In addition, a number of pharmaceutical manufacturers have reached substantial financial settlements in connection with allegedly causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses. Certain marketing practices, including off-label promotion, may also violate false claims laws, as might violations of the federal physician self-referral laws, such as the Stark laws, which prohibit a physician from making a referral to certain designated health services with which the physician or the physician's family member has a financial interest and prohibit submission of a claim for reimbursement pursuant to the prohibited referral. The "qui tam" provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In addition, various states have enacted similar fraud and abuse statutes or regulations, including, without limitation, false claims laws analogous to the False Claims Act, and laws analogous to the federal Anti-Kickback Statute, that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer, and there are also federal criminal false claims laws.

Separately, there are a number of other fraud and abuse laws that pharmaceutical manufacturers must be mindful of, particularly after a medicine candidate has been approved for marketing in the United States. For example, a federal criminal law enacted as part of, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. There are also federal civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, as well as federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Healthcare Privacy and Security Laws. We may be subject to, or our marketing activities may be limited by, HIPAA, as amended by the Health Information Technology and Clinical Health Act and their respective implementing regulations, which established uniform standards for certain "covered entities" (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. Among other things, HIPAA's privacy and security standards are directly applicable to "business associates" — independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. In addition to possible civil and criminal penalties for violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. In the EU/EEA, Directive 95/46/EEC (as amended) or its successor applies to identified or identifiable personal data processed by automated means (for example, a computer database of customers) and data contained in, or intended to be part of, non-automated filing systems (traditional paper files) as well as transfer of such data to a country outside of the EU/EEA.

"Sunshine" and Marketing Disclosure Laws. There are an increasing number of federal and state "sunshine" laws that require pharmaceutical manufacturers to make reports to states on pricing and marketing information. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, and make periodic public disclosures on sales and marketing activities, and prohibiting certain other sales and marketing practices. In addition, a similar federal requirement requires manufacturers, including pharmaceutical manufacturers, to track and report to the federal government certain payments and other transfers of value made to physicians and other healthcare professionals and teaching hospitals and ownership or investment interests held by physicians and their immediate family members. The federal government began disclosing the reported information on a publicly available website in 2014. These laws may adversely affect our sales, marketing, and other activities with respect to our medicines in the United States by imposing administrative and compliance burdens on us. If we fail to track and report as required by these laws or otherwise comply with these laws, we could be subject to the penalty provisions of the pertinent state and federal authorities. In the EU/EEA, declaration of transfers of value to healthcare professionals is subject to the requirements under the voluntary industry code of practice. France however has a statutory regime similar to the U.S. Sunshine Act.

Government Price Reporting. For those marketed medicines which are covered in the United States by the Medicaid programs, we have various obligations, including government price reporting and rebate requirements, which generally require medicines be offered at substantial rebates/discounts to Medicaid and certain purchasers (including "covered entities" purchasing under the 340B Drug Discount Program). We are also required to discount such medicines to authorized users of the Federal Supply Schedule of the General Services Administration, under which additional laws and requirements apply. These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations, and the guidance governing such calculations is not always clear. Compliance with such requirements can require significant investment in personnel, systems and resources, but failure to properly calculate our prices, or offer required discounts or rebates could subject us to substantial penalties. One component of the rebate and discount calculations under the Medicaid and 340B programs, respectively, is the "additional rebate", a complex calculation which is based, in part, on the rate at which a branded drug price increases over time more than the rate of inflation (based on the CPI-U). This comparison is based on the baseline pricing data for the first full quarter of sales associated with a branded drug's NDA, and baseline data cannot generally be reset, even on transfer of the NDA to another manufacturer. This "additional rebate" calculation can, in some cases where price increase have been relatively high versus the first quarter of sales of the NDA, result in Medicaid rebates up to 100 percent of a drug's "average manufacturer price" and 340B prices of one penny. Subject to the control of Directive 89/105/EEC, pricing and reimbursement in the EU/EEA is governed by national rules and policy and may vary from Member State to Member State.

In General. Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities, in the United States, could be subject to challenge under one or more of such laws. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including significant civil and criminal penalties, damages, fines, imprisonment, exclusion from participation in U.S. federal or state healthcare programs, additional reporting requirements and/or oversight and the curtailment or restructuring of our operations. To the extent that any medicine we make is sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, sunshine, government price reporting, and fraud laws may prove costly.

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Impact of Healthcare Reform and Recent Public Scrutiny of Specialty Drug Pricing on Coverage, Reimbursement, and Pricing. In the United States and other potentially significant markets for our medicines, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative medicines and therapies, which has resulted in lower average selling prices. Further, the increased scrutiny of prescription drug pricing practices and emphasis on managed healthcare in the United States and on country-specific and regional pricing and reimbursement controls in the EU will put additional pressure on medicine pricing, reimbursement and usage, which may adversely affect our future medicine sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

The U.S. and some foreign jurisdictions are considering or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our medicines profitably. Among policy makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs (including a number of proposals pertaining to prescription drugs, specifically), improving quality and/or expanding access. There has been particular and increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices over the course of 2015 and 2016, particularly with respect to drugs that have been subject to relatively large price increases over relatively short time periods. There have been several recent U.S. Congressional inquiries and proposed legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient assistance programs, and reform government program reimbursement methodologies for drugs. In the United States, the pharmaceutical industry has already been significantly affected by major legislative initiatives, including, for example, the ACA. The ACA, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription drug medicines. It also contains substantial provisions intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, and impose additional health policy reforms, any or all of which may affect our business. Since its enactment, there have been judicial and Congressional challenges to numerous provisions of the ACA. In January, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law, but it is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed. We will continue to evaluate the effect that the ACA and any future measures to repeal or replace the ACA have on our business. The intense public scrutiny of drug pricing in the United States, is likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Other legislative changes have also been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of up to two percent per fiscal year, starting in 2013, and the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Such laws, and others that may affect our business that have been recently enacted or may in the future be enacted, may result in additional reductions in Medicare and other healthcare funding. In the future, there will likely continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit coverage and reimbursement of medicines, including our medicine candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our medicines.

Irish Law Matters

As a result of the Vidara Merger, the outstanding shares of the common stock of HPI were canceled and automatically converted into the right to receive our ordinary shares. As we are an Irish-incorporated company, the following matters of Irish law are relevant to the holders of our ordinary shares.

Irish Restrictions on Import and Export of Capital. Except as indicated below, there are no restrictions imposed specifically on non-residents of Ireland dealing in Irish domestic securities, which includes ordinary shares of Irish companies. Dividends and redemption proceeds also continue to be freely transferable to non-resident holders of such securities. The Financial Transfers Act 1992 gives power to the Minister for Finance of Ireland to restrict financial transfers between Ireland and other countries and persons. Financial transfers are broadly defined and include all transfers that would be movements of capital or payments within the meaning of the treaties governing the member states of the EU. The acquisition or disposal of interests in shares issued by an Irish incorporated company and associated payments falls within this definition. In addition, dividends or payments on redemption or purchase of shares and payments on a liquidation of an Irish incorporated company would fall within this definition. The Criminal Justice (Terrorist Offences) Act 2005 also gives the Minister of Finance of Ireland the power to take various measures, including the freezing or seizure of assets, in order to combat terrorism. At present the Financial Transfers Act 1992 and the Criminal Justice (Terrorist Offences) Act 2005 prohibit financial transfers involving the late Slobodan Milosevic and associated persons, Republic of Guinea-Bissau, Myanmar/Burma, Belarus, certain persons indicted by the International Criminal Tribunal for the former Yugoslavia, the late Osama bin Laden, Al-Qaida, the Taliban of Afghanistan, Democratic Republic of Congo, Democratic People's Republic of Korea (North Korea), Iran, Iraq, Côte d'Ivoire, Lebanon, Liberia, Zimbabwe, Sudan, Somalia, Republic of Guinea, Afghanistan, Egypt, Eritrea, Libya, Syria, Tunisia, Burundi, the Central African Republic, Ukraine, Yemen, certain known terrorists and terrorist groups, and countries that harbor certain terrorist groups, without the prior permission of the Central Bank of Ireland or the Minister of Finance (as applicable).

Any transfer of, or payment in respect of, a share or interest in a share involving the government of any country that is currently the subject of United Nations sanctions, any person or body controlled by any of the foregoing, or by any person acting on behalf of the foregoing, may be subject to restrictions pursuant to such sanctions as implemented into Irish law.

Irish Taxes Applicable to U.S. Holders

Withholding Tax on Dividends. While we have no current plans to pay dividends, dividends on our ordinary shares would generally be subject to Irish Dividend Withholding Tax, or DWT, at the standard rate of income tax (currently twenty percent), unless an exemption applies.

Dividends on our ordinary shares that are owned by residents of the United States and held beneficially through the Depositary Trust Company, or DTC, will not be subject to DWT provided that the address of the beneficial owner of the ordinary shares in the records of the broker is in the United States.

Dividends on our ordinary shares that are owned by residents of the United States and held directly (outside of DTC) will not be subject to DWT provided that the shareholder has completed the appropriate Irish DWT form and this form remains valid. Such shareholders must provide the appropriate Irish DWT form to our transfer agent at least seven business days before the record date for the first dividend payment to which they are entitled.

If any shareholder who is resident in the United States receives a dividend subject to DWT, he or she should generally be able to make an application for a refund from the Irish Revenue Commissioners on the prescribed form.

While the U.S./Ireland Double Tax Treaty contains provisions regarding withholding, due to the wide scope of the exemptions from DWT available under Irish domestic law, it would generally be unnecessary for a U.S. resident shareholder to rely on the treaty provisions.

Income Tax on Dividends. A shareholder who is neither resident nor ordinarily resident in Ireland and who is entitled to an exemption from DWT generally has no additional liability to Irish income tax or to the universal social charge on a dividend from us unless that shareholder holds our ordinary shares through a branch or agency in Ireland through which a trade is carried on.

A shareholder who is neither resident nor ordinarily resident in Ireland and who is not entitled to an exemption from DWT generally has no additional liability to Irish income tax or to the universal social charge on a dividend from us. The DWT deducted by us discharges the liability to Irish income tax and to the universal social charge. This however is not the case where the shareholder holds the ordinary shares through a branch or agency in Ireland through which a trade is carried on.

Irish Tax on Capital Gains. A shareholder who is neither resident nor ordinarily resident in Ireland and does not hold our ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency should not be within the charge to Irish tax on capital gains on a disposal of our ordinary shares.

Capital Acquisitions Tax. Irish capital acquisitions tax, or CAT, is composed principally of gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares are regarded as property situated in Ireland as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33 percent above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (i) the relationship between the donor and the donee and (ii) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same category of relationship for CAT purposes. Gifts and inheritances passing between spouses are exempt from CAT. Our shareholders should consult their own tax advisers as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

Stamp Duty. Irish stamp duty (if any) may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. A transfer of our ordinary shares (i) by a seller who holds ordinary shares outside of DTC to any buyer, or (ii) by a seller who holds the ordinary shares through DTC to a buyer who holds the acquired ordinary shares outside of DTC, may be subject to Irish stamp duty (currently at the rate of one percent of the price paid or the market value of the ordinary shares acquired, if greater). The person accountable for payment of stamp duty is the buyer or, in the case of a transfer by way of a gift or for less than market value, all parties to the transfer.

A shareholder who holds ordinary shares outside of DTC may transfer those ordinary shares into DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) as a result of the transfer and at the time of the transfer into DTC there is no sale of those book-entry interests to a third party being contemplated by the shareholder. Similarly, a shareholder who holds ordinary shares through DTC may transfer those ordinary shares out of DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the ordinary shares (and in exactly the same proportions) as a result of the transfer, and at the time of the transfer out of DTC there is no sale of those ordinary shares to a third party being contemplated by the shareholder. In order for the share registrar to be satisfied as to the application of this Irish stamp duty treatment where relevant, the shareholder must confirm to us that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) (or vice-versa) as a result of the transfer and there is no agreement for the sale of the related book-entry interest or the ordinary shares or an interest in the ordinary shares, as the case may be, by the shareholder to a third party being contemplated.

Employees

As of December 31, 2016, we had approximately 1,050 full-time employees. Of our employees as of December 31, 2016, approximately 185 were engaged in development, regulatory and manufacturing activities, approximately 650 were engaged in sales and marketing and approximately 215 were engaged in administration, including business development, finance, legal, information systems, facilities and human resources. None of our employees is subject to a collective bargaining agreement. We consider our employee relations to be satisfactory.

Available Information

We make available free of charge on or through our internet website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with or furnished to the Securities and Exchange Commission. We also regularly post copies of our press releases as well as copies of presentations and other updates about our business on our website. Our website address is www.horizonpharma.com. The information contained in or that can be accessed through our website is not part of this report. Information is also available through the Securities and Exchange Commission's website at www.sec.gov or is available at the Securities and Exchange Commission's Public Reference Room located at 100 F Street, NE, Washington DC, 20549. Information on the operation of the Public Reference Room is available by calling the Securities and Exchange Commission at 800-SEC-0330.

Item 1A. Risk Factors

Certain factors may have a material adverse effect on our business, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors in its entirety, in addition to other information contained in this report as well as our other public filings with the Securities and Exchange Commission, or SEC.

Risks Related to Our Business and Industry

Our ability to generate revenues from our medicines is subject to attaining significant market acceptance among physicians, patients and healthcare payers.

Our current medicines, and other medicines or medicine candidates that we may develop or acquire, may not attain market acceptance among physicians, patients, healthcare payers or the medical community. We have a limited history of commercializing medicines and most of our medicines have not been on the market for an extensive period of time, which subjects us to numerous risks as we attempt to increase our market share. We believe that the degree of market acceptance and our ability to generate revenues from our medicines will depend on a number of factors, including:

- timing of market introduction of our medicines as well as competitive medicines;
- efficacy and safety of our medicines;
- continued projected growth of the markets in which our medicines compete;
- prevalence and severity of any side effects;
- if and when we are able to obtain regulatory approvals for additional indications for our medicines;
- acceptance by patients, primary care physicians and key specialists;
- availability of coverage and adequate reimbursement and pricing from government and other third-party payers;
- potential or perceived advantages or disadvantages of our medicines over alternative treatments, including cost of treatment and relative convenience and ease of administration;
- strength of sales, marketing and distribution support;
- the price of our medicines, both in absolute terms and relative to alternative treatments;
- impact of past and limitation of future medicine price increases;
- our ability to maintain a continuous supply of medicine for commercial sale;
- the effect of current and future healthcare laws;
- the performance of third-party distribution partners, over which we have limited control; and
- medicine labeling or medicine insert requirements of the U.S. Food and Drug Administration, or FDA, or other regulatory authorities.

With respect to DUEXIS and VIMOVO, studies indicate that physicians do not commonly co-prescribe gastrointestinal, or GI, protective agents to high-risk patients taking nonsteroidal anti-inflammatory drugs, or NSAIDs. We believe this is due in part to a lack of awareness among physicians prescribing NSAIDs regarding the risk of NSAID-induced upper GI ulcers, in addition to the inconvenience of prescribing two separate medications and patient compliance issues associated with multiple prescriptions. If physicians remain unaware of, or do not otherwise believe in, the benefits of combining GI protective agents with NSAIDs, our market opportunity for DUEXIS and VIMOVO will be limited. Some physicians may also be reluctant to prescribe DUEXIS or VIMOVO due to the inability to vary the dose of ibuprofen and naproxen, respectively, or if they believe treatment with NSAIDs or GI protective agents other than those contained in DUEXIS and VIMOVO, including those of its competitors, would be more effective for their patients. With respect to each of DUEXIS, PENNSAID 2% w/w, or PENNSAID 2%, RAYOS/LODOTRA, VIMOVO and BUPHENYL, their higher cost compared to the generic or branded forms of their active ingredients alone may limit adoption by physicians, patients and healthcare payers. With respect to ACTIMMUNE, while it is the only FDA-approved treatment for chronic granulomatous disease, or CGD, and severe, malignant osteopetrosis, or SMO, they are very rare conditions and, as a result, our ability to grow ACTIMMUNE sales will depend on our ability to further penetrate this limited market and obtain marketing approval for additional indications. With respect to RAVICTI, which is also approved to treat a very limited patient population, our ability to grow sales will depend in large part on our ability to transition urea cycle disorder, or UCD, patients from BUPHENYL or generic equivalents, which are comparatively much less expensive, to RAVICTI. With respect to KRYSTEXXA, our ability to grow sales will be affected by the success of our sales and marketing strategies and life cycle management, including studies designed to test reduction of immunogenicity in KRYSTEXXA which could expand the patient population and usage of KRYSTEXXA. With respect to MIGERGOT, our ability to sustain sales will depend on the management of inventory levels and the continued awareness of its benefits among physicians. With respect to PROCYSBI, which is approved to treat a very limited patient population, our ability to grow sales will depend in large part on our ability to transition patients from the first-generation immediate-release cysteamine therapy to PROCYSBI, to identify additional patients with nephropathic cystinosis, and expand commercialization in Europe. Unless QUINSAIR is approved for marketing in additional countries, our ability to drive growth of this medicine will largely depend on expanding its use in Europe and Canada. If our current medicines or any other medicine that we may seek approval for or acquire fail to attain market acceptance, we may not be able to generate significant revenue to achieve or sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects (including, possibly, the value of our ordinary shares).

Our future prospects are highly dependent on our ability to successfully formulate and execute commercialization strategies for each of our medicines. Failure to do so would adversely impact our financial condition and prospects.

A substantial majority of our resources are focused on the commercialization of our current medicines. Our ability to generate significant medicine revenues and to achieve commercial success in the near-term will initially depend almost entirely on our ability to successfully commercialize these medicines in the United States.

With respect to our orphan business unit medicines, ACTIMMUNE, BUPHENYL, PROCYSBI, QUINSAIR and RAVICTI, and with respect to our rheumatology business unit medicine, KRYSTEXXA, our commercialization strategy includes efforts to increase awareness of the rare conditions that each medicine is designed to treat, enhancing efforts to identify target patients and in certain cases pursue opportunities for label expansion and more effective use through clinical trials. In addition, our strategy with respect to ACTIMMUNE includes pursuing label expansion for additional indications, such as for advanced urothelial carcinoma and renal cell carcinoma, and price increases but we cannot be certain that our pricing strategy will not result in downward pressure on sales or that we or others will be able to successfully complete clinical trials and obtain regulatory approvals in additional indications. With respect to PROCYSBI and RAVICTI, our strategy includes accelerating the transition of patients from first-generation therapies, and increasing the diagnosis of the associated rare conditions through patient and physician outreach. Part of our success in our strategy for RAVICTI will also depend on obtaining approval of RAVICTI for the treatment of UCD in patients less than two years of age. However, we cannot guarantee that on-going studies will be positive or that we will be able to expand the labeling for RAVICTI on our anticipated timeline or at all. Our strategy with respect to

KRYSTEXXA includes the continued enhancement of the marketing campaign with improved immunogenicity data, continued volume growth and pricing optimization.

With respect to our primary care medicines DUEXIS, PENNSAID 2% and VIMOVO, our strategy has more recently included entering into rebate agreements with pharmacy benefit managers, or PBMs, for certain of our primary care medicines where we believe the rebates and costs justify expanded formulary access for patients. However, we cannot guarantee that we will be able to secure additional rebate agreements on commercially reasonable terms or that expected volume growth will sufficiently offset the rebates and fees paid to PBMs or that our existing agreements with PBMs will have the intended impact on formulary access. For each of our primary care medicines, we expect that our commercial success will depend on our sales and marketing efforts in the United States.

Our strategy for RAYOS in the United States is to focus on the rheumatology indications approved for RAYOS, including our collaboration with the Alliance for Lupus Research, or ALR, to study the effect of RAYOS on the fatigue experienced by systemic lupus erythematosus, or SLE, patients.

Our overall commercialization strategy also includes plans to expand sales in Europe and other countries outside the United States directly or through distributors for certain of our orphan and rheumatology medicines. In November 2015, we received approval of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, for RAVICTI for use as an adjunctive therapy for chronic management of adult and pediatric UCD patients greater than two months of age. This authorizes us to market RAVICTI in all 28 Member States of the European Union, or EU, and will form the basis for recognition by the Member States of the European Economic Area, or EEA, namely Norway, Iceland and Liechtenstein, for the medicine to be placed on the market. In June 2016, we partnered with Clinigen Group plc's Idis managed access division to initiate a managed access program in selected European countries, which agreement will terminate on April 10, 2017 and after which we will partner with Swedish Orphan Biovitrum AB, or SOBI, to continue our managed access program in selected European countries. While we expect to commercially launch RAVICTI in Europe in 2017 through an exclusive distribution agreement with SOBI, we cannot guarantee we will be able to successfully implement our commercial plans for RAVICTI in Europe. With respect to PROCYSBI and QUINSAIR, which are approved for marketing in the EU, we intend to continue evaluating commercial launches in additional EU countries as well as pursuing early access programs. Although LODOTRA is approved for marketing in countries outside the United States, to date it has only been marketed in a limited number of countries.

If any of our commercial strategies are unsuccessful or we fail to successfully modify our strategies over time due to changing market conditions, our ability to increase market share for our medicines, grow revenues and sustain profitability will be harmed.

In order to increase adoption and sales of our medicines, we will need to continue developing our commercial organization as well as recruit and retain qualified sales representatives.

Part of our strategy is to continue to build a biopharmaceutical company to successfully execute the commercialization of our medicines in the U.S. market, and in selected markets outside the United States where we have commercial rights. We may not be able to successfully commercialize our medicines in the United States or in any other territories where we have commercial rights. In order to commercialize any approved medicines, we must continue to build our sales, marketing, distribution, managerial and other non-technical capabilities. Although we had expanded our sales force to approximately 480 sales representatives as of December 31, 2016, consisting of approximately 20 orphan disease sales representatives, 100 rheumatology sales specialists and 360 primary care sales representatives, we currently have limited resources compared to some of our competitors, and the continued development of our own commercial organization to market our medicines and any additional medicines we may acquire will be expensive and time-consuming. We also cannot be certain that we will be able to continue to successfully develop this capability.

As a result of the evolving role of various constituents in the prescription decision making process, we focus on hiring sales representatives for our primary care and rheumatology business units with successful business to business experience. For example, we have faced challenges due to pharmacists increasingly switching a patient's intended prescription from DUEXIS and VIMOVO to a generic or over-the-counter brand of their active ingredients. We have faced similar challenges for RAYOS, BUPHENYL and PENNSAID 2% with respect to generic brands. While we believe the profile of our representatives is better suited for this evolving environment, we cannot be certain that our representatives will be able to successfully protect our market for DUEXIS, PENNSAID 2%, RAYOS, BUPHENYL and VIMOVO or that we will be able to continue attracting and retaining sales representatives with our desired profile and skills. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain commercial personnel. To the extent we rely on additional third parties to commercialize any approved medicines, we may receive less revenue than if we commercialized these medicines ourselves. In addition, we may have little or no control over the sales efforts of any third parties involved in our commercialization efforts. In the event we are unable to successfully develop and maintain our own commercial organization or collaborate with a third-party sales and marketing organization, we may not be able to commercialize our medicines and medicine candidates and execute on our business plan.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize our medicines will be harmed.

As we continue to acquire additional medicines through acquisition transactions, the members of our sales force may have limited experience promoting certain of our medicines. To the extent we employ an acquired entity's original sales forces to promote acquired medicines, we may not be successful in continuing to retain these employees and we otherwise will have limited experience marketing these medicines under our commercial organization. As a result, we are required to expend significant time and resources to train our sales force to be credible and persuasive in convincing physicians to prescribe and pharmacists to dispense our medicines. In addition, we must train our sales force to ensure that a consistent and appropriate message about our medicines is being delivered to our potential customers. Our sales representatives may also experience challenges promoting multiple medicines when we call on physicians and their office staff. We have experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire, requiring us to train new sales representatives. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate physicians about the benefits of our medicines and their proper administration and label indication, as well as our patient access programs, our efforts to successfully commercialize our medicines could be put in jeopardy, which could have a material adverse effect on our financial condition, share price and operations.

If we cannot successfully implement our patient access programs or increase formulary access and reimbursement for our medicines in the face of increasing pressure to reduce the price of medications, the adoption of our medicines by physicians, patients and payers may decline.

There continues to be immense pressure from healthcare payers and PBMs to use less expensive generics or over-the-counter brands instead of branded medicines. For example, some of the largest PBMs previously placed DUEXIS and VIMOVO on their formulary exclusion lists. Additional healthcare plans, including those that contract with these PBMs but use different formularies, may also choose to exclude our medicines from their formularies or restrict coverage to situations where a generic or over-the-counter medicine has been tried first. Many payers and PBMs also require patients to make co-payments for branded medicines, including many of our medicines, in order to incentivize the use of generic or other lower-priced alternatives instead. Legislation enacted in most states in the United States allows, or in some instances mandates, that a pharmacist dispenses an available generic equivalent when filling a prescription for a branded medicine, in the absence of specific instructions from the prescribing physician. Because our medicines (other than BUPHENYL) do not currently have FDA-approved generic equivalents in the United States, we do not believe our medicines should be subject to mandatory generic substitution laws. However, we understand that some pharmacies may attempt to obtain physician authorization to switch prescriptions for DUEXIS or VIMOVO to prescriptions for multiple generic medicines with similar active pharmaceutical ingredients,

or APIs, to ensure payment for the medicine if the physician's prescription for the branded medicine is not immediately covered by the payer, despite such substitution being off-label in the case of DUEXIS and VIMOVO. If these limitations in coverage and other incentives result in patients refusing to fill prescriptions or being dissatisfied with the out-of-pocket costs of their medications, or if pharmacies otherwise seek and receive physician authorization to switch prescriptions, not only would we lose sales on prescriptions that are ultimately not filled, but physicians may be dissuaded from writing prescriptions for our medicines in the first place in order to avoid potential patient non-compliance or dissatisfaction over medication costs, or to avoid spending the time and effort of responding to pharmacy requests to switch prescriptions.

Part of our commercial strategy to increase adoption and access to our medicines in the face of these incentives to use generic alternatives is to offer physicians the opportunity to have patients fill prescriptions through independent pharmacies participating in our HorizonCares patient access program. Through HorizonCares, financial assistance may be available to reduce eligible patients' out-of-pocket costs for prescriptions filled. Because of this assistance, eligible patients' out-of-pocket cost for our medicines when dispensed through HorizonCares may be significantly lower than such costs when our medicines are dispensed outside of the HorizonCares program. However, to the extent physicians do not direct prescriptions currently filled through traditional pharmacies, including those associated with or controlled by PBMs, to pharmacies participating in our HorizonCares program, we may experience a significant decline in DUEXIS, VIMOVO and PENNSAID 2% prescriptions as a result of formulary exclusions, co-payment requirements or other incentives to use lower-priced alternatives to our medicines. Our ability to increase utilization of our patient access programs will depend on physician and patient awareness and comfort with the programs, and we have limited ability to influence whether physicians use our patient access programs to prescribe our medicines or whether patients will agree to receive our medicines through our HorizonCares program. In addition, the HorizonCares program is not available to federal health care program (such as Medicare and Medicaid) beneficiaries. We have also contracted with certain PBMs and other payers to secure formulary status and reimbursement for certain of our primary care medicines, which generally require us to pay administrative fees and rebates to the PBMs and other payers for qualifying prescriptions. While we recently announced business relationships with two of the largest PBMs, Express Scripts, Inc., or Express Scripts, and CVS Caremark, that have resulted in DUEXIS and VIMOVO being removed from the Express Scripts and CVS Caremark 2017 exclusion lists, as well as a rebate agreement with another PBM, Prime Therapeutics LLC, and we believe these agreements will secure formulary status for certain of our medicines, we cannot guarantee that we will be able to agree to terms with other PBMs and other payers, or that such terms will be commercially reasonable to us. In addition, despite our agreements with PBMs, the extent of formulary status and reimbursement will ultimately depend to a large extent upon individual healthcare plan formulary decisions. If healthcare plans that contract with PBMs with which we have agreements do not adopt formulary changes recommended by the PBMs with respect to our medicines, we may not realize the expected access and reimbursement benefits from these agreements. If we are unable to increase adoption of HorizonCares for filling prescriptions of our medicines or to secure formulary status and reimbursement through arrangements with PBMs and other payers, our ability to maintain or increase prescriptions for our medicines could be impaired.

There has been negative publicity and inquiries from Congress and enforcement authorities regarding the use of specialty pharmacies and drug pricing. Our patient access programs are not involved in the prescribing of medicines and are solely to assist in ensuring that when a physician determines one of our medicines offers a potential clinical benefit to their patients and they prescribe one for an eligible patient, financial assistance may be available to reduce the patient's out-of-pocket costs. In addition, all pharmacies that fill prescriptions for our medicines are fully independent, including those that participate in HorizonCares. We do not own or possess any option to purchase an ownership stake in any pharmacy that distributes our medicines, and our relationship with each pharmacy is non-exclusive and arm's length. All of our sales are processed through pharmacies independent of us. Despite this, the negative publicity and interest from Congress and enforcement authorities regarding specialty pharmacies may result in physicians being less willing to participate in our patient access programs and thereby limit our ability to increase patient access and adoption of our medicines.

We may also encounter difficulty in forming and maintaining relationships with pharmacies that participate in our patient access programs. We currently depend on a limited number of pharmacies participating in HorizonCares to fulfill patient prescriptions under the HorizonCares program. If these HorizonCares participating pharmacies are unable to process and fulfill the volume of patient prescriptions directed to them under the HorizonCares program, our ability to maintain or increase prescriptions for our medicines will be impaired. The commercialization of our medicines and our operating results could be affected should any of the HorizonCares participating pharmacies choose not to continue participation in our HorizonCares program or by any adverse events at any of those HorizonCares participating pharmacies. For example, pharmacies that dispense our medicines could lose contracts that they currently maintain with managed care organizations, or MCOs, including PBMs. Pharmacies often enter into agreements with MCOs. They may be required to abide by certain terms and conditions to maintain access to MCO

networks, including terms and conditions that could limit their ability to participate in patient access programs like ours. Failure to comply with the terms of their agreements with MCOs could result in a variety of penalties, including termination of their agreement, which could negatively impact the ability of those pharmacies to dispense our medicines and collect reimbursement from MCOs for such medicines.

The HorizonCares program may implicate certain state laws related to, among other things, unlawful schemes to defraud, excessive fees for services, tortious interference with patient contracts and statutory or common law fraud. We have a comprehensive compliance program in place to address adherence with various laws and regulations relating to the selling, marketing and manufacturing of our medicines, as well as certain third-party relationships, including pharmacies. Specifically with respect to pharmacies, the compliance program utilizes a variety of methods and tools to monitor and audit pharmacies, including those that participate in the HorizonCares program, to confirm their activities, adjudication and practices are consistent with our compliance policies and guidance. Despite our compliance efforts, to the extent the HorizonCares program is found to be inconsistent with applicable laws or the pharmacies that participate in our patient access programs do not comply with applicable laws, we may be required to restructure or discontinue such programs, terminate our relationship with certain pharmacies, or be subject to other significant penalties. In November 2015, we received a subpoena from the U.S. Attorney's Office for the Southern District of New York requesting documents and information related to our patient access programs and other aspects of our marketing and commercialization activities. We are unable to predict how long this investigation will continue or its outcome, but we have incurred and anticipate that we may continue to incur significant costs in connection with the investigation, regardless of the outcome. We may also become subject to similar investigations by other governmental agencies or Congress. The investigation by the U.S. Attorney's Office and any additional investigations of our patient access programs and sales and marketing activities may result in damages, fines, penalties, exclusion, additional reporting requirements and/or oversight or other administrative sanctions against us.

If the cost of maintaining our patient access programs increases relative to our sales revenues, we could be forced to reduce the amount of patient financial assistance that we offer or otherwise scale back or eliminate such programs, which could in turn have a negative impact on physicians' willingness to prescribe and patients' willingness to fill prescriptions of our medicines. While we believe that our recent arrangements with PBMs will result in broader inclusion of certain of our primary care medicines on healthcare plan formularies, and therefore increase payer reimbursement and lower our cost of providing patient access programs, these arrangements generally require us to pay administrative and rebate payments to the PBMs and/or other payers and their effectiveness will ultimately depend to a large extent upon individual healthcare plan formulary decisions that are beyond the control of the PBMs. If our arrangements with PBMs and other payers do not result in increased prescriptions and reductions in our costs to provide our patient access programs that are sufficient to offset the administrative fees and rebate payments to the PBMs and/or other payers, our financial results may be harmed.

If we are unable to successfully implement our commercial plans and facilitate adoption by patients and physicians of any approved medicines through our sales, marketing and commercialization efforts, then we will not be able to generate sustainable revenues from medicine sales which will have a material adverse effect on our business and prospects.

We are solely dependent on third parties to commercialize certain of our medicines outside the United States. Failure of these third parties or any other third parties to successfully commercialize our medicines and medicine candidates in the applicable jurisdictions could have a material adverse effect on our business.

Mundipharma International Corporation Limited, or Mundipharma, is our exclusive distributor for LODOTRA in Europe, Asia and Latin America. We rely on other third-party distributors for commercialization of BUPHENYL (known as AMMONAPS in certain European countries) in certain territories outside the United States for which we currently have rights. We have limited contractual rights to force these third parties to invest significantly in commercialization of these medicines in our markets. In the event that Mundipharma or our current ex-U.S. distributors for BUPHENYL or any other third-party with any future commercialization rights to any of our medicines or medicine candidates fail to adequately commercialize those medicines or medicine candidates because they lack adequate financial or other resources, decide to focus on other initiatives or otherwise, our ability to successfully commercialize our medicines or medicine candidates in the applicable jurisdictions would be limited, which would adversely affect our business, financial condition, results of operations and prospects. We have had disagreements with Mundipharma under our European agreements and may continue to have disagreements, which could harm

commercialization of LODOTRA in Europe or result in the termination of our agreements with Mundipharma. In addition, our agreements with Mundipharma and our agreements with our current ex-U.S. distributors for BUPHENYL may be terminated by either party in the event of a bankruptcy of the other party or upon an uncured material breach by the other party. If these third parties terminated their agreements, we may not be able to secure an alternative distributor in the applicable territory on a timely basis or at all, in which case our ability to generate revenues from the sale of LODOTRA, QUINSAIR, RAVICTI or BUPHENYL outside the United States would be materially harmed.

Our medicines are subject to extensive regulation, and we may not obtain additional regulatory approvals for our medicines.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, marketing and distribution and other possible activities relating to our medicines and our medicine candidates are, and will be, subject to extensive regulation by the FDA and other regulatory agencies. Failure to comply with FDA and other applicable regulatory requirements may, either before or after medicine approval, subject us to administrative or judicially imposed sanctions.

To market any drugs or biologics outside of the United States, we and current or future collaborators must comply with numerous and varying regulatory and compliance related requirements of other countries. Approval procedures vary among countries and can involve additional medicine testing and additional administrative review periods, including obtaining reimbursement and pricing approval in select markets. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks associated with FDA approval as well as additional, presently unanticipated, risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Applications for regulatory approval, including a marketing authorization application, or MAA, for marketing new drugs in Europe, must be supported by extensive clinical and preclinical data, as well as extensive information regarding chemistry, manufacturing and controls, or CMC, to demonstrate the safety and effectiveness of the applicable medicine candidate. The number and types of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the medicine candidate, the disease or the condition that the medicine candidate is designed to target and the regulations applicable to any particular medicine candidate. Despite the time and expense associated with preclinical and clinical studies, failure can occur at any stage, and we could encounter problems that cause us to repeat or perform additional preclinical studies, CMC studies or clinical trials. Regulatory authorities could delay, limit or deny approval of a medicine candidate for many reasons, including because they:

- may not deem a medicine candidate to be adequately safe and effective;
- may not find the data from preclinical studies, CMC studies and clinical trials to be sufficient to support a claim of safety and efficacy;
- may interpret data from preclinical studies, CMC studies and clinical trials significantly differently than we do;
- may not approve the manufacturing processes or facilities associated with our medicine candidates;
- may conclude that we have not sufficiently demonstrated long-term stability of the formulation for which we are seeking marketing approval;
- may change approval policies (including with respect to our medicine candidates' class of drugs) or adopt new regulations; or
- may not accept a submission due to, among other reasons, the content or formatting of the submission.

Even if we believe that data collected from our preclinical studies, CMC studies and clinical trials of our medicine candidates are promising and that our information and procedures regarding CMC are sufficient, our data may not be sufficient to support marketing approval by regulatory authorities, or regulatory interpretation of these data and procedures may be unfavorable. Even if approved, medicine candidates may not be approved for all indications requested and such approval may be subject to limitations on the indicated uses for which the medicine may be marketed, restricted distribution methods or other limitations. Our business and reputation may be harmed by any failure or significant delay in obtaining regulatory approval for the sale of any of our medicine candidates. We cannot predict when or whether regulatory approval will be obtained for any medicine candidate we develop.

If we are unable to obtain any further approvals for RAVICTI outside the United States, Canada and Europe, or determine that commercializing RAVICTI outside the United States, Canada and Europe is not economically viable, the market potential of RAVICTI may be limited.

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On July 12, 2016, Raptor Pharmaceutical Corp., or Raptor, received a notice of deficiency, or NOD, from Health Canada, or HC, dated July 11, 2016 relating to the New Drug Submission, or NDS, Raptor submitted for PROCYSBI in January 2016. The NOD outlined specific deficiencies in the NDS that needed to be addressed for HC to complete its review. A complete response was submitted to HC to address the NOD on November 3, 2016. HC completed the screening process and accepted the NOD response for review on December 16, 2016. Based on a 180-day review for priority applications, we anticipate that HC will complete its review of the NDS and decide whether to grant marketing approval for PROCYSBI for the treatment of nephropathic cystinosis by June 14, 2017.

With respect to QUINSAIR, the FDA has indicated in previous written and verbal communications with Raptor and with the drug's previous sponsor that it believes the data submitted in connection with EMA's subsequent approval of QUINSAIR for the management of chronic pulmonary infections due to Pseudomonas aeruginosa in adults with cystic fibrosis does not provide substantial evidence of efficacy and safety to support FDA approval of QUINSAIR for treatment of patients with cystic fibrosis. On October 27, 2016, the FDA expressed its recommendation that an additional clinical trial should be conducted, and noted that if Raptor submits a new drug application, or NDA, without conducting an additional clinical trial, the FDA will review the submission to determine whether it is acceptable for filing. Based upon the FDA's feedback, we have made the decision not to pursue an NDA for U.S. approval of QUINSAIR as a treatment of Pseudomonas aeruginosa in adults with cystic fibrosis.

Prior to our acquisition of Raptor, Raptor planned to pursue the development of QUINSAIR for use in the indication of bronchiectasis, or BE, not associated with cystic fibrosis. On September 8, 2016, Raptor met the Medicines and Healthcare Products Regulatory Agency, or the MHRA, to discuss non-clinical and clinical development aspects of QUINSAIR for the treatment of BE. On September 29, 2016, Raptor received a written response from the MHRA, which included answers to questions on trial design, among other responses. Raptor submitted a protocol to FDA on August 18, 2016 for a Phase 2, placebo-controlled study of QUINSAIR in adults with BE. Feedback from FDA was received on October 17, 2016 requesting additional information and changes to the proposed study protocol. Raptor was also exploring further clinical development of QUINSAIR for the treatment of pulmonary nontuberculous mycobacteria, or NTM, infection, based on third-party data generated pertaining to the susceptibility of certain pathogens to treatment with levofloxacin and other fluoroquinolone molecules. No clinical data has been generated with QUINSAIR in patients with BE or with NTM infections, either by Raptor, by us or by other parties. This creates uncertainty regarding the potential efficacy of QUINSAIR in these indications.

We will evaluate all development opportunities, including all obligations to use commercial reasonable efforts to further develop QUINSAIR. However, we may determine not to pursue such further development.

The ultimate approval and commercial marketing of any of our medicines in additional indications or geographies is subject to substantial uncertainty. Failure to gain additional regulatory approvals would limit the potential revenues and value of our medicines and could cause our share price to decline.

The amount of our medicine sales in the EEA is dependent in part upon the pricing and reimbursement decisions adopted in each of the EEA countries, which may not be at acceptable levels to us.

One or more EEA countries may not support pricing within our target pricing and reimbursement range for our medicines due to budgetary decisions made by regional, national and local health authorities and third-party payers in the EEA, which would negatively affect our revenues. The pricing and reimbursement process in EEA countries can be lengthy, involved and difficult to predict. Failure to timely complete the pricing and reimbursement process in the EEA countries will delay our ability to market PROCYSBI, to bring QUINSAIR to market in the EEA and to derive revenues from those countries.

We may be subject to penalties and litigation and large incremental expenses if we fail to comply with regulatory requirements or experience problems with our medicines.

Even after we achieve regulatory approvals, we are subject to ongoing obligations and continued regulatory review with respect to many operational aspects including our manufacturing processes, labeling, packaging, distribution, storage, adverse event monitoring and reporting, dispensation, advertising, promotion and recordkeeping. These requirements include submissions of safety and other post-marketing information and reports, ongoing maintenance of medicine registration and continued compliance with current good manufacturing practices, or cGMPs, GCPs, good pharmacovigilance practice, good distribution practices and good laboratory practices, or GLPs. If we, our medicines or medicine candidates, or the third-party manufacturing facilities for our medicines or medicine candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose injunctions or restrictions on the marketing, manufacturing or distribution of a medicine, suspend or withdraw medicine approvals, revoke necessary licenses or suspend medicine reimbursement;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- suspend any ongoing clinical trials or delay or prevent the initiation of clinical trials;
- delay or refuse to approve pending applications or supplements to approved applications we have filed;
- refuse to permit drugs or precursor or intermediary chemicals to be imported or exported to or from the United States;
- suspend or impose restrictions or additional requirements on operations, including costly new manufacturing quality or pharmacovigilance requirements;
- seize or detain medicines or require us to initiate a medicine recall; and/or
- commence criminal investigations and prosecutions.

Moreover, existing regulatory approvals and any future regulatory approvals that we obtain will be subject to limitations on the approved indicated uses and patient populations for which our medicines may be marketed, the conditions of approval, requirements for potentially costly, post-market testing and requirements for surveillance to monitor the safety and efficacy of the medicines. In the EEA, the advertising and promotion of pharmaceuticals is strictly regulated. The direct-to-consumer promotion of prescription pharmaceuticals is not permitted, and some countries in the EEA require the notification and/or prior authorization of promotional or advertising materials directed at healthcare professionals. The FDA, EMA and other authorities in the EEA countries strictly regulate the promotional claims that may be made about prescription medicines, and our medicine labeling, advertising and promotion are subject to continuing regulatory review. Physicians nevertheless may prescribe our medicines to their patients in a manner that is inconsistent with the approved label or that is off-label. Positive clinical trial results in any of our medicine development programs increase the risk that approved pharmaceutical forms of the same APIs may be used off-label in those indications. Our investigational medicine candidate RP103 is comprised of the same API as PROCYSBI. If we are found to have improperly promoted off-label uses of approved medicines, we may be subject to significant sanctions, civil and criminal fines and injunctions prohibiting us from engaging in specified promotional conduct.

In addition, engaging in improper promotion of our medicines for off-label uses in the United States can subject us to false claims litigation under federal and state statutes. These false claims statutes in the United States include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims or causing to present such false or fraudulent claims for payment by a federal program such as Medicare or Medicaid. Growth in false claims litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay civil money penalties, settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs.

The regulations, policies or guidance of regulatory agencies may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our medicine candidates or further restrict or regulate post-approval activities. For example, the Food and Drug Administration Safety and Innovation Act requires the FDA to issue new guidance describing its policy regarding internet and social media promotion of regulated medical products, and the FDA may soon specify new restrictions on this type of promotion. In January 2014, the FDA released draft guidance on how drug companies can fulfill their regulatory requirements for post-marketing submission of interactive promotional media, and though the guidance provided insight into how the FDA views a company's responsibility for certain types of social media promotion, there remains a substantial amount of uncertainty. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are unable to achieve and maintain regulatory compliance, we will not be permitted to market our drugs, which would materially adversely affect our business, results of operations and financial condition.

Our limited history of commercial operations makes evaluating our business and future prospects difficult and may increase the risk of any investment in our ordinary shares.

We face considerable risks and difficulties as a company with limited commercial operating history, particularly as a global consolidated entity with operating subsidiaries that also have limited operating histories. If we do not successfully address these risks, our business, prospects, operating results and financial condition will be materially and adversely harmed. Our limited commercial operating history, including our limited history commercializing our current medicines, makes it particularly difficult for us to predict our future operating results and appropriately budget for our expenses. In the event that actual results differ from our estimates or we adjust our estimates in future periods, our operating results and financial position could be materially affected. For example, we may underestimate the resources we will require to successfully integrate recent or future medicine or company acquisitions, or to commercialize our medicines, or not realize the benefits we expect to derive from our recent or future acquisitions. In addition, we have a limited history implementing our commercialization strategy focused on patient access, and we cannot guarantee that we will be able to successfully implement this strategy or that it will represent a viable strategy over the long term.

We have rights to medicines in certain jurisdictions but have no control over third parties that have rights to commercialize those medicines in other jurisdictions, which could adversely affect our commercialization of these medicines.

Boehringer Ingelheim International GmbH, or Boehringer Ingelheim International, currently has certain rights to commercialize interferon gamma 1b, known as IMUKIN, outside the United States, Canada and Japan. On May 18, 2016, we entered into a definitive agreement with Boehringer Ingelheim International to acquire such rights to IMUKIN, or the IMUKIN Acquisition. The transaction is expected to close in 2017 and we are continuing to work with Boehringer Ingelheim International to enable the transfer of applicable marketing authorizations. AstraZeneca AB, or AstraZeneca, has retained its existing rights to VIMOVO in territories outside of the United States, including the right to use the VIMOVO name and related trademark. While we have the worldwide rights to BUPHENYL, the marketing and distribution rights are granted to SOBI. Similarly, Nuvo Research Inc., or Nuvo, has retained its rights to PENNSAID 2% in territories outside of the United States and has announced its intention to seek commercialization partners outside the United States. We have little or no control over Boehringer Ingelheim International's activities with respect to IMUKIN outside the United States, Canada and Japan, over AstraZeneca's activities with respect to VIMOVO outside of the United States, over SOBI's activities with respect to BUPHENYL in Europe, certain Asian, Latin American, Middle Eastern, North African and other countries or over Nuvo's or its future commercial partners' activities with respect to PENNSAID 2% outside of the United States, even though those activities could impact our ability to successfully commercialize these medicines. For example, AstraZeneca or its assignees or Nuvo or its assignees can make statements or use promotional materials with respect to VIMOVO or PENNSAID 2%, respectively, outside of the United States that are inconsistent with our positioning of the medicines in the United States, and could sell VIMOVO or PENNSAID 2%, respectively, in foreign countries, including

Canada, at prices that are dramatically lower than the prices we charge in the United States. These activities and decisions, while occurring outside of the United States, could harm our commercialization strategy in the United States, in particular because AstraZeneca is continuing to market VIMOVO outside the United States under the same VIMOVO brand name that we are using in the United States. In addition, medicine recalls or safety issues with these medicines outside the United States, even if not related to the commercial medicine we sell in the United States, could result in serious damage to the brand in the United States and impair our ability to successfully market them. We also rely on Boehringer Ingelheim International, AstraZeneca, SOBI and Nuvo or their assignees to provide us with timely and accurate safety information regarding the use of these medicines outside of the United States (and outside of Canada and Japan with regards to Boehringer Ingelheim International), as we have or will have limited access to this information ourselves.

We rely on third parties to manufacture commercial supplies of all of our medicines, and we currently intend to rely on third parties to manufacture commercial supplies of any other approved medicines. The commercialization of any of our medicines could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of medicine or fail to do so at acceptable quality levels or prices or fail to maintain or achieve satisfactory regulatory compliance.

The facilities used by our third-party manufacturers to manufacture our medicines and medicine candidates must be approved by the applicable regulatory authorities. We do not control the manufacturing processes of third-party manufacturers and are currently completely dependent on our third-party manufacturing partners. In addition, we are required to obtain AstraZeneca's consent prior to engaging any third-party manufacturers for esomeprazole, one of the APIs in VIMOVO, other than the third-party manufacturer(s) used by AstraZeneca or its affiliates or licensees. To the extent such manufacturers are unwilling or unable to manufacture esomeprazole for us on commercially acceptable terms, we cannot guarantee that AstraZeneca would consent to our use of alternate sources of supply.

We rely on an exclusive supply agreement with Boehringer Ingelheim RCV GmbH & Co. KG, or Boehringer Ingelheim, for manufacturing and supply of ACTIMMUNE. However, Boehringer Ingelheim also currently manufactures interferon gamma-1b to supply its own commercial needs in its licensed territory, and this may lead to capacity allocation issues and supply constraints to our company. ACTIMMUNE is manufactured by starting with cells from working cell bank samples which are derived from a master cell bank. We and Boehringer Ingelheim separately store multiple vials of the master cell bank. In the event of catastrophic loss at our or Boehringer Ingelheim's storage facility, it is possible that we could lose multiple cell banks and have the manufacturing capacity of ACTIMMUNE severely impacted by the need to substitute or replace the cell banks. In addition, a key excipient used in PENNSAID 2% as a penetration enhancer is dimethyl sulfoxide, or DMSO. We and Nuvo, our exclusive supplier of PENNSAID 2%, rely on a sole proprietary form of DMSO for which we maintain a substantial safety stock. However, should this supply become inadequate, damaged, destroyed or unusable, we and Nuvo may not be able to qualify a second source. We rely on NOF Corporation, or NOF, as our exclusive supplier of the PEGylation agent that is a critical raw material in the manufacture of KRYSTEXXA. If NOF failed to supply such PEGylation agent, it may lead to KRYSTEXXA supply constraints.

If any of our third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, or pass regulatory inspection, they will not be able to secure or maintain regulatory approval for the manufacturing facilities. For example, Pharmaceutics International, Inc., or PII, our manufacturer of BUPHENYL, was found to be non-compliant for cGMPs by the MHRA, which could restrict PII from supplying BUPHENYL in the EU. However, BUPHENYL was considered to be critical to public health and as a result, the MHRA issued a certificate of cGMP compliance for PII which is valid until June 30, 2017. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve these facilities for the manufacture of our medicines or if they withdraw any such approval in the future, or if our suppliers or third-party manufacturers decide they no longer want to supply our primary active ingredients or manufacture our medicines, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our medicines. To the extent any third-party manufacturers that we engage with respect to our medicines are different from those currently being used for commercial supply in the United States, the FDA will need to approve the facilities of those third-party manufacturers used in the manufacture of our medicines prior to our sale of any medicine using these facilities.

Although we have entered into supply agreements for the manufacture and packaging of our medicines, our manufacturers may not perform as agreed or may terminate their agreements with us. We currently rely on single source suppliers for certain of our medicines. If our manufacturers terminate their agreements with us, we may have to qualify new back-up manufacturers. We rely on safety stock to mitigate the risk of our current suppliers electing to cease producing bulk drug medicine or ceasing to do so at acceptable prices and quality. However, we can provide no assurance that such safety stocks would be sufficient to avoid supply shortfalls in the event we have to identify and

qualify new contract manufacturers.

The manufacture of medicines requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of medicines often encounter difficulties in production, particularly in scaling up and validating initial production. These problems include difficulties with production costs and yields, quality control, including stability of the medicine, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if microbial, viral or other contaminations are discovered in the medicines or in the manufacturing facilities in which our medicines are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that issues relating to the manufacture of any of our medicines will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to commercialize our medicines in the United States or provide any medicine candidates to patients in clinical trials would be jeopardized.

Any delay or interruption in our ability to meet commercial demand for our medicines will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these medicines. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of any of our medicines or medicine candidates and could have a material adverse effect on our business, results of operations, financial condition and prospects.

We have experienced recent growth and expanded the size of our organization substantially in connection with our recent acquisition transactions, and we may experience difficulties in managing this growth as well as potential additional growth in connection with future medicine, development program or company acquisitions.

As of December 31, 2010 and prior to the commercial launch of DUEXIS, we employed approximately 40 full-time employees as a consolidated entity. As of December 31, 2016, we employed approximately 1,050 full-time employees, including approximately 480 sales representatives, representing a substantial change to the size of our organization. We have also experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire in connection with the commercialization of our medicines, requiring us to hire and train new sales representatives. Our management, personnel, systems and facilities currently in place may not be adequate to support this recent and anticipated growth, and we may not be able to retain or recruit qualified personnel in the future due to competition for personnel among pharmaceutical businesses.

As our commercialization plans and strategies continue to develop, we will need to continue to recruit and train sales and marketing personnel and expect to need to expand the size of our employee base for managerial, operational, financial and other resources as a result of our recent acquisitions. Our ability to manage any future growth effectively may require us to, among other things:

- continue to manage and expand the sales and marketing efforts for our existing medicines;
- enhance our operational, financial and management controls, reporting systems and procedures;
- expand our international resources;
- successfully identify, recruit, hire, train, maintain, motivate and integrate additional employees;
- establish and increase our access to commercial supplies of our medicines and medicine candidates;
- expand our facilities and equipment; and
- manage our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors, collaborators, distributors and other third parties.

Our recent acquisitions have resulted in many changes, including significant changes in the corporate business and legal entity structure, the integration of other companies and their personnel with us, and changes in systems. We are currently undertaking numerous complex transition activities associated with our recent acquisitions, and we may encounter unexpected difficulties or incur unexpected costs, including:

- difficulties in achieving growth prospects from combining third-party businesses with our business;
- difficulties in the integration of operations and systems;
- difficulties in the assimilation of employees and corporate cultures;
- challenges in preparing financial statements and reporting timely results at both a statutory level for multiple entities and jurisdictions and at a consolidated level for public reporting;
- challenges in keeping existing physician prescribers and patients and increasing adoption of acquired medicines;
- difficulties in achieving anticipated cost savings, synergies, business opportunities and growth prospects from the combination;
- potential unknown liabilities, adverse consequences and unforeseen increased expenses associated with the transaction; and
- challenges in attracting and retaining key personnel.

If any of these factors impair our ability to continue to integrate our operations with those of any companies or businesses we acquire, we may not be able to realize the business opportunities, growth prospects and anticipated tax synergies from combining the businesses. In addition, we may be required to spend additional time or money on integration that otherwise would be spent on the development and expansion of our business.

As a result of our acquisition of Raptor and our plans to launch RAVICTI in Europe, we may continue expanding our operations and add commercial personnel in Europe. We may not be successful in integrating Raptor's existing European operations and personnel with our own or in otherwise growing our commercial operations outside the United States, and could encounter other challenges in growing our commercial presence in Europe, including due to risks associated with political and economic instability, operating under different legal requirements and tax complexities. If we are unable to manage our commercial growth outside of the Unites States, our opportunities to expand sales in other countries will be limited or we may experience greater costs with respect to our ex-U.S. commercial operations.

We are also broadening our acquisition strategy to potentially include development-stage assets or programs, which entails additional risk to us. For example, if we are unable to identify programs that ultimately result in approved medicines, we may spend material amounts of our capital and other resources evaluating, acquiring and developing medicines that ultimately do not provide a return on our investment. We have less experience evaluating development-stage assets and may be at a disadvantage compared to other entities pursuing similar opportunities. Regardless, development-stage programs generally have a high rate of failure and we cannot guarantee that any such programs will ultimately be successful. We will also need to enhance our clinical development and regulatory functions to properly evaluate and develop earlier-stage opportunities, which may include recruiting personnel that are knowledgeable in therapeutic areas we have not yet pursued. If we are unable to acquire promising development-stage assets or eventually obtain marketing approval for them, we may not be able to create a meaningful pipeline of new medicines and eventually realize a return on our investments.

Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities and toward managing these growth and integration activities. Our future financial performance and our ability to execute on our business plan will depend, in part, on our ability to effectively manage any future growth and our failure to effectively manage growth could have a material adverse effect on our business, results of operations, financial condition and prospects.

We face significant competition from other biotechnology and pharmaceutical companies, including those marketing generic medicines and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and international markets, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, experienced marketing and manufacturing organizations and well-established sales forces. Additional consolidations in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors and we will have to find new ways to compete and may have to potentially merge with or acquire other businesses to stay competitive. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or in-licensing on an exclusive basis, medicines that are more effective and/or less costly than our medicines.

DUEXIS and VIMOVO face competition from other NSAIDs, including Celebrex®, which was marketed by Pfizer Inc., and is also a generic medicine known as celecoxib and marketed by other pharmaceutical companies. DUEXIS and VIMOVO also face significant competition from the separate use of NSAIDs for pain relief and GI protective medications to reduce the risk of NSAID-induced upper GI ulcers. Both NSAIDs and GI protective medications are available in generic form and may be less expensive to use separately than DUEXIS or VIMOVO. PENNSAID 2% faces competition from generic versions of diclofenac sodium topical solutions that are priced significantly less than the price we charge for PENNSAID 2%, and Voltaren Gel, marketed by Endo Pharmaceuticals Solutions Inc., which is the market leader in the topical NSAID category. Legislation enacted in most states in the United States allows, or in some instances mandates, that a pharmacist dispense an available generic equivalent when filling a prescription for a branded medicine, in the absence of specific instructions from the prescribing physician. Because pharmacists often have economic and other incentives to prescribe lower-cost generics, if physicians prescribe DUEXIS, PENNSAID 2% or VIMOVO, those prescriptions may not result in sales. If physicians do not complete prescriptions through our HorizonCares program or otherwise provide prescribing instructions prohibiting the substitution of generic ibuprofen and famotidine separately as a substitution for DUEXIS or generic naproxen and branded Nexium® (esomeprazole) as a substitute for VIMOVO or generic diclofenac sodium topical solutions as a substitute for PENNSAID 2%, sales of DUEXIS, PENNSAID 2% and VIMOVO may suffer despite any success we may have in promoting DUEXIS, PENNSAID 2% or VIMOVO to physicians. In addition, other medicine candidates that contain ibuprofen and famotidine in combination or naproxen and esomeprazole in combination, while not currently known or FDA approved, may be developed and compete with DUEXIS or VIMOVO, respectively, in the future. While KRYSTEXXA faces limited direct competition, a number of competitors have drugs in Phase 1 or Phase 2 trials. On December 22, 2015, AstraZeneca secured approval from the FDA for ZURAMPIC (lesinurad) 200mg tablets in combination with a xanthine oxidase inhibitor, or XOI, for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with an XOI alone. In April 2016, the U.S. rights to ZURAMPIC were licensed to Ironwood Pharmaceuticals Inc. Although ZURAMPIC is not a direct competitor because it has not been approved for refractory gout, this therapy could be used prior to use of KRYSTEXXA and if effective, could reduce the target patient population for KRYSTEXXA. PROCYSBI faces competition from Cystagon (immediate-release cysteamine bitartrate capsules) for the treatment of cystinosis and Cystaran (cysteamine ophthalmic solution) for treatment of corneal crystal accumulation in patients with cystinosis. QUINSAIR faces competition from Tobramycin solution, which is available as a generic medicine for treatment of chronic Pseudomonas aeruginosa lung infections in patients with cystic fibrosis, TOBI Podhaler, Cayston and colistimethate.

We have also entered into settlement and license agreements that may allow certain of our competitors to sell generic versions of certain of our medicines in the United States, subject to the terms of such agreements. We granted a non-exclusive license (that is only royalty-bearing in some circumstances), to manufacture and commercialize a generic version of DUEXIS in the United States after January 1, 2023, or earlier under certain circumstances. We granted non-exclusive licenses to manufacture and commercialize generic versions of PENNSAID 2% in the United States after January 10, 2029, or earlier under certain circumstances. We granted a non-exclusive license to

manufacture and commercialize a generic version of RAYOS tablets in the United States after December 23, 2022, or earlier under certain circumstances.

Patent litigation is currently pending in the United States District Court for the District of New Jersey against several companies intending to market a generic version of PENNSAID 2% prior to the expiration of certain of our patents listed in the FDA's Orange Book, or the Orange Book. These cases are collectively known as the PENNSAID 2% cases, and involve the following sets of defendants: (i) Actavis Laboratories UT, Inc., formerly known as Watson Laboratories, Inc., Actavis, Inc. and Actavis plc, or collectively Actavis; and (ii) Lupin Limited and Lupin Pharmaceuticals, Inc., or collectively Lupin. These cases arise from Paragraph IV Patent Certification notice letters from each of Actavis and Lupin advising each had filed an Abbreviated New Drug Application, or ANDA, with the FDA seeking approval to market a generic version of PENNSAID 2% before the expiration of the patents-in-suit. In Horizon Pharma Ireland Limited, et al v. Actavis Laboratories UT, Inc., C.A. No. 14-cv-7992-NLH-AMD, a bench trial is scheduled to begin on March 21, 2017. No trial date has been set in any other PENNSAID 2% case.

We received from Actavis a Paragraph IV Patent Certification Notice Letter dated September 27, 2016, against Orange Book listed U.S. Patent No. 9,415,029 advising that Actavis had filed an ANDA with the FDA for a generic version of PENNSAID 2%.

We received from Apotex Inc., or Apotex, three Paragraph IV Patent Certification Notice Letters dated April 1, 2016, June 30, 2016, and September 21, 2016 against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, 8,871,809, 9,066,913, 9,101,591, 9,132,110, 9,168,304, 9,168,305, 9,220,784, 9,339,551, 9,339,552 and 9,415,029, advising that Apotex had filed an ANDA with the FDA for a generic version of PENNSAID 2%.

Patent litigation is currently pending in the United States District Court for the District of New Jersey against several companies intending to market a generic version of VIMOVO before the expiration of certain of our patents listed in the Orange Book. These cases are collectively known as the VIMOVO cases, and involve the following sets of defendants: (i) Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd., or collectively Dr. Reddy's; (ii) Lupin; and (iii) Mylan Pharmaceuticals Inc., Mylan Laboratories Limited, and Mylan Inc., or collectively Mylan. Patent litigation is currently pending before the Court of Appeals for the Federal Circuit against a fourth generic company, Actavis Laboratories FL., Inc. and Actavis Pharma, Inc., or collectively Actavis Pharma. The cases arise from Paragraph IV Patent Certification notice letters from each of Dr. Reddy's, Lupin and Mylan advising each had filed an ANDA with the FDA seeking approval to market generic versions of VIMOVO before the expiration of the patents-in-suit.

Patent litigation is currently pending in the United States District Court for the Eastern District of Texas against Par Pharmaceutical, Inc., or Par Pharmaceutical, and in the United States District Court for the District of New Jersey against Par Pharmaceutical and against Lupin, who are each intending to market generic versions of RAVICTI prior to the expiration of certain of our patents listed in the Orange Book. These cases are collectively known as the RAVICTI cases and arise from Paragraph IV Patent Certification notice letters from each of Par Pharmaceutical and Lupin advising each had filed an ANDA with the FDA seeking approval to market a generic version of RAVICTI before the expiration of the patents-in-suit.

If we are unsuccessful in any of the VIMOVO cases or PENNSAID 2% cases, we will likely face generic competition with respect to VIMOVO and/or PENNSAID 2% and sales of VIMOVO and/or PENNSAID 2% will be substantially harmed. If we are unsuccessful in any of the RAVICTI cases, RAVICTI would likely face generic competition in the United States when its orphan exclusivity expires (currently scheduled to occur in February 2020), and its sales would likely materially decline.

ACTIMMUNE is the only medicine currently approved by the FDA specifically for the treatment of CGD and SMO. While there are additional or alternative approaches used to treat patients with CGD and SMO, there are currently no medicines on the market that compete directly with ACTIMMUNE. A widely accepted protocol to treat CGD in the United States is the use of concomitant "triple prophylactic therapy" comprising ACTIMMUNE, an oral antibiotic agent and an oral antifungal agent. However, the FDA-approved labeling for ACTIMMUNE does not discuss this "triple prophylactic therapy," and physicians may choose to prescribe one or both of the other modalities in the absence of ACTIMMUNE. Because of the immediate and life-threatening nature of SMO, the preferred treatment option for SMO is often to have the patient undergo a bone marrow transplant which, if successful, will likely obviate the need for further use of ACTIMMUNE in that patient. Likewise, the use of bone marrow transplants in the treatment of patients with CGD is becoming more prevalent, which could have a material adverse effect on sales of ACTIMMUNE and its profitability. We are aware of a number of research programs investigating the potential of gene therapy as a possible cure for CGD. Additionally, other companies may be pursuing the development of medicines and treatments that target the same diseases and conditions which ACTIMMUNE is currently approved to treat. As a result, it is possible that our competitors may develop new medicines that manage CGD or SMO more effectively, cost less or possibly even cure CGD or SMO. In addition, U.S. healthcare legislation passed in March 2010 authorized the FDA to approve biological products, known as biosimilars, that are similar to or interchangeable with previously approved biological products, like ACTIMMUNE, based upon potentially abbreviated data packages. Biosimilars are likely to be sold at substantially lower prices than branded medicines because the biosimilar manufacturer would not have to recoup the research and development and marketing costs associated with the branded medicine. Though we are not currently aware of any biosimilar under development, the development and commercialization of any competing medicines or the discovery of any new alternative treatment for CGD or SMO could have a material adverse effect on sales of ACTIMMUNE and its profitability.

BUPHENYL's composition of matter patent protection and orphan drug exclusivity have expired. Because BUPHENYL has no regulatory exclusivity or listed patents, there is nothing to prevent a competitor from submitting an ANDA for a generic version of BUPHENYL and receiving FDA approval. In November 2011, Ampolgen Pharmaceuticals, LLC received FDA approval for a generic version of NaPBA tablets, which may compete with RAVICTI and BUPHENYL in treating UCD. In March 2013, SigmaPharm Laboratories, LLC received FDA approval for a generic version of NaPBA powder, which competes with BUPHENYL and may compete with RAVICTI in treating UCD. In July 2013, Lucane Pharma, or Lucane, received marketing approval from the EMA for taste-masked NaPBA and has announced a distribution partnership in Canada. In January 2015, Lucane announced it had received marketing approval for its taste-masked NaPBA in Canada. We believe Lucane is also seeking approval via an ANDA in the United States. If this ANDA is approved, this formulation may compete with RAVICTI and BUPHENYL in treating UCD in the United States. Generic versions of BUPHENYL to date have been priced at a discount relative to BUPHENYL or RAVICTI, and physicians, patients, or payers may decide that this less expensive alternative is preferable to BUPHENYL and RAVICTI. If this occurs, sales of BUPHENYL and/or RAVICTI could be materially reduced, but we would nevertheless be required to make royalty payments to Ucyclyd Pharma, Inc., or Ucyclyd, and another external party, at the same royalty rates. While Ucyclyd and its affiliates are generally contractually prohibited from developing or commercializing new medicines, anywhere in the world, for the treatment of UCD or hepatic encephalopathy, or HE, which are chemically similar to RAVICTI, they may still develop and commercialize medicines that compete with RAVICTI. For example, medicines approved for indications other than UCD and HE may still compete with RAVICTI if physicians prescribe such medicines off-label for UCD or HE. We are also aware that Orphan Europe SARL, or Orphan Europe, is conducting a clinical trial of carglumic acid to treat some of the UCD enzyme deficiencies for which RAVICTI was approved. Promethera Biosciences SA has successfully completed Phase I/II trials of its cell-based therapy for the treatment of UCD and plans to conduct a Phase IIb/III clinical trial. Carglumic acid is approved for maintenance therapy for chronic hyperammonemia and to treat hyperammonenic crises in Nacetylglutamate synthase deficiency, a rare UCD subtype, and is sold under the name Carbaglu. If the results of this trial are successful and Orphan Europe is able to complete development and obtain approval of Carbaglu to treat additional UCD enzyme deficiencies, RAVICTI would face additional competition from this compound.

The availability and price of our competitors' medicines could limit the demand, and the price we are able to charge, for our medicines. We will not successfully execute on our business objectives if the market acceptance of our medicines is inhibited by price competition, if physicians are reluctant to switch from existing medicines to our medicines, or if physicians switch to other new medicines or choose to reserve our medicines for use in limited patient populations.

In addition, established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to acquire novel compounds that could make our medicines obsolete. Our ability to compete successfully with these companies and other potential competitors will depend largely on our ability to leverage our experience in clinical, regulatory and commercial development to:

- develop and acquire medicines that are superior to other medicines in the market;
- attract qualified clinical, regulatory, and sales and marketing personnel;
- obtain patent and/or other proprietary protection for our medicines and technologies;
- obtain required regulatory approvals; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicine candidates.

If we are unable to maintain or realize the benefits of orphan drug exclusivity, we may face increased competition with respect to certain of our medicines.

Under the Orphan Drug Act of 1983, the FDA may designate a medicine as an orphan drug if it is a drug intended to treat a rare disease or condition affecting fewer than 200,000 people in the United States. A company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years from the date of its approval. RAVICTI, KRYSTEXXA and PROCYSBI have been granted orphan drug exclusivity by the FDA, which we expect will provide orphan drug marketing exclusivity in the United States until February 2020, September 2017 and December 2020, respectively, with exclusivity for PROCYSBI extending to 2022 for patients ages two to six years. However, despite orphan drug exclusivity, the FDA can still approve another drug containing the same active ingredient and used for the same orphan indication if it determines that a subsequent drug is safer, more effective or makes a major contribution to patient care, and orphan exclusivity can be lost if the orphan drug manufacturer is unable to ensure that a sufficient quantity of the orphan drug is available to meet the needs of patients with the rare disease or condition. Orphan drug exclusivity may also be lost if the FDA later determines that the initial request for designation was materially defective. In addition, orphan drug exclusivity does not prevent the FDA from approving competing drugs for the same or similar indication containing a different active ingredient. If orphan drug exclusivity is lost and we were unable to successfully enforce any remaining patents covering RAVICTI, KRYSTEXXA or PROCYSBI, we could be subject to generic competition and revenues from RAVICTI, KRYSTEXXA or PROCYSBI could decrease materially. In addition, if a subsequent drug is approved for marketing for the same or a similar indication as RAVICTI, KRYSTEXXA or PROCYSBI despite orphan drug exclusivity, we may face increased competition and lose market share with respect to these medicines. KRYSTEXXA does not have orphan drug exclusivity in the EU or other regions of the world. RAVICTI will benefit from a period of 10 years of orphan market exclusivity in the EU, concurrently applied to each of the approved six sub-types of the UCDs. This will run concurrently with its marketing exclusivity status. PROCYSBI received marketing authorization in September 2013 from the European Commission for marketing in the EU as an orphan medicine for the management of proven nephropathic cystinosis. PROCYSBI received seven years of market exclusivity, through 2020 for patients six years and older as an orphan drug in the United States and ten years of market exclusivity, through 2023, as an orphan drug in Europe. QUINSAIR received 10 years of market exclusivity in the EU, beginning with its March 2015 marketing authorization. Orphan market exclusivity may be reduced to six years in the EU if the orphan drug designation criteria are no longer met after five years, including where it is shown that the medicine is sufficiently profitable. As in the United States, loss of orphan marketing exclusivity in the EU may result in early generic competition, which could substantially reduce our revenues from EU sales of these medicines.

Our business operations may subject us to numerous commercial disputes, claims and/or lawsuits and such litigation may be costly and time-consuming and could materially and adversely impact our financial position and results of operations.

Operating in the pharmaceutical industry, particularly the commercialization of medicines, involves numerous commercial relationships, complex contractual arrangements, uncertain intellectual property rights, potential product liability and other aspects that create heightened risks of disputes, claims and lawsuits. In particular, we may face claims related to the safety of our medicines, intellectual property matters, employment matters, tax matters, commercial disputes, competition, sales and marketing practices, environmental matters, personal injury, insurance coverage and acquisition or divestiture-related matters. For example, the active ingredient in QUINSAIR, levofloxacin, is currently subject to product liability claims. Any commercial dispute, claim or lawsuit may divert management's attention away from our business, we may incur significant expenses in addressing or defending any commercial dispute, claim or lawsuit, and we may be required to pay damage awards or settlements or become subject to equitable remedies that could adversely affect our operations and financial results.

We are currently in litigation with multiple generic drug manufacturers regarding intellectual property infringement. For example, we are currently involved in Hatch Waxman litigation with generic drug manufacturers related to VIMOVO, PENNSAID 2% and RAVICTI.

Similarly, from time to time we are involved in disputes with distributors, PBMs and licensing partners regarding our rights and performance of obligations under contractual arrangements. For example, we were previously in litigation with Express Scripts, related to alleged breach of contract claims and in which Express Scripts was seeking payment for rebates relating to DUEXIS, RAYOS and VIMOVO. We counterclaimed against Express Scripts, contesting the amount owed and contending Express Scripts had breached the rebate agreement. In September 2016, we entered into a settlement agreement and mutual release with Express Scripts pursuant to which we and Express Scripts were released from any and all claims relating to the litigation without admitting any fault or wrongdoing and we agreed to pay Express Scripts $65.0 million.

Litigation related to these disputes may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us.

A variety of risks associated with operating our business and marketing our medicines internationally could materially adversely affect our business.

In addition to our U.S. operations, we have operations in Ireland, Bermuda, the Grand Duchy of Luxembourg, or Luxembourg, the Netherlands, France, Switzerland, Germany, Canada, the Grand Cayman Islands and in Israel (through Andromeda Biotech Ltd). Moreover, Grünenthal S.A. is in the registration process for the commercialization of DUEXIS in Latin America. BUPHENYL is currently marketed in various territories outside the United States by third-party distributors. RAVICTI received marketing authorization from HC in March 2016 and marketing approval in the EU in November 2015. We launched RAVICTI in Canada in November 2016 and plan to begin commercializing RAVICTI in Europe in 2017. PROCYSBI received marketing authorization from the EMA in September 2013 and is marketed in various countries within the EEA. QUINSAIR received marketing authorization from the EMA in March 2015 and is also marketed in several countries within the EEA. QUINSAIR received marketing authorization from HC in June 2015 and we launched QUINSAIR in Canada in December 2016. We face risks associated with our international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. We are subject to numerous risks associated with international business activities, including:

- compliance with differing or unexpected regulatory requirements for our medicines;
- compliance with Irish laws and the maintenance of our Irish tax residency with respect to our overall corporate structure and administrative operations, including the need to generally hold meetings of our board of directors and

make decisions in Ireland, which may make certain corporate actions more cumbersome, costly and time-consuming;

- difficulties in staffing and managing foreign operations;
- in certain circumstances, including with respect to the commercialization of LODOTRA in Europe and certain Asian, Latin American, Middle Eastern and African countries, commercialization of BUPHENYL in select countries throughout Europe, the Middle East, and the Asia-Pacific region, commercialization of RAVICTI in select countries throughout Europe and commercialization of DUEXIS in Latin America, increased dependence on the commercialization efforts and regulatory compliance of third-party distributors or strategic partners;

- compliance with German laws with respect to our Horizon Pharma GmbH subsidiary through which Horizon Pharma Switzerland GmbH conducts most of its European operations;
- foreign government taxes, regulations and permit requirements;
- U.S. and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;
    - anti-corruption laws, including the Foreign Corrupt Practices Act, or the FCPA;
- economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries;
- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues, and other obligations related to doing business in another country;
- compliance with tax, employment, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- changes in diplomatic and trade relationships; and
- challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States.

Our business activities outside of the United States are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the United Kingdom's Bribery Act 2010, or the U.K. Bribery Act. The FCPA and similar anti-corruption laws generally prohibit offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to non-U.S. government officials in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The U.K. Bribery Act prohibits giving, offering, or promising bribes to any person, including non-United Kingdom, or U.K., government officials and private persons, as well as requesting, agreeing to receive, or accepting bribes from any person. In addition, under the U.K. Bribery Act, companies which carry on a business or part of a business in the U.K. may be held liable for bribes given, offered or promised to any person, including non-U.K. government officials and private persons, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Liability is strict, with no element of a corrupt state of mind, but a defense of having in place adequate procedures designed to prevent bribery is available. Furthermore, under the U.K. Bribery Act there is no exception for facilitation payments. As described above, our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. Recently the SEC and the U.S. Department of Justice have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd–Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We are engaged in ongoing efforts that are designed to ensure our compliance with these laws, including due diligence, training, policies, procedures and internal controls. However, there is no certainty that all employees and third-party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of manufacturers and other third-party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

These and other risks associated with our international operations may materially adversely affect our business, financial condition and results of operations.

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If we fail to develop or acquire other medicine candidates or medicines, our business and prospects would be limited.

A key element of our strategy is to develop or acquire and commercialize a portfolio of other medicines or medicine candidates in addition to our current medicines, through business or medicine acquisitions. Because we do not engage in proprietary drug discovery, the success of this strategy depends in large part upon the combination of our regulatory, development and commercial capabilities and expertise and our ability to identify, select and acquire approved or clinically enabled medicine candidates for therapeutic indications that complement or augment our current medicines, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Identifying, selecting and acquiring promising medicines or medicine candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular medicine or medicine candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to identify, select and acquire suitable medicines or medicine candidates from third parties or acquire businesses at valuations and on other terms acceptable to us, or if we are unable to raise capital required to acquire businesses or new medicines, our business and prospects will be limited.

Moreover, any medicine candidate we acquire may require additional, time-consuming development or regulatory efforts prior to commercial sale or prior to expansion into other indications, including preclinical studies if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All medicine candidates are prone to the risk of failure that is inherent in pharmaceutical medicine development, including the possibility that the medicine candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such medicines that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective or desired than other commercially available alternatives.

In addition, if we fail to successfully commercialize and further develop our medicines, there is a greater likelihood that we will fail to successfully develop a pipeline of other medicine candidates to follow our existing medicines or be able to acquire other medicines to expand our existing portfolio, and our business and prospects would be harmed.

Our recent medicine and company acquisitions and any other strategic transactions that we may pursue in the future could have a variety of negative consequences, and we may not realize the benefits of such transactions or attempts to engage in such transactions.

We have recently completed multiple medicine and company acquisitions and our strategy is to engage in additional strategic transactions with third parties, such as acquisitions of companies or divisions of companies and asset purchases of medicines, medicine candidates or technologies that we believe will complement or augment our existing business. We may also consider a variety of other business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and other investments. Any such transaction may require us to incur non-recurring and other charges, increase our near and long-term expenditures, pose significant integration challenges, create additional tax, legal, accounting and operational complexities in our business, require additional expertise, result in dilution to our existing shareholders and disrupt our management and business, which could harm our operations and financial results. For example, in connection with our acquisition of the U.S. rights to VIMOVO, we assumed primary responsibility for the existing patent infringement litigation with respect to VIMOVO, and have also agreed to reimburse certain legal expenses of Pozen Inc., who subsequently entered into a business combination with Tribute Pharmaceuticals Canada Inc. to become known as Aralez Pharmaceuticals Inc., or Aralez, with respect to its continued involvement in such litigation. We also assumed responsibility for the existing patent infringement litigation with respect to RAVICTI upon the closing of our acquisition of Hyperion Therapeutics Inc., or Hyperion, and have assumed responsibility for completing post-marketing clinical trials of RAVICTI that are required by the FDA and are ongoing. We expect that the RAVICTI litigation will result in substantial on-going expenses and potential distractions to our management team.

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In connection with our acquisition of Raptor, we assumed Raptor's post-marketing clinical study obligations in the MAA for QUINSAIR and contractual obligations under agreements with Tripex Pharmaceuticals, LLC, or Tripex, and PARI Pharma GmbH, or PARI, related to QUINSAIR. Under the agreement with Tripex, we are required to pursue commercially reasonable efforts to initiate, and subsequently to complete, an additional clinical trial of QUINSAIR in a non-cystic fibrosis patient population within a specified period of time and an obligation to progress toward submitting an NDA for approval of QUINSAIR in the United States for use in all or part of the cystic fibrosis patient population. These obligations are subject to certain exceptions due to, for example, manufacturing delays not under our control, or delays caused by the FDA. If we fail to properly exercise such efforts to initiate and complete an appropriate clinical trial, or fail to submit an NDA for U.S. approval in the cystic fibrosis patient population, during the time periods specified in the agreement, we may be subject to various claims by Tripex and parties affiliated with Tripex. In addition, if we do not spend a minimum amount on QUINSAIR development in each of the three years following our acquisition of Raptor, we may also be obligated to pre-pay a milestone payment related to initiating a clinical trial for QUINSAIR in a non-cystic fibrosis indication. Under the license agreement with PARI, we are required to comply with diligence milestones related to development and commercialization of QUINSAIR in the United States and to spend a specified minimum amount per year on development activities in the United States until submission of the NDA for QUINSAIR in the United States. If we do not comply with these obligations, our licenses to certain intellectual property related to QUINSAIR may become non-exclusive in the United States or could be terminated. We are also now subject to contractual obligations under license agreements with the Regents of the University of California, San Diego, or UCSD, with respect to PROCYSBI, including diligence obligations to develop PROCYSBI for the treatment of non-alcoholic steatohepatitis, or NASH, and Huntington's disease, with which we currently are not in compliance. To the extent that we fail to perform the diligence obligations under the agreement, UCSD may, with respect to such indication, terminate the license or otherwise cause the license to become non-exclusive. If one or more of these licenses was terminated, we would have no further right to use or exploit the related intellectual property, which would limit our ability to develop PROCYSBI or QUINSAIR in other indications, and could impact our ability to continue commercializing PROCYSBI or QUINSAIR in their approved indications.

We face significant competition in seeking appropriate strategic transaction opportunities and the negotiation process for any strategic transaction can be time-consuming and complex. In addition, we may not be successful in our efforts to engage in certain strategic transactions because our financial resources may be insufficient and/or third parties may not view our commercial and development capabilities as being adequate. We may not be able to expand our business or realize our strategic goals if we do not have sufficient funding or cannot borrow or raise additional capital. There is no assurance that following any of our recent acquisition transactions or any other strategic transaction, we will achieve the anticipated revenues, net income, tax or other benefits that we believe justify such transactions. In addition, any failures or delays in entering into strategic transactions anticipated by analysts or the investment community could seriously harm our consolidated business, financial condition, results of operations or cash flow.

Our parent company may not be able to successfully maintain its current advantageous tax status and resulting tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

Our parent company is incorporated in Ireland and maintains subsidiaries in multiple jurisdictions, including Ireland, the U.K, the United States, Switzerland, Luxembourg, Germany, France, the Netherlands, Canada and Bermuda. Prior to our merger transaction with Vidara Therapeutics International Public Limited Company, or Vidara, and such transaction, the Vidara Merger, Vidara was able to achieve a favorable tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, including Ireland and Bermuda, together with intra-group service and transfer pricing agreements, each on an arm's length basis. We are continuing a substantially similar structure and arrangements. Taxing authorities, such as the U.S. Internal Revenue Service, or IRS, actively audit and otherwise challenge these types of arrangements, and have done so in the pharmaceutical industry. We expect that these challenges will continue as a result of the recent increase in scrutiny and political attention on corporate tax structures. The IRS may challenge our structure and transfer pricing arrangements through an audit or lawsuit. Responding to or defending such a challenge could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We cannot predict whether taxing authorities will

conduct an audit or file a lawsuit challenging this structure, the cost involved in responding to any such audit or lawsuit, or the outcome. If we are unsuccessful in defending such a challenge, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our medicines or seek to raise additional funds, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The IRS may not agree with our conclusion that our parent company should be treated as a foreign corporation for U.S. federal income tax purposes following the combination of the businesses of Horizon Pharma, Inc., or HPI, and Vidara.

Although our parent company is incorporated in Ireland, the IRS may assert that it should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal income tax purposes pursuant to Section 7874 of the Internal Revenue Code of 1986, as amended, or the Code. A corporation is generally considered a tax resident in the jurisdiction of its organization or incorporation for U.S. federal income tax purposes. Because our parent company is an Irish incorporated entity, it would generally be classified as a foreign corporation (and, therefore, a non-U.S. tax resident) under these rules. Section 7874 of the Code provides an exception pursuant to which a foreign incorporated entity may, in certain circumstances, be treated as a U.S. corporation for U.S. federal income tax purposes.

Under Section 7874 of the Code, a foreign corporation will be treated as a U.S. corporation for U.S. federal tax purposes if, due to an acquisition of a U.S. corporation, at least 80 percent of its stock (by vote or value) is held by former stockholders of the acquired U.S. corporation. We believe that we should be treated as a foreign corporation because the former stockholders of HPI owned (within the meaning of Section 7874 of the Code) less than 80 percent (by both vote and value) of the combined entity's stock immediately after the Vidara Merger. However, there can be no assurance that there will not exist in the future a subsequent change in the facts or in law which might cause our parent company to be treated as a domestic corporation for U.S. federal income tax purposes, including with retroactive effect.

Further, there can be no assurance that the IRS will agree with the position that the ownership test was satisfied. There is limited guidance regarding the application of Section 7874 of the Code, including with respect to the provisions regarding the application of the ownership test. If our parent company were unable to be treated as a foreign corporation for U.S. federal income tax purposes, one of our significant strategic reasons for completing the Vidara Merger would be nullified and we may not be able to recoup the significant investment in completing the transaction.

Future changes to U.S. and non-U.S. tax laws could materially adversely affect our company.

Under current law, we expect our parent company to be treated as a foreign corporation for U.S. federal income tax purposes. However, changes to the rules in Section 7874 of the Code or regulations promulgated thereunder or other guidance issued by the U.S. Department of the Treasury, or the U.S. Treasury, or the IRS could adversely affect our parent company's status as a foreign corporation for U.S. federal income tax purposes, and any such changes could have prospective or retroactive application. If our parent company is treated as a domestic corporation, more of our income will be taxed by the United States which may substantially increase our effective tax rate.

On April 4, 2016, the U.S. Treasury and the IRS issued temporary regulations that expand the scope of transactions subject to the rules designed to eliminate the U.S. tax benefits of inversions. Under the temporary regulations, the former stockholders of U.S. corporations acquired by a foreign corporation within 36 months of the signing date of the last such acquisition are aggregated for the purpose of determining whether the foreign corporation will be treated as a domestic corporation for U.S. federal tax purposes because at least 80 percent of the stock of the foreign corporation is held by former stockholders of a U.S. corporation. The requirement to aggregate the stockholders in such acquisitions for the purpose of determining whether the 80 percent threshold is met may limit our ability to use our stock to acquire U.S. corporations or their assets in the future.

The U.S. Treasury and the IRS also issued proposed regulations on April 4, 2016 that address whether an interest in a related corporation is debt or equity. The proposed regulations would treat certain inter-company debt issued on or after that date as equity including, subject to certain exceptions, inter-company debt issued in certain distributions, acquisitions of related party stock and asset reorganizations. As drafted, the proposed regulations would limit the ability of our U.S. group to deduct interest on such new inter-company debt. The proposed regulations could also result in recharacterization of inter-company debt to equity for inter-company debt incurred to provide funding for an

acquisition by the U.S. group if, and to the extent of, certain cash or property transfers by our U.S. group to the foreign affiliates within 36 months before or after these inter-company borrowings. These limitations could result in more of our future income being taxed by the United States and thereby increase our effective tax rate.

In July 2015, the International Tax Bipartisan Tax Working Group of the United States Senate Committee on Finance, or the Finance Committee, issued its report on international tax reform. The Finance Committee's co-chairs concluded that it will be necessary to limit earnings stripping by foreign multinationals through interest deductions on inter-company debt in order to eliminate a competitive advantage that foreign multinationals would otherwise have over domestic multinational companies. The status of the recommendations from the International Tax Bipartisan Tax Working Group, including regulations aimed at curbing earnings stripping, as well as the status of United States tax reform in general, is subject to significant uncertainty as the White House and both houses of Congress are considering several material tax reform proposals. These proposals include, among other items, a significant reduction to the United States corporate tax rate and a possible "border adjustment tax" that would effectively increase the economic cost of imports. At this point in time it is not possible to determine all of the possible consequences to us of the various tax reform proposals that are under consideration. However, any tax reform could significantly impact our United States and worldwide tax liabilities.

In addition, the Organization for Economic Co-operation and Development released its Base Erosion and Profit Shifting project final report on October 5, 2015. This report provides the basis for international standards for corporate taxation that are designed to prevent, among other things, the artificial shifting of income to tax havens and low-tax jurisdictions, the erosion of the tax base through interest deductions on inter-company debt and the artificial avoidance of permanent establishments (i.e., tax nexus with a jurisdiction). Legislation to adopt these standards has been enacted or is currently under consideration in a number of jurisdictions. As a result, our income may be taxed in jurisdictions where it is not currently taxed and at higher rates of tax than it is currently taxed, which may substantially increase our effective tax rate.

The U.S. federal government has called for substantial changes to U.S. tax policy and laws. We do not currently have sufficient information that would allow us to predict what U.S. tax reform, if any, may be enacted in the future or what impact any such changes would have on our business. Changes to U.S. tax laws could significantly impact our business, financial condition, results of operations, or cash flows.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, sales and marketing and scientific and medical personnel, including our executive committee composed of our Chairman, President and Chief Executive Officer, Timothy P. Walbert; our Executive Vice President, Chief Business Officer, Robert F. Carey; our Executive Vice President, Chief Financial Officer, Paul W. Hoelscher; our Executive Vice President, Chief Administrative Officer, Barry J. Moze; our Executive Vice President, Research and Development and Chief Medical Officer, Jeffrey W. Sherman, M.D., FACP; our Executive Vice President, General Counsel, Brian K. Beeler; our Executive Vice President, Primary Care Business Unit, George Hampton; our Executive Vice President, Orphan Business Unit, Dave Happel; our Executive Vice President, Technical Operations, Michael A. DesJardin and our Senior Vice President, Rheumatology Business Unit, Vikram Karnani. In order to retain valuable employees at our company, in addition to salary and cash incentives, we provide performance stock units, or PSUs, and stock options and restricted stock units that vest over time. The value to employees of PSUs, stock options and restricted stock units will be significantly affected by movements in our share price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, sales and marketing, regulatory affairs, clinical development, medical affairs and development teams may terminate their employment with us on short notice. Although we have written employment arrangements with all of our employees, these employment arrangements generally provide for at-will employment, which means that our employees can leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our

inability to find suitable replacements could potentially harm our business, financial condition and prospects. We do not maintain “key man” insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior sales and marketing and scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize medicines and medicine candidates will be limited.

We are, with respect to our current medicines, and will be, with respect to any other medicine or medicine candidate for which we obtain FDA or EMA approval or which we acquire, subject to ongoing FDA or the EMA obligations and continued regulatory review, which may result in significant additional expense. Additionally, any other medicine candidate, if approved by the FDA or the EMA, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our medicines.

Any regulatory approvals that we obtain for our medicine candidates may also be subject to limitations on the approved indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the medicine candidate. In addition, with respect to our current FDA-approved medicines (and with respect to our medicine candidates, if approved), the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the medicine are subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs, GCPs, international conference on harmonization regulations, or ICH regulations, and GLPs, which are regulations and guidelines enforced by the FDA for all of our medicines in clinical development, for any clinical trials that we conduct post-approval. With respect to RAVICTI, the FDA imposed several post-marketing requirements and a post-marketing commitment, which include remaining obligations to conduct studies in UCD patients during the first two months of life and from two months to two years of age, including a study of the pharmacokinetics in both age groups, and a randomized study to determine the safety and efficacy in UCD patients who are treatment naïve to phenylbutyrate treatment. Although we are committed to carrying out these commitments, there are challenges in conducting studies in pediatric patients including availability of study sites, patients, and obtaining parental informed consent. On June 29, 2016, we submitted a supplemental new drug application, or sNDA, to the FDA for RAVICTI to expand the age range for chronic management of UCDs from two years of age and older to two months of age and older. Subject to positive data from on-going studies, we have targeted an sNDA submission in the first quarter of 2018 in relation to UCD patients during the first two months of life. In connection with our acquisition of Crealta Holdings LLC, or Crealta, in January 2016, we assumed responsibility for an observational study related to KRYSTEXXA. Thus far in this study there have been no new safety signals and the reported safety results parallel those in the KRYSTEXXA product label. We are continuing to screen and enroll patients in the near term. With respect to QUINSAIR, we are required to conduct post-marketing clinical studies in cystic fibrosis patients pursuant to obligations in the MAA for QUINSAIR and submit data to the EMA regularly regarding observed clinical medicine profile and safety assessment.

In addition, the FDA closely regulates the marketing and promotion of drugs and biologics. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' promotional communications. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of medicines for off-label uses and other sales practices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, false claims laws, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of medicines for unapproved uses, pricing and Medicare and/or Medicaid reimbursement.

Later discovery of previously unknown problems with a medicine, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the medicine, withdrawal of the medicine from the market, or voluntary or mandatory medicine recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of medicine license approvals;

- medicine seizure or detention, or refusal to permit the import or export of medicines; and
- injunctions, the imposition of civil or criminal penalties, or exclusion, debarment or suspension from government healthcare programs.

If we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects.

Coverage and reimbursement may not be available, or reimbursement may be available at only limited levels, for our medicines, which could make it difficult for us to sell our medicines profitably or to successfully execute planned medicine price increases.

Market acceptance and sales of our medicines will depend in large part on global coverage and reimbursement policies and may be affected by future healthcare reform measures, both in the United States and other key international markets. Successful commercialization of our medicines will depend in part on the availability of governmental and third-party payer reimbursement for the cost of our medicines. Government health administration authorities, private health insurers and other organizations generally provide reimbursement for healthcare. In particular, in the United States, private health insurers and other third-party payers often provide reimbursement for medicines and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the United States, the EU and other significant or potentially significant markets for our medicines and medicine candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medicines and services, particularly for new and innovative medicines and therapies, which has resulted in lower average selling prices. Further, the increased scrutiny of prescription drug pricing practices and emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU will put additional pressure on medicine pricing, reimbursement and usage, which may adversely affect our medicine sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. These pressures may create negative reactions to any medicine price increases, or limit the amount by which we may be able to increase our medicine prices, which may adversely affect our medicine sales and results of operations.

Patients are unlikely to use our medicines unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our medicines. Third-party payers may limit coverage to specific medicines on an approved list, also known as a formulary, which might not include all of the FDA-approved medicines for a particular indication. Moreover, a third-party payer’s decision to provide coverage for a medicine does not imply that an adequate reimbursement rate will be approved. Additionally, one third-party payer’s decision to cover a particular medicine does not ensure that other payers will also provide coverage for the medicine, or will provide coverage at an adequate reimbursement rate. Even though we have contracts with some PBMs in the United States, that does not guarantee that they will perform in accordance with the contracts, nor does that preclude them from taking adverse actions against us, which could materially adversely affect our operating results. In addition, the existence of such PBM contracts does not guarantee coverage by such PBM’s contracted health plans or adequate reimbursement to their respective providers for our medicines. For example, two significant PBMs placed DUEXIS and VIMOVO on their exclusion lists beginning in 2015, which has resulted in a loss of coverage for patients whose healthcare plans have adopted these PBM lists. While DUEXIS and VIMOVO were removed from the Express Scripts and CVS Caremark 2017 exclusion lists, we cannot guarantee that Express Scripts or CVS Caremark will not later add these medicines back to their exclusion lists or that we will be able to otherwise expand formulary access for DUEXIS and VIMOVO under health plans that contract with Express Scripts and/or CVS Caremark. Additional healthcare plan formularies may also exclude our medicines from coverage due to the actions of certain PBMs, future price increases we may implement, our use of the HorizonCares program or any other co-pay programs, or other reasons. If our strategies to mitigate formulary exclusions are not effective, these events may reduce the likelihood that physicians prescribe our medicines and increase the likelihood that prescriptions for our medicines are not filled.

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Outside of the United States, the success of our medicines, including BUPHENYL, LODOTRA, PROCYSBI, QUINSAIR, RAVICTI and, following the IMUKIN Acquisition, interferon gamma-1b (currently commercialized under the trade names IMUKIN, IMUKINE, IMMUKIN and IMMUKINE), will depend largely on obtaining and maintaining government coverage, because in many countries patients are unlikely to use prescription drugs that are not covered by their government healthcare programs. The majority of LODOTRA sales are in Germany and Italy where reimbursement has been approved. BUPHENYL is marketed in select countries throughout Europe, the Middle East and the Asia-Pacific region. We launched RAVICTI in Canada in November 2016 and we expect to begin commercializing RAVICTI in Europe in 2017. PROCYSBI is marketed in select countries in Europe and QUINSAIR was recently launched in certain countries in Europe and in Canada, but we cannot be certain that existing reimbursement in EU countries will be maintained or that we will be able to secure reimbursement in additional countries. Negotiating coverage and reimbursement with governmental authorities can delay commercialization by 12 months or more. Coverage and reimbursement policies may adversely affect our ability to sell our medicines on a profitable basis. In many international markets, governments control the prices of prescription pharmaceuticals, including through the implementation of reference pricing, price cuts, rebates, revenue-related taxes and profit control, and we expect prices of prescription pharmaceuticals to decline over the life of the medicine or as volumes increase. Many countries in the EU have increased the amount of discounts required on medicines, and we expect these discounts to continue as countries attempt to manage healthcare expenditures, especially in light of current economic conditions. As a result of these pricing practices, it may become difficult to achieve or sustain profitability or expected rates of growth in revenue or results of operations. Any shortfalls in revenue could adversely affect our business, financial condition and results of operations.

In light of such policies and the uncertainty surrounding proposed regulations and changes in the coverage and reimbursement policies of governments and third-party payers, we cannot be sure that coverage and reimbursement will be available for any of our medicines in any additional markets or for any other medicine candidates that we may develop. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our medicines. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize our medicines.

We expect to experience pricing pressures in connection with the sale of our medicines due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals relating to outcomes and quality. For example, the ACA increased the mandated Medicaid rebate from 15.1% to 23.1%, expanded the rebate to Medicaid managed care utilization and increased the types of entities eligible for the federal 340B drug discount program. On January 30, 2017, the White House Office of Management and Budget withdrew the draft August 2015 Omnibus Guidance document that was issued by the Department of Health and Human Services Health Resources and Services Administration, or HRSA, that addressed a broad range of topics including, among other items, the definition of a patient’s eligibility for 340B drug pricing. However, as concerns over drug pricing have not abated, there remains the possibility that HRSA will propose a similar regulation or that Congress will explore changes to the program through legislation. Also, in March 2016, the Centers for Medicare & Medicaid Services, or CMS, announced a Proposed Rule that would test new payment models for Medicare Part B prescription drugs, and provider services incident to, or otherwise related to, such drugs. Generally, the Proposed Rule included payment models designed on quality and value propositions and incentives to drive utilization of efficient therapies and payments based on clinical outcomes. The Proposed Rule greatly differs from the current reimbursement methodology for Medicare Part B drugs and was subject to significant discussion among stakeholders including Congress, industry, payers, healthcare providers and other interested organizations. Although the Proposed Rule was withdrawn by CMS in December, we will continue to monitor for legislative developments and new regulatory proposals.

There may be additional pressure by payers, healthcare providers, and Congress, to use generic drugs that contain the active ingredients found in our medicines or any other medicine candidates that we may develop or acquire. If we fail to successfully secure and maintain coverage and adequate reimbursement for our medicines or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our medicines and expected revenue and

profitability which would have a material adverse effect on our business, results of operations, financial condition and prospects.

We may also experience pressure from payers concerning certain promotional approaches that we may implement such as our HorizonCares program or any other co-pay or free medicine programs whereby we assist qualified patients with certain out-of-pocket expenditures for our medicine. If we are unsuccessful with our HorizonCares program or any other co-pay initiatives or free medicine programs, or we alternatively are unable to secure expanded formulary access through additional arrangements with PBMs or other payers, we would be at a competitive disadvantage in terms of pricing versus preferred branded and generic competitors. We may also experience financial pressure in the future which would make it difficult to support investment levels in areas such as managed care contract rebates, HorizonCares and other access tools.

We are subject to federal, state and foreign healthcare laws and regulations and implementation or changes to such healthcare laws and regulations could adversely affect our business and results of operations.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to regulate and to change the healthcare system in ways that could affect our ability to sell our medicines profitably. In the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs (including a number of proposals pertaining to prescription drugs, specifically), improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

If we are found to be in violation of any of these laws or any other federal or state regulations, we may be subject to civil and/or criminal penalties, damages, fines, exclusion, additional reporting requirements and/or oversight from federal health care programs and the restructuring of our operations. Any of these could have a material adverse effect on our business and financial results. Since many of these laws have not been fully interpreted by the courts, there is an increased risk that we may be found in violation of one or more of their provisions. Any action against us for violation of these laws, even if we ultimately are successful in our defense, will cause us to incur significant legal expenses and divert our management's attention away from the operation of our business.

In January 2017, the United States House of Representatives and Senate passed legislation, the concurrent budget resolution for fiscal year 2017, which initiates actions that would repeal certain aspects of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA, to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed.

Moreover, certain politicians, including President Trump, have called for federal legislation to regulate the prices of medicines. The majority of our medicines are purchased by private payers, and we do not believe that any such legislation, if enacted, would have a material effect on us or our business. However, we cannot know what form any such legislation may take, the likelihood it would be signed into law or the market's perception of how such legislation would affect us. Any reduction in reimbursement from government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our current medicines and/or those for which we may receive regulatory approval in the future.

We are subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. Prosecutions under such laws have increased in recent years and we may become subject to such litigation. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

In the United States, we are subject directly, or indirectly through our customers, to various state and federal fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, civil monetary penalty statutes prohibiting beneficiary inducements, and similar state laws, federal and state privacy and security laws, sunshine laws, government price reporting laws, and other fraud laws. These laws may impact, among other things, our current and proposed sales, marketing and educational programs, as well as other possible relationships with customers, pharmacies, physicians, payers, and patients.

Compliance with these laws, including the development of a comprehensive compliance program, is difficult, costly and time consuming. Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. These risks may be increased where there are evolving interpretations of applicable regulatory requirements, such as those applicable to manufacturer co-pay initiatives. Pharmaceutical manufacturer co-pay initiatives and free medicine programs are the subject of ongoing litigation (involving other manufacturers and to which we are not a party) and evolving interpretations of applicable regulatory requirements and certain state laws, and any change in the regulatory or enforcement environment regarding such programs could impact our ability to offer such programs. If we are unsuccessful with our HorizonCares programs, any other co-pay initiatives or free medicine programs, we would be at a competitive disadvantage in terms of pricing versus preferred branded and generic competitors, or be subject to significant penalties. We are engaged in various business arrangements with current and potential customers, and we can give no assurance that such arrangements would not be subject to scrutiny under such laws, despite our efforts to properly structure such arrangements. Even if we structure our programs with the intent of compliance with such laws, there can be no certainty that we would not need to defend our business activities against enforcement or litigation. Further, we cannot give any assurances that prior business activities or arrangements of other companies that we acquire will not be scrutinized or subject to enforcement or litigation.

There has also been a trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposed reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in significant civil monetary penalties.

We are unable to predict whether we could be subject to actions under any of these or other healthcare laws, or the impact of such actions. If we are found to be in violation of, or to encourage or assist the violation by third parties of any of the laws described above or other applicable state and federal fraud and abuse laws, we may be subject to penalties, including administrative, civil and criminal penalties, damages, fines, withdrawal of regulatory approval, imprisonment, exclusion from government healthcare reimbursement programs, contractual damages, reputational harm, diminished profits and future earnings, injunctions and other associated remedies, or private “qui tam” actions brought by individual whistleblowers in the name of the government, and the curtailment or restructuring of our operations, all of which could have a material adverse effect on our business and results of operations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business.

Our medicines or any other medicine candidate that we develop may cause undesirable side effects or have other properties that could delay or prevent regulatory approval or commercialization, result in medicine re-labeling or withdrawal from the market or have a significant impact on customer demand.

Undesirable side effects caused by any medicine candidate that we develop could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, or cause us to evaluate the future of our development programs. In our two Phase 3 clinical trials with DUEXIS, the most commonly reported treatment-emergent adverse events were nausea, dyspepsia, diarrhea, constipation and upper respiratory tract infection. In Phase 3 endoscopic registration clinical trials with VIMOVO, the most commonly reported treatment-emergent adverse events were erosive gastritis, dyspepsia, gastritis, diarrhea, gastric ulcer, upper abdominal pain, nausea and upper respiratory tract infection. The most common side effects observed in pivotal trials for ACTIMMUNE were “flu-like” or constitutional symptoms such as fever, headache, chills, myalgia and fatigue. The most commonly reported treatment-emergent adverse events in the Phase 3 clinical trials with RAYOS/LODOTRA included flare in rheumatoid arthritis related symptoms, abdominal pain, nasopharyngitis, headache, flushing, upper respiratory tract infection, back pain and weight gain. The most common adverse events reported in a Phase 2 clinical trial of PENNSAID 2% were application site reactions, such as dryness, exfoliation, erythema, pruritus, pain, induration, rash and scabbing. With respect to BUPHENYL, the most common side effects are change in the frequency of breathing, lack of or irregular menstruation, lower back, side, or stomach pain, mood or mental changes, muscle pain or twitching, nausea or vomiting, nervousness or restlessness, swelling of the feet or lower legs, unpleasant taste and unusual tiredness or weakness. With respect to RAVICTI, the most common side effects are diarrhea, nausea, decreased appetite, gas, vomiting, high blood levels of ammonia, headache, tiredness and dizziness. With respect to KRYSTEXXA, the most commonly reported serious adverse reactions in the pivotal trial were gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis, exacerbation of pre-existing congestive heart failure and vomiting. With respect to MIGERGOT, the most commonly reported adverse reactions are ischemia, cyanosis, absence of pulse, cold extremities, gangrene, precordial distress and pain, electrocardiogram change, muscle pain, nausea and vomiting, rectal or anal ulcer, parathesias, numbness weakness, vertigo, localized edemas and itching. With respect to PROCYSBI, the most common side effects include vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue, rash and headache. With respect to QUINSAIR, the most common side effects include itching, wheezing, hives, rash, swelling, pale skin color, fast heartbeat and faintness.

The FDA or other regulatory authorities may also require, or we may undertake, additional clinical trials to support the safety profile of our medicines or medicine candidates.

In addition, if we or others identify undesirable side effects caused by our medicines or any other medicine candidate that we may develop that receives marketing approval, or if there is a perception that the medicine is associated with undesirable side effects:

- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- regulatory authorities may withdraw their approval of the medicine or place restrictions on the way it is prescribed;
- we may be required to change the way the medicine is administered, conduct additional clinical trials or change the labeling of the medicine or implement a risk evaluation and mitigation strategy; and
- we may be subject to increased exposure to product liability and/or personal injury claims.

If any of these events occurred with respect to our medicines, our ability to generate significant revenues from the sale of these medicines would be significantly harmed.

We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or if they experience regulatory compliance issues, we may not be able to obtain regulatory approval for or commercialize our medicine candidates and our business could be substantially harmed.

We have agreements with third-party contract research organizations, or CROs, to conduct our clinical programs, including those required for post-marketing commitments, and we expect to continue to rely on CROs for the completion of on-going and planned clinical trials. We may also have the need to enter into other such agreements in the future if we were to develop other medicine candidates or conduct clinical trials in additional indications for our existing medicines. In connection with the investigator-initiated study to evaluate ACTIMMUNE in combination with PD-1/PD-L1 inhibitors in various forms of cancer including advanced urothelial carcinoma (bladder cancer) and renal cell carcinoma, we are collaborating with Fox Chase Cancer Center. In connection with our ongoing study to evaluate RAYOS/LODOTRA on the fatigue experienced by SLE patients, we are collaborating with the ALR. We rely heavily on these parties for the execution of our clinical studies and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol. We, our CROs and our academic research organizations are required to comply with current GCP or ICH regulations. The FDA enforces these GCP or ICH regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs or collaborators fail to comply with applicable GCP or ICH regulations, the data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply or complied with GCP or ICH regulations. In addition, our clinical trials must be conducted with medicine produced under cGMP regulations, and may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our CROs or collaborators violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. We must also obtain certain third-party institutional review board, or IRB, and ethics committee approvals in order to conduct our clinical trials. Delays by IRBs and ethics committees in providing such approvals may delay our clinical trials.

If any of our relationships with these third-party CROs or collaborators terminate, we may not be able to enter into similar arrangements on commercially reasonable terms, or at all. If CROs or collaborators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our medicines and medicine candidates. As a result, our results of operations and the commercial prospects for our medicines and medicine candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs or collaborators can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO or collaborator commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs and collaborators, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition or prospects.

Clinical development of drugs and biologics involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of potential medicine candidates may not be predictive of the results of later-stage clinical trials. Medicine candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical testing. For example, Raptor announced in September 2015, based on information then available, that it would not advance its program for the treatment of pediatric NASH with PROCYSBI after a Phase 2b trial failed achieve its primary endpoints. Also, on December 8, 2016, we announced that the Phase 3 trial, Safety, Tolerability and Efficacy of ACTIMMUNE Dose Escalation in Friedreich's Ataxia study evaluating ACTIMMUNE for the treatment of Friedreich's ataxia, or FA, did not meet its primary endpoint of a statistically significant change from baseline in the modified Friedreich's Ataxia Rating Scale at twenty-six weeks versus treatment with placebo. In addition, the secondary endpoints did not meet statistical significance. We, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and the Friedreich's Ataxia Research Alliance Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study.

With respect to the investigator-initiated study to evaluate ACTIMMUNE in combination with OPDIVO® (nivolumab) in advanced solid tumors and to the extent that we are required to conduct additional clinical development of any of our existing or later acquired medicines or we conduct clinical development of earlier stage medicine candidates or for other additional indications for RAYOS/LODOTRA, we may experience delays in these clinical trials or investigator-initiated studies. We do not know whether any additional clinical trials will be initiated in the future, begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB or ethics committee approval at each site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial;
- adding new sites; or
- manufacturing sufficient quantities of medicine candidates for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the medicine candidate being studied in relation to other available therapies, including any new drugs or biologics that may be approved for the indications we are investigating. Furthermore, we rely and expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our future clinical trials and while we have and intend to have agreements governing their committed activities, we will have limited influence over their actual performance.

We could encounter delays if prescribing physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our medicine candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, our collaborators, the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a medicine candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or if we terminate, any clinical trial of our medicine candidates, the commercial prospects of our medicine candidates will be harmed, and our ability to generate medicine revenues from any of these medicine candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our medicine development and approval process and jeopardize our ability to commence medicine sales and generate revenues.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of one or more of our medicine candidates.

Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our medicine candidates.

Business interruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions. While we carry insurance for certain of these events and have implemented disaster management plans and contingencies, the occurrence of any of these business interruptions could seriously harm our business and financial condition and increase our costs and expenses. We conduct significant management operations at both our global headquarters located in Dublin, Ireland and our U.S. office located in Lake Forest, Illinois. If our Dublin or Lake Forest offices were affected by a natural or man-made disaster or other business interruption, our ability to manage our domestic and foreign operations could be impaired, which could materially and adversely affect our results of operations and financial condition. We currently rely, and intend to rely in the future, on third-party manufacturers and suppliers to produce our medicines and third-party logistics partners to ship our medicines. Our ability to obtain commercial supplies of our medicines could be disrupted and our results of operations and financial condition could be materially and adversely affected if the operations of these third-party suppliers or logistics partners were affected by a man-made or natural disaster or other business interruption. The ultimate impact of such events on us, our significant suppliers and our general infrastructure is unknown.

We are dependent on information technology systems, infrastructure and data, which exposes us to data security risks.

We are dependent upon information technology systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems make them inherently vulnerable to service interruption or destruction, malicious intrusion and random attack. Likewise, data privacy or security breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity. Cyber-attacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business partners face similar risks and any security breach of their systems could adversely affect our security posture. A security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, any of which could disrupt our business and/or result in increased costs or loss of revenue. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our medicines.

We face an inherent risk of product liability claims as a result of the commercial sales of our medicines and the clinical testing of our medicine candidates. For example, we may be sued if any of our medicines or medicine candidates allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the medicine, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our medicines and medicine candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our medicines or medicine candidates that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and resources;
- substantial monetary awards to trial participants or patients;
- medicine recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize our medicines or medicine candidates.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of medicines we develop. We currently carry product liability insurance covering our clinical studies and commercial medicine sales in the amount of $75 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to the on-going commercialization of our current medicines in the United States, and/or the potential commercial launches of any of our medicines in additional markets or for additional indications, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our business involves the use of hazardous materials, and we and our third-party manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our medicine candidates and other hazardous compounds. We and our manufacturers are subject to federal, state and local as well as foreign laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state, federal or foreign authorities may curtail the use of these materials and interrupt our business operations. We do not currently maintain hazardous materials insurance coverage. If we are subject to any liability as a result of our third-party manufacturers' activities involving hazardous materials, our business and financial condition may be adversely affected. In the future we may seek to establish longer-term third-party manufacturing arrangements, pursuant to which we would seek to obtain contractual indemnification protection from such third-party manufacturers potentially limiting this liability exposure.

Our employees, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by our employees and other third parties may also include the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare

programs and imprisonment.

Risks Related to our Financial Position and Capital Requirements

In the past we have incurred significant operating losses.

We have a limited operating history and even less history operating as a combined organization following the acquisitions of Vidara, Hyperion, Crealta and Raptor. We have financed our operations primarily through equity and debt financings and have incurred significant operating losses in the past. We had an operating loss of $147.2 million for the year ended December 31, 2016, operating income of $55.4 million for the year ended December 31, 2015 and an operating loss of $8.5 million for the year ended December 31, 2014. We had a net loss of $166.8 million and a net income of $39.5 million for the years ended December 31, 2016 and 2015, respectively, and a net loss of $263.6 million for the year ended December 31, 2014. As of December 31, 2016, we had an accumulated deficit of $848.0 million. Our prior losses have resulted principally from costs incurred in our development activities for our medicines and medicine candidates, commercialization activities related to our medicines, costs associated with our acquisition transactions and costs associated with derivative liability accounting. Our prior losses, combined with possible future losses, have had and will continue to have an adverse effect on our shareholders' deficit and working capital. While we anticipate that we will continue to generate operating profits in the future, whether we can sustain this will depend on the revenues we generate from the sale of our medicines being sufficient to cover our operating expenses.

We have limited sources of revenues and significant expenses. We cannot be certain that we will sustain profitability, which would depress the market price of our ordinary shares and could cause our investors to lose all or a part of their investment.

Our ability to sustain profitability depends upon our ability to generate sales of our medicines. We have a limited history of commercializing our medicines as a company, and commercialization has been primarily in the United States. We may never be able to successfully commercialize our medicines or develop or commercialize other medicines in the United States or in the EU, which we believe represents our most significant commercial opportunity. Our ability to generate future revenues depends heavily on our success in:

- continued commercialization of our existing medicines and any other medicine candidates for which we obtain approval;
- obtaining FDA approvals for additional indications for ACTIMMUNE and RAVICTI;
- securing additional foreign regulatory approvals for our medicines in territories where we have commercial rights; and
- developing, acquiring and commercializing a portfolio of other medicines or medicine candidates in addition to our current medicines.

Even if we do generate additional medicine sales, we may not be able to sustain profitability on a quarterly or annual basis. Our failure to remain profitable would depress the market price of our ordinary shares and could impair our ability to raise capital, expand our business, diversify our medicine offerings or continue our operations.

We may need to obtain additional financing to fund additional acquisitions.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to:

- commercialize our existing medicines in the United States, including the substantial expansion of our sales force in recent years;
- complete the regulatory approval process, and any future required clinical development related thereto, for our medicines and medicine candidates;
- potentially acquire other businesses or additional complementary medicines or medicines that augment our current medicine portfolio, including costs associated with refinancing debt of acquired companies; and
-

conduct clinical trials with respect to potential additional indications, as well as conduct post-marketing requirements and commitments, with respect to our medicines and medicines we acquire.

While we believe that our existing cash and cash equivalents will be sufficient to fund our operations based on our current expectations of continued revenue growth, we may need to raise additional funds if we choose to expand our commercialization or development efforts more rapidly than presently anticipated, if we develop or acquire additional medicines or acquire companies, or if our revenue does not meet expectations.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our medicines or medicine candidates or one or more of our other research and development initiatives, or delay, cut back or abandon our plans to grow the business through acquisition. We also could be required to:

- seek collaborators for one or more of our current or future medicine candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms our rights to technologies or medicine candidates that we would otherwise seek to develop or commercialize ourselves.

In addition, if we are unable to secure financing to support future acquisitions, our ability to execute on a key aspect of our overall growth strategy would be impaired.

Any of the above events could significantly harm our business, financial condition and prospects.

We have incurred a substantial amount of debt, which could adversely affect our business, including by restricting our ability to engage in additional transactions or incur additional indebtedness, and prevent us from meeting our debt obligations.

As of December 31, 2016, we had $1,807.5 million book value, or $1,944.0 million principal amount, of indebtedness, including $769.0 million in secured indebtedness. In connection with the acquisition of Hyperion, we issued $475.0 million aggregate principal amount of 6.625% Senior Notes due 2023, or the 2023 Senior Notes, in April 2015 and borrowed $400.0 million in principal amount of secured loans pursuant to a credit agreement we entered into in May 2015 with Citibank, N.A., as administrative and collateral agent, and the lenders from time to time party thereto providing for (i) the six-year $400.0 million term loan facility; (ii) an uncommitted accordion facility subject to the satisfaction of certain financial and other conditions; and (iii) one or more uncommitted refinancing loan facilities with respect to loans thereunder, or the 2015 Senior Secured Credit Facility. We repaid $1.0 million in principal amount from this facility quarterly from the third quarter of 2015 to the fourth quarter of 2016. In connection with the acquisition of Raptor, we issued $300.0 million aggregate principal amount of 8.75% Senior Notes due 2024, or the 2024 Senior Notes, in October 2016 and borrowed $375.0 million in principal amount of secured loans, or the 2016 Incremental Loan Facility, pursuant to an amendment to our credit agreement, or as amended, the credit agreement. Accordingly, we have a significant amount of debt outstanding on a consolidated basis.

This substantial level of debt could have important consequences to our business, including, but not limited to:

- reducing the benefits we expect to receive from our recent and any future acquisition transactions;
- making it more difficult for us to satisfy our obligations;
- requiring a substantial portion of our cash flows from operations to be dedicated to the payment of principal and interest on our indebtedness, therefore reducing our ability to use our cash flows to fund acquisitions, capital expenditures, and future business opportunities;
- exposing us to the risk of increased interest rates to the extent of any future borrowings, including borrowings under our credit agreement, at variable rates of interest;
- making it more difficult for us to satisfy our obligations with respect to our indebtedness, including our outstanding notes, our credit agreement, and any failure to comply with the obligations of any of our debt instruments, including restrictive covenants and borrowing conditions, could result in an event of default under the agreements governing such indebtedness;

- increasing our vulnerability to, and reducing our flexibility to respond to, changes in our business or general adverse economic and industry conditions;

- limiting our ability to obtain additional financing for working capital, capital expenditures, debt service requirements, acquisitions, and general corporate or other purposes and increasing the cost of any such financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; and placing us at a competitive disadvantage as compared to our competitors, to the extent they are not as highly leveraged and who, therefore, may be able to take advantage of opportunities that our leverage may prevent us from exploiting; and
- restricting us from pursuing certain business opportunities.

The credit agreement and the indentures governing the 2024 Senior Notes and the 2023 Senior Notes impose, and the terms of any future indebtedness may impose, various covenants that limit our ability and/or the ability of our restricted subsidiaries' (as designated under such agreements) to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales, consolidate with or merge or sell all or substantially all of our assets, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries, and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to us.

Our ability to obtain future financing and engage in other transactions may be restricted by these covenants. In addition, any credit ratings will impact the cost and availability of future borrowings and our cost of capital. Our ratings at any time will reflect each rating organization's then opinion of our financial strength, operating performance and ability to meet our debt obligations. There can be no assurance that we will achieve a particular rating or maintain a particular rating in the future. A reduction in our credit ratings may limit our ability to borrow at acceptable interest rates. If our credit ratings were downgraded or put on watch for a potential downgrade, we may not be able to sell additional debt securities or borrow money in the amounts, at the times or interest rates or upon the more favorable terms and conditions that might otherwise be available. Any impairment of our ability to obtain future financing on favorable terms could have an adverse effect on our ability to refinance any of our then-existing debt and may severely restrict our ability to execute on our business strategy, which includes the continued acquisition of additional medicines or businesses.

We may not be able to generate sufficient cash to service all of our indebtedness and may be forced to take other actions to satisfy our obligations under our indebtedness, which may not be successful.

Our ability to make scheduled payments under or to refinance our debt obligations depends on our financial condition and operating performance, which is subject to prevailing economic, industry and competitive conditions and to certain financial, business and other factors beyond our control. Our ability to generate cash flow to meet our payment obligations under our debt may also depend on the successful implementation of our operating and growth strategies. Any refinancing of our debt could be at higher interest rates and may require us to comply with more onerous covenants, which could further restrict our business operations. We cannot assure you that we will maintain a level of cash flows from operating activities sufficient to pay the principal, premium, if any, and interest on our indebtedness.

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay capital expenditures, sell assets or business operations, seek additional capital or restructure or refinance our indebtedness. We cannot ensure that we would be able to take any of these actions, that these actions would be successful and permit us to meet our scheduled debt service obligations or that these actions would be permitted under the terms of existing or future debt agreements, including the indentures that govern the 2024 Senior Notes and the 2023 Senior Notes and the credit agreement. In addition, any failure to make payments of interest and principal on our outstanding indebtedness on a timely basis would likely result in a reduction of our credit rating, which could harm our ability to incur additional indebtedness.

If we cannot make scheduled payments on our debt, we will be in default and, as a result:

- our debt holders could declare all outstanding principal and interest to be due and payable;
-

the administrative agent and/or the lenders under the credit agreement could foreclose against the assets securing the borrowings then outstanding; and

- we could be forced into bankruptcy or liquidation, which could result in you losing your investment.

We generally have broad discretion in the use of our cash and may not use it effectively.

Our management has broad discretion in the application of our cash, and investors will be relying on the judgment of our management regarding the use of our cash. Our management may not apply our cash in ways that ultimately increase the value of any investment in our securities. We expect to use our existing cash to fund commercialization activities for our medicines, to potentially fund additional medicine or business acquisitions, to potentially fund additional regulatory approvals of certain of our medicines, to potentially fund development, life cycle management or manufacturing activities of our medicines for other indications, to potentially fund share repurchases, and for working capital, capital expenditures and general corporate purposes. We may also invest our cash in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our shareholders. If we do not invest or apply our cash in ways that enhance shareholder value, we may fail to achieve expected financial results, which could cause the price of our ordinary shares to decline.

Our ability to use net operating loss carryforwards and certain other tax attributes may be limited.

Under Sections 382 and 383 of the Code, if a corporation undergoes an “ownership change” (generally defined as a greater than 50 percent change (by value) in its equity ownership over a three-year period), the corporation’s ability to use pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change income may be limited. We continue to carry forward our annual limitation resulting from an ownership change date of August 2, 2012. The limitation on pre-change net operating losses incurred prior to the August 2, 2012 change date is approximately $14.7 million for 2017 and $7.7 million for 2018 through 2028. During the third quarter of 2016, we also recognized additional net operating losses and federal and state tax credits as a result of our acquisition of Raptor on October 25, 2016 in the amount of approximately $97.3 million of federal net operating losses, state operating losses of approximately $177.5 million and approximately $22.4 million of federal and state tax credits. We continue to carry forward the annual limitation related to Hyperion of $50 million resulting from the last ownership change date in 2014. The net operating loss carryforward limitation is cumulative such that any use of the carryforwards below the limitations in one year will result in a corresponding increase in the limitations for the subsequent tax year.

Following certain acquisitions of a U.S. corporation by a foreign corporation, Section 7874 of the Code limits the ability of the acquired U.S. corporation and its U.S. affiliates to utilize U.S. tax attributes such as net operating losses to offset U.S. taxable income resulting from certain transactions. Based on the limited guidance available, we expect this limitation is applicable following the Vidara Merger. As a result, it is not currently expected that we or our other U.S. affiliates will be able to utilize their U.S. tax attributes to offset their U.S. taxable income, if any, resulting from certain taxable transactions following the Vidara Merger. Notwithstanding this limitation, we expect that we will be able to fully use our U.S. net operating losses prior to their expiration. As a result of this limitation, however, it may take HPI longer to use its net operating losses. Moreover, contrary to these expectations, it is possible that the limitation under Section 7874 of the Code on the utilization of U.S. tax attributes could prevent us from fully utilizing our U.S. tax attributes prior to their expiration if we do not generate sufficient taxable income.

Any limitation on our ability to use our net operating loss and tax credit carryforwards, including the carryforwards of companies that we acquire, will likely increase the taxes we would otherwise pay in future years if we were not subject to such limitations.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price.

As widely reported, global credit and financial markets have experienced extreme disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. While there has been some recent improvement in some of these financial metrics, there can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be

adversely affected by any such economic downturn, volatile business environment and continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate again, or do not improve, it may make any necessary debt or equity financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and share price and could require us to delay or abandon commercialization or development plans. There is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

The U.K.'s referendum to leave the EU or "Brexit," has and may continue to cause disruptions to capital and currency markets worldwide. The full impact of the Brexit decision, however, remains uncertain. A process of negotiation will determine the future terms of the U.K.'s relationship with the EU. During this period of negotiation, our results of operations and access to capital may be negatively affected by interest rate, exchange rate and other market and economic volatility, as well as regulatory and political uncertainty. Brexit may also have a detrimental effect on our customers, distributors and suppliers, which would, in turn, adversely affect our revenues and financial condition.

At December 31, 2016, we had $509.1 million of cash and cash equivalents consisting of cash and money market funds. While we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents since December 31, 2016, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Further dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

Changes in accounting rules or policies may affect our financial position and results of operations.

Accounting principles generally accepted in the United States, or GAAP, and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. Changes in these rules or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our operation as an Irish company with multiple subsidiaries in different jurisdictions adds additional complexity to the application of GAAP and this complexity will be exacerbated further if we complete additional strategic transactions. Changes in the application of existing rules or guidance applicable to us or our wholly owned subsidiaries could significantly affect our consolidated financial position and results of operations.

Covenants under the indentures governing our 2024 Senior Notes and 2023 Senior Notes and the credit agreement may restrict our business and operations in many ways, and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected.

The indentures governing the 2024 Senior Notes and the 2023 Senior Notes and the credit agreement impose various covenants that limit our ability and/or our restricted subsidiaries' ability to, among other things:

- pay dividends or distributions, repurchase equity, prepay, redeem or repurchase certain debt and make certain investments;
- incur additional debt and issue certain preferred stock;
- provide guarantees in respect of obligations of other persons;
- incur liens on assets;
- engage in certain asset sales;
- merge, consolidate with or sell all or substantially all of our assets to another person;
- enter into transactions with affiliates;
- sell assets and capital stock of our subsidiaries;
- enter into agreements that restrict distributions from our subsidiaries;
- designate subsidiaries as unrestricted subsidiaries; and
- allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to us.

These covenants may:

- limit our ability to borrow additional funds for working capital, capital expenditures, acquisitions or other general business purposes;
- limit our ability to use our cash flow or obtain additional financing for future working capital, capital expenditures, acquisitions or other general business purposes;

- require us to use a substantial portion of our cash flow from operations to make debt service payments;

- limit our flexibility to plan for, or react to, changes in our business and industry;
- place us at a competitive disadvantage compared to less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

If we are unable to successfully manage the limitations and decreased flexibility on our business due to our significant debt obligations, we may not be able to capitalize on strategic opportunities or grow our business to the extent we would be able to without these limitations.

Our failure to comply with any of the covenants could result in a default under the credit agreement or the indentures governing the 2024 Senior Notes or the 2023 Senior Notes, which could permit the administrative agent or the trustee, as applicable, or permit the lenders or the holders of the 2024 Senior Notes or the 2023 Senior Notes to cause the administrative agent or the trustee, as applicable, to declare all or part of any outstanding senior secured term loans, the 2023 Senior Notes or the 2024 Senior Notes to be immediately due and payable or to exercise any remedies provided to the administrative agent or the trustee, including, in the case of the credit agreement proceeding against the collateral granted to secure our obligations under the credit agreement. An event of default under the credit agreement or the indentures governing the 2024 Senior Notes or the 2023 Senior Notes could also lead to an event of default under the terms of the other agreements and the indenture governing our 2.50% Exchangeable Senior Notes due 2022, or the Exchangeable Senior Notes. Any such event of default or any exercise of rights and remedies by our creditors could seriously harm our business.

If intangible assets that we have recorded in connection with our acquisition transactions become impaired, we could have to take significant charges against earnings.

In connection with the accounting for our various acquisition transactions, we have recorded significant amounts of intangible assets. Under GAAP, we must assess, at least annually and potentially more frequently, whether the value of goodwill and other indefinite-lived intangible assets has been impaired. Amortizing intangible assets will be assessed for impairment in the event of an impairment indicator. Any reduction or impairment of the value of goodwill or other intangible assets will result in a charge against earnings, which could materially adversely affect our results of operations and shareholders' equity in future periods.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our medicines and medicine candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our medicines and medicine candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own may fail to result in issued patents with claims that cover our medicines in the United States or in other foreign countries. If this were to occur, early generic competition could be expected against our current medicines and other medicine candidates in development. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which prior art can invalidate a patent or prevent a patent from issuing based on a pending patent application. In particular, because the APIs in DUEXIS, VIMOVO and RAYOS/LODOTRA have been on the market as separate medicines for many years, it is possible that these medicines have previously been used off-label in such a manner that such prior usage would affect the validity of our patents or our ability to obtain patents based on our patent applications. In addition, claims directed to dosing and dose adjustment may be substantially less likely to issue in light of the Supreme Court decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., where the court held that claims directed to methods of determining whether to adjust drug dosing levels based on drug metabolite levels in the red blood cells were not patent eligible because they were directed to a law of nature. This decision may have wide-ranging implications on the validity and scope of pharmaceutical method claims.

Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated.

Patent litigation is currently pending in the United States District Court for the District of New Jersey against several companies intending to market a generic version of VIMOVO before the expiration of certain of our patents listed in the Orange Book. These cases are collectively known as the VIMOVO cases, and involve the following sets of defendants: (i) Dr. Reddy's; (ii) Lupin; and (iii) Mylan. Patent litigation against a fourth generic company, Actavis, is currently pending in the Court of Appeals for the Federal Circuit. Patent litigation against a fourth generic company, Actavis, is currently pending in the Court of Appeals for the Federal Circuit. The cases arise from Paragraph IV Patent Certification notice letters from each of Dr. Reddy's, Lupin, Mylan and Actavis advising each had filed an ANDA with the FDA seeking approval to market generic versions of VIMOVO before the expiration of the patents-in-suit.

On January 12, 2017, a six-day bench trial commenced against defendants Dr. Reddy's and Mylan before the Honorable Judge Mary Cooper in the District of New Jersey. The patents at issue in this trial included two Orange Book listed patents: U.S. Patent Nos. 6,926,907 and 8,557,285. Defendant Lupin formerly entered into a stay pending entry of judgment in this consolidated action. Currently, closing arguments and post-trial filings are not scheduled.

On August 19, 2015, Lupin filed Petitions for inter partes review, or IPR, of U.S. Patent No. 8,858,996, or the '996 patent, and U.S. Patent Nos. 8,852,636 and 8,865,190, or the '190 patent, all patents in litigation in the above referenced VIMOVO cases. On March 1, 2016, the Patent Trial and Appeal Board, or the PTAB, issued decisions to institute the IPRs for the '996 patent and the '190 patent. The PTAB must issue a final written decision on the IPRs of the '996 patent and the '190 patent no later than March 1, 2017. Also on March 1, 2016, the PTAB denied the Petition for IPR for U.S. Patent No. 8,852,636. The PTAB hearings for the '996 and '190 patents were both held on November 29, 2016. The PTAB must issue final written decision on the IPRs of the '996 and '190 patents no later than March 1, 2017.

Patent litigation is currently pending in the United States District Court for the District of New Jersey against several companies intending to market a generic version of PENNSAID 2% prior to the expiration of certain of our patents listed in the Orange Book. These cases are collectively known as the PENNSAID 2% cases, and involve the following sets of defendants: (i) Actavis and (ii) Lupin. These cases arise from Paragraph IV Patent Certification notice letters from each of Actavis and Lupin advising each had filed an ANDA with the FDA seeking approval to market a generic version of PENNSAID 2% before the expiration of the patents-in-suit. The status of these cases is as set forth below.

We received from Actavis a Paragraph IV Patent Certification Notice Letter dated September 27, 2016, against Orange Book listed U.S. Patent No. 9,415,029, advising that Actavis had filed an ANDA with the FDA for a generic version of PENNSAID 2%.

We have received from Apotex three Paragraph IV Patent Certification Notice Letters dated April 1, 2016, June 30, 2016, and September 21, 2016 against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, 8,871,809, 9,066,913, 9,101,591, 9,132,110, 9,168,304, 9,168,305, 9,220,784, 9,339,551, 9,339,552 and 9,415,029, advising that Apotex had filed an ANDA with the FDA for a generic version of PENNSAID 2%.

Patent litigation is currently pending in the United States District Court for the Eastern District of Texas against Par Pharmaceutical and in the United States District Court for the District of New Jersey against Lupin and against Par Pharmaceutical, who are each intending to market generic versions of RAVICTI prior to the expiration of certain of our patents listed in the Orange Book. These cases are collectively known as the RAVICTI cases, and arise from Paragraph IV Patent Certification notice letters from each of Par Pharmaceutical and Lupin advising each had filed an ANDA with the FDA seeking approval to market a generic version of RAVICTI before the expiration of the patents-in-suit.

On April 29, 2015, Par Pharmaceutical filed Petitions for IPR of U.S. Patent No. 8,404,215 and U.S. Patent No. 8,642,012, two of the patents involved in the above mentioned RAVICTI cases. On November 4, 2015, the PTAB issued decisions instituting such IPRs and on December 14, 2015, the District Court Judge Roy Payne issued a stay

pending a final written decision from the PTAB with respect to such IPRs. On September 29, 2016, the PTAB found all of the claims in U.S. Patent No. 8,404,215 to be unpatentable. Horizon has not appealed the PTAB's final written decision with respect to U.S. Patent No. 8,404,215. On November 3, 2016, the PTAB issued a final written decision holding all of the claims of U.S. Patent No. 8,642,012 patentable. On December 29, 2016, Par filed a notice of appeal with the Federal Circuit to appeal the final written decision of the PTAB concerning the patentability of U.S. Patent No. 8,642,012.

On April 1, 2016, Lupin filed a Petition for IPR of U.S. Patent No. 9,095,559, a patent currently at issue in the Lupin RAVICTI case. On September 30, 2016, the PTAB issued a decision instituting the IPR. The PTAB must issue a final written decision on the IPR no later than September 30, 2017.

We intend to vigorously defend our intellectual property rights relating to our medicines, but we cannot predict the outcome of the VIMOVO cases, the PENNSAID 2% cases, the RAVICTI cases or the IPRs. Any adverse outcome in these matters or any new generic challenges that may arise could result in one or more generic versions of our medicines being launched before the expiration of the listed patents, which could adversely affect our ability to successfully execute our business strategy to increase sales of our medicines, and would negatively impact our financial condition and results of operations, including causing a significant decrease in our revenues and cash flows.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the patent applications we hold with respect to our medicines fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop them and threaten our ability to commercialize our medicines. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found not invalid and not unenforceable or will go unthreatened by third parties. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to our medicines or any other medicine candidates. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be provoked by a third-party or instituted by us to determine which party was the first to invent any of the subject matter covered by the patent claims of our applications.

With respect to RAVICTI, the composition of matter patent we hold would have expired in the United States in February 2015 without term extension. However, Hyperion applied for a term extension for this patent under the Drug Price Competition and Patent Term Restoration Act and received notice that the United States Patent and Trademark Office, or the U.S. PTO, extended the expiration date of the patent to July 28, 2018. We cannot guarantee that pending patent applications related to RAVICTI will result in additional patents or that other existing and future patents related to RAVICTI will be held valid and enforceable or will be sufficient to deter generic competition in the United States. Therefore, it is possible that upon expiration of the RAVICTI composition of matter patent, we would need to rely on forms of regulatory exclusivity, to the extent available, to protect against generic competition.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the United States and the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific and factual issues. Changes in either patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The U.S. PTO has developed new and untested regulations and procedures to govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective in March 2013. The Leahy-Smith Act has also introduced procedures making it easier for third-parties to challenge issued patents, as well as to intervene in the prosecution of patent applications. Finally, the Leahy-Smith Act contains new

statutory provisions that still require the U.S. PTO to issue new regulations for their implementation and it may take the courts years to interpret the provisions of the new statute. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In addition, the ACA allows applicants seeking approval of biosimilar or interchangeable versions of biological products such as ACTIMMUNE to initiate a process for challenging some or all of the patents covering the innovator biological product used as the reference product. This process is complicated and could result in the limitation or loss of certain patent rights. An inability to obtain, enforce and defend patents covering our proprietary technologies would materially and adversely affect our business prospects and financial condition.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. For example, if the issuance, in a given country, of a patent to us, covering an invention, is not followed by the issuance, in other countries, of patents covering the same invention, or if any judicial interpretation of the validity, enforceability, or scope of the claims in, or the written description or enablement in, a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on us avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party reexamination proceedings before the U.S. PTO. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which our collaborators are developing medicine candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our medicine candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our medicines and/or any other medicine candidates. Because patent applications can take many years to issue, there may be currently pending patent applications, which may later result in issued patents that our medicine candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our medicine candidates, any molecules formed during the manufacturing process or any final medicine itself, the holders of any such patents may be able to block our ability to commercialize such medicine candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable medicine candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our medicine candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing medicines, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our medicine candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or

on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our medicine candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our medicines, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

If we fail to comply with our obligations in the agreements under which we license rights to technology from third parties, we could lose license rights that are important to our business.

We are party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. For example, we hold an exclusive license to Vectura Group plc's, or Vectura, proprietary technology and know-how covering the delayed-release of corticosteroids relating to RAYOS/LODOTRA. If we fail to comply with our obligations under our agreement with Vectura or our other license agreements, or if we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market medicines covered by the license, including RAYOS/ LODOTRA.

In connection with our November 2013 acquisition of the U.S. rights to VIMOVO, we (i) received the benefit of a covenant not to sue under AstraZeneca's patent portfolio with respect to Nexium (which shall automatically become a license under such patent portfolio if and when AstraZeneca reacquires control of such patent portfolio from Merck Sharp & Dohme Corp. and certain of its affiliates), (ii) were assigned AstraZeneca's amended and restated collaboration and license agreement for the United States with Aralez, under which AstraZeneca has in-licensed exclusive rights under certain of Aralez's patents with respect to VIMOVO, and (iii) acquired AstraZeneca's co-ownership rights with Aralez with respect to certain joint patents covering VIMOVO, all for the commercialization of VIMOVO in the United States. If we fail to comply with our obligations under our agreements with AstraZeneca or if we fail to comply with our obligations under our agreements with Aralez, our rights to commercialize VIMOVO in the United States may be adversely affected or terminated by AstraZeneca or Aralez.

We also license rights to patents, know-how and trademarks for ACTIMMUNE from Genentech Inc., or Genentech, under an agreement that remains in effect for so long as we continue to commercialize and sell ACTIMMUNE. However, Genentech may terminate the agreement upon our material default, if not cured within a specified period of time. Genentech may also terminate the agreement in the event of our bankruptcy or insolvency. Upon such a termination of the agreement, all intellectual property rights conveyed to us under the agreement, including the rights to the ACTIMMUNE trademark, revert to Genentech. If we fail to comply with our obligations under this agreement, we could lose the ability to market and distribute ACTIMMUNE, which would have a material adverse effect on our business, financial condition and results of operations.

We rely on a license from Ucyclyd with respect to technology developed by Ucyclyd in connection with the manufacturing of RAVICTI. The purchase agreement under which Hyperion purchased the worldwide rights to RAVICTI contains obligations to pay Ucyclyd regulatory and sales milestone payments relating to RAVICTI, as well as royalties on the net sales of RAVICTI. On May 31, 2013, when Hyperion acquired BUPHENYL under a restated collaboration agreement with Ucyclyd, Hyperion received a license to use some of the manufacturing technology developed by Ucyclyd in connection with the manufacturing of BUPHENYL. The restated collaboration agreement also contains obligations to pay Ucyclyd regulatory and sales milestone payments, as well as royalties on net sales of BUPHENYL. If we fail to make a required payment to Ucyclyd and do not cure the failure within the required time period, Ucyclyd may be able to terminate the license to use its manufacturing technology for RAVICTI and BUPHENYL. If we lose access to the Ucyclyd manufacturing technology, we cannot guarantee that an acceptable alternative method of manufacture could be developed or acquired. Even if alternative technology could be developed or acquired, the loss of the Ucyclyd technology could still result in substantial costs and potential periods where we would not be able to market and sell RAVICTI and/or BUPHENYL. We also license intellectual property necessary for commercialization of RAVICTI from an external party. This party may be entitled to terminate the license if we breach the agreement, including failure to pay required royalties on net sales of RAVICTI, or we do not meet specified diligence obligations in our development and commercialization of RAVICTI, and we do not cure the failure within the required time period. If the license is terminated, it may be difficult or impossible for us to continue to commercialize RAVICTI, which would have a material adverse effect on our business, financial condition and results of operations.

We also hold an exclusive license to patents and technology from Duke University, or Duke, and Mountain View Pharmaceuticals, Inc., or MVP, covering KRYSTEXXA. Duke and MVP may terminate the license if we commit fraud or for our willful misconduct or illegal conduct. Duke and MVP may also terminate the license upon our material breach of the agreement, if not cured within a specified period of time, or upon written notice if we have committed two or more material breaches under the agreement. Duke and MVP may also terminate the license in the event of our bankruptcy or insolvency. If the license is terminated, it may be impossible for us to continue to commercialize KRYSTEXXA, which would have a material adverse effect on our business, financial condition and results of operations.

In addition, we are subject to contractual obligations under our agreements with Tripex and PARI related to QUINSAIR. Under the agreement with Tripex, we are required to pursue commercially reasonable efforts to initiate, and subsequently to complete, an additional clinical trial of QUINSAIR in a non-cystic fibrosis patient population within a specified period of time and an obligation to progress toward submitting an NDA for approval of QUINSAIR in the United States for use in all or part of the cystic fibrosis patient population. These obligations are subject to certain exceptions due to, for example, manufacturing delays not under our control, or delays caused by the FDA. If we fail to properly exercise such efforts to initiate and complete an appropriate clinical trial, or fail to submit an NDA for U.S. approval in the cystic fibrosis patient population, during the time periods specified in the agreement, we may be subject to various claims by Tripex and parties affiliated with Tripex. In addition, if we do not spend a minimum amount on QUINSAIR development in each of the three years following our acquisition of Raptor, we may also be obligated to pre-pay a milestone payment related to initiating a clinical trial for QUINSAIR in a non-cystic fibrosis indication. Under the license agreement with PARI, we are required to comply with diligence milestones related to development and commercialization of QUINSAIR in the United States and to spend a specified minimum amount per year on development activities in the United States until submission of the NDA for QUINSAIR in the United States. If we do not comply with these obligations, our licenses to certain intellectual property related to QUINSAIR may become non-exclusive in the United States or could be terminated. We are also subject to contractual obligations under our license agreements with the UCSD with respect to PROCYSBI, including diligence obligations to develop PROCYSBI for the treatment of NASH and Huntington's disease, with which we currently are not in compliance. To the extent that we fail to perform the diligence obligations under the agreement, UCSD may, with respect to such indication, terminate the license or otherwise cause the license to become non-exclusive. If one or more of these licenses was terminated, we would have no further right to use or exploit the related intellectual property, which would limit our ability to develop PROCYSBI or QUINSAIR in other indications, and could impact our ability to continue commercializing PROCYSBI or QUINSAIR in their approved indications.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one of our patents, or a patent of one of our licensors, is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

There are numerous post grant review proceedings available at the U.S. PTO (including IPR, post-grant review and ex-parte reexamination) and similar proceedings in other countries of the world that could be initiated by a third-party that could potentially negatively impact our issued patents.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our collaborators or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim

proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our ordinary shares.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our medicine candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Risks Related to Ownership of Our Ordinary Shares

The market price of our ordinary shares historically has been volatile and is likely to continue to be volatile, and you could lose all or part of any investment in our ordinary shares.

The trading price of our ordinary shares has been volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- our failure to successfully execute our commercialization strategy with respect to our approved medicines, particularly our commercialization of our medicines in the United States;
- actions or announcements by third-party or government payers with respect to coverage and reimbursement of our medicines;
- disputes or other developments relating to intellectual property and other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our medicines and medicine candidates;
- unanticipated serious safety concerns related to the use of our medicines;
- adverse regulatory decisions;
- changes in laws or regulations applicable to our business, medicines or medicine candidates, including but not limited to clinical trial requirements for approvals or tax laws;
- inability to comply with our debt covenants and to make payments as they become due;
- inability to obtain adequate commercial supply for any approved medicine or inability to do so at acceptable prices;
- developments concerning our commercial partners, including but not limited to those with our sources of manufacturing supply;

- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse results or delays in clinical trials;

- our failure to successfully develop and/or acquire additional medicine candidates or obtain approvals for additional indications for our existing medicine candidates;
- introduction of new medicines or services offered by us or our competitors;
- overall performance of the equity markets, including the pharmaceutical sector, and general political and economic conditions;
- failure to meet or exceed revenue and financial projections that we may provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- inaccurate or significant adverse media coverage;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- our inability to successfully enter new markets;
- the termination of a collaboration or the inability to establish additional collaborations;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our inability to maintain an adequate rate of growth;
- ineffectiveness of our internal controls or our inability to otherwise comply with financial reporting requirements;
- adverse U.S. and foreign tax exposure;
- additions or departures of key management, commercial or regulatory personnel;
- issuances of debt or equity securities;
- significant lawsuits, including patent or shareholder litigation;
- changes in the market valuations of similar companies to us;
- sales of our ordinary shares by us or our shareholders in the future;
- trading volume of our ordinary shares;
- effects of natural or man-made catastrophic events or other business interruptions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and The NASDAQ Global Select Market and the stock of biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may adversely affect the market price of our ordinary shares, regardless of our actual operating performance.

We have never declared or paid dividends on our share capital and we do not anticipate paying dividends in the foreseeable future.

We have never declared or paid any cash dividends on our ordinary shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future, including due to limitations that are currently imposed by the 2015 Senior Secured Credit Facility, the 2016 Incremental Loan Facility, the 2024 Senior Notes and the 2023 Senior Notes. Any return to shareholders will therefore be limited to the increase, if any, of our ordinary share price.

We have incurred and will continue to incur significant increased costs as a result of operating as a public company and our management will be required to devote substantial time to compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In particular, the Sarbanes-Oxley Act of 2000, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the NASDAQ Stock Market, Inc., or NASDAQ, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. These rules and regulations have substantially increased our legal and financial compliance costs and have made some activities more time-consuming and costly. These effects are exacerbated by our transition to an Irish company and the integration of numerous acquired businesses and operations into our historical business and operating structure. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will continue to decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our medicines or services. For example, these rules and regulations make it more difficult and more expensive for us to obtain and maintain director and officer liability insurance. We cannot predict or estimate the amount or timing of additional costs that we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. If we fail to comply with the continued listing requirements of NASDAQ, our ordinary shares could be delisted from The NASDAQ Global Select Market, which would adversely affect the liquidity of our ordinary shares and our ability to obtain future financing.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform annual system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, or Section 404. Our independent registered public accounting firm is also required to deliver a report on the effectiveness of our internal control over financial reporting. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 requires that we incur substantial expense and expend significant management efforts, particularly because of our Irish parent company structure and international operations. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm identify deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our ordinary shares could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs as we respond to their requirements.

Sales of a substantial number of our ordinary shares in the public market could cause our share price to decline.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of such ordinary shares could decline. In addition, our ordinary shares that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are or may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act. If these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

Certain holders of our ordinary shares are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by our affiliates. For example, we are subject to a registration rights agreement with certain former Vidara shareholders that acquired our ordinary shares in connection with our acquisition of Vidara. Pursuant to this agreement, we filed and are required to maintain a registration statement covering the resale of ordinary shares held by these shareholders and in certain circumstances, these holders can require us to participate in an underwritten public offering of their ordinary shares. Any sales of securities by these shareholders or a public announcement of such sales could have a material adverse effect on the trading price of our ordinary shares.

In addition, any conversion or exchange of our Exchangeable Senior Notes, whether pursuant to their terms or pursuant to privately negotiated transactions between the issuer and/or us and a holder of such securities, could depress the market price for our ordinary shares.

Future sales and issuances of our ordinary shares, securities convertible into our ordinary shares or rights to purchase ordinary shares or convertible securities could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to decline.

Additional capital may be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities or securities convertible into or exchangeable for ordinary shares, our shareholders may experience substantial dilution. We may sell ordinary shares, and we may sell convertible or exchangeable securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell such ordinary shares, convertible or exchangeable securities or other equity securities in subsequent transactions, existing shareholders may be materially diluted. New investors in such subsequent transactions could gain rights, preferences and privileges senior to those of holders of ordinary shares. We also maintain equity incentive plans, including our Amended and Restated 2014 Equity Incentive Plan, 2014 Non-Employee Equity Plan and 2014 Employee Share Purchase Plan, and intend to grant additional ordinary share awards under these and future plans, which will result in additional dilution to our existing shareholders.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our securities.

It may not be possible to enforce court judgments obtained in the United States against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U.S. currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish company, we are governed by the Irish Companies Acts, which differ in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the United States.

Provisions of our articles of association could delay or prevent a takeover of us by a third-party.

Our articles of association could delay, defer or prevent a third-party from acquiring us, despite the possible benefit to our shareholders, or otherwise adversely affect the price of our ordinary shares. For example, our articles of association:

- impose advance notice requirements for shareholder proposals and nominations of directors to be considered at shareholder meetings;
- stagger the terms of our board of directors into three classes; and
- require the approval of a supermajority of the voting power of the shares of our share capital entitled to vote generally at a meeting of shareholders to amend or repeal our articles of association.

In addition, several mandatory provisions of Irish law could prevent or delay an acquisition of us. For example, Irish law does not permit shareholders of an Irish public limited company to take action by written consent with less than

unanimous consent. We are also subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in our ordinary shares in certain circumstances.

These provisions may discourage potential takeover attempts, discourage bids for our ordinary shares at a premium over the market price or adversely affect the market price of, and the voting and other rights of the holders of, our ordinary shares. These provisions could also discourage proxy contests and make it more difficult for you and our other shareholders to elect directors other than the candidates nominated by our board of directors, and could depress the market price of our ordinary shares.

A transfer of our ordinary shares may be subject to Irish stamp duty.

In certain circumstances, the transfer of shares in an Irish incorporated company will be subject to Irish stamp duty, which is a legal obligation of the buyer. This duty is currently charged at the rate of 1.0 percent of the price paid or the market value of the shares acquired, if higher. Because our ordinary shares are traded on a recognized stock exchange in the United States, an exemption from this stamp duty is available to transfers by shareholders who hold ordinary shares beneficially through brokers which in turn hold those shares through the Depositary Trust Company, or DTC, to holders who also hold through DTC. However, a transfer by or to a record holder who holds ordinary shares directly in his, her or its own name could be subject to this stamp duty. We, in our absolute discretion and insofar as the Companies Acts or any other applicable law permit, may, or may provide that one of our subsidiaries will pay Irish stamp duty arising on a transfer of our ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of ordinary shares which would otherwise be payable by the transferee is paid by us or any of our subsidiaries on behalf of the transferee, then in those circumstances, we will, on our behalf or on behalf of such subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) claim a first and permanent lien on the ordinary shares on which stamp duty has been paid by us or such subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares.

Dividends paid by us may be subject to Irish dividend withholding tax.

In certain circumstances, as an Irish tax resident company, we will be required to deduct Irish dividend withholding tax (currently at the rate of 20%) from dividends paid to our shareholders. Shareholders that are resident in the United States, EU countries (other than Ireland) or other countries with which Ireland has signed a tax treaty (whether the treaty has been ratified or not) generally should not be subject to Irish withholding tax so long as the shareholder has provided its broker, for onward transmission to our qualifying intermediary or other designated agent (in the case of shares held beneficially), or our or its transfer agent (in the case of shares held directly), with all the necessary documentation by the appropriate due date prior to payment of the dividend. However, some shareholders may be subject to withholding tax, which could adversely affect the price of our ordinary shares.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our ordinary shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our rating or publish inaccurate or unfavorable research about our business, our share price could decline. If one or more of these analysts cease coverage of our company or fail to publish reports on our company regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline.

Securities class action litigation could divert our management's attention and harm our business and could subject us to significant liabilities.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the equity securities of pharmaceutical companies. These broad market fluctuations may cause the market price of our ordinary shares to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. For example, following declines in our stock price, two federal securities class action lawsuits were filed in March 2016 against us and certain of our current and former officers alleging violations of the Securities Exchange Act of 1934, as amended. Subsequently, the two actions were consolidated, and plaintiff added claims under the Securities Act and named additional defendants. This consolidated class action (captioned Schaffer v. Horizon Pharma plc, et al., Case No. 1:16-cv-01763) is currently pending in the United States District Court for the Southern District of New York. In November 2016, defendants filed motions to dismiss plaintiffs' consolidated amended complaint, which are fully briefed but have not yet been decided by the court. Even if we are successful in defending against this action or any similar claims that may be brought in the future, such litigation could result in substantial costs and may be a distraction to our management, and may lead to an unfavorable outcome that could adversely impact our financial condition and prospects.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Location	Approximate Square Footage	Lease Expiry Date
Dublin, Ireland	18,900	November 3, 2029
Lake Forest, Illinois	160,000	March 31, 2024
Novato, California	61,000	August 31, 2021
Deerfield, Illinois (1)	53,500	June 30, 2018
Brisbane, California	20,100	November 30, 2019
Mannheim, Germany	14,300	December 31, 2018
Chicago, Illinois	6,500	December 31, 2018
Utrecht, the Netherlands	5,400	October 31, 2019
Reinach, Switzerland	3,500	May 31, 2020

(1) We vacated the premises in Deerfield, Illinois, and began occupying the premises in Lake Forest, Illinois, in January 2016.

Item 3. Legal Proceedings

For a description of our legal proceedings, see Note 16 of the Notes to Consolidated Financial Statements, included in Item 15 of this Annual Report on Form 10-K.

Item 4. Mine Safety Disclosures

None.

PART II

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

Market Information

Our ordinary shares trade on The NASDAQ Global Select Market under the trading symbol "HZNP".

The following table sets forth the high and low sales prices per share of our ordinary shares as reported on The NASDAQ Global Select Market for the periods indicated.

	High	Low
2016		
First quarter	$22.02	$13.36
Second quarter	19.45	13.05
Third quarter	23.44	16.18
Fourth quarter	21.98	14.16

	High	Low
2015		
First quarter	$26.46	$12.64
Second quarter	34.99	25.26
Third quarter	39.49	16.22
Fourth quarter	23.70	12.86

Holders of Record

The closing price of our ordinary shares on February 22, 2017 was $17.04. As of February 22, 2017, there were approximately thirteen holders of record of our ordinary shares.

Performance Graph

The following graph shows a comparison from December 31, 2011 through December 31, 2016 of the cumulative total return for (i) our ordinary shares, (ii) the NASDAQ U.S. Benchmark TR Index and (iii) NASDAQ Pharmaceuticals.

Information set forth in the graph below represents the performance of the Horizon Pharma, Inc. common stock from December 31, 2011 until September 18, 2014, the day before the consummation of the Vidara Merger, and the performance of our ordinary shares from September 19, 2014 through December 31, 2016. Our ordinary shares trade on the same exchange, the NASDAQ Global Select Market, and under the same trading symbol, “HZNP”, as the Horizon Pharma, Inc. common stock prior to the Vidara Merger. The graph assumes an initial investment of $100 on December 31, 2011. The comparisons in the graph are required by the Securities and Exchange Commission and are not intended to forecast or be indicative of possible future performance of our ordinary shares.

	12/31/2011	12/31/2012	12/31/2013	12/31/2014	12/31/2015	12/31/2016
Cumulative Returns						
Horizon Pharma plc	$ 100.00	$ 58.25	$ 190.50	$ 322.25	$ 541.75	$ 404.50
NASDAQ Pharmaceuticals	100.00	114.32	155.11	188.95	199.22	197.05
NASDAQ U.S. Benchmark TR Index	100.00	116.43	155.41	174.78	175.62	198.47

The foregoing graph and table are furnished solely with this report, and are not filed with this report, and shall not be deemed incorporated by reference into any other filing under the Securities Act of 1933, as amended, or the Securities Act, or the Securities Exchange Act of 1934, as amended, whether made by us before or after the date hereof, regardless of any general incorporation language in any such filing, except to the extent we specifically incorporate this material by reference into any such filing.

Dividend Policy

We have never declared or paid cash dividends on our common equity. We currently intend to retain all available funds and any future earnings to support operations and finance the growth and development of our business and do not intend to pay cash dividends on our ordinary shares for the foreseeable future. Under Irish law, dividends may only be paid, and share repurchases and redemptions must generally be funded only out of, “distributable reserves.” In addition, our ability to pay cash dividends is currently prohibited by the terms of our credit agreement we entered into in May 2015 with Citibank, N.A., as administrative and collateral agent, as amended, $475.0 million aggregate principal amount of 6.625% Senior Notes due 2023 and the $300.0 million aggregate principal amount of 8.75% Senior Notes due 2024, subject to customary exceptions. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors our board of directors deems relevant.

Securities Authorized for Issuance under Equity Compensation Plans

See Item 12 of Part III of this Annual Report on Form 10-K regarding information about securities authorized for issuance under our equity compensation plans.

Recent Sales of Unregistered Securities

We completed the following issuances of unregistered securities during the year ended December 31, 2016 which were not previously reported in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K:

- In December 2016, we issued an aggregate of 500 ordinary shares to Peter Orlando upon the cash exercise of warrants and we received proceeds of $2,285 representing the aggregate exercise price of such warrants.
- In December 2016, we issued an aggregate of 500 ordinary shares to Troon Capital upon the cash exercise of warrants and we received proceeds of $2,285 representing the aggregate exercise price of such warrants.
- In December 2016, we issued an aggregate of 750 ordinary shares to Foster Equities LP upon the cash exercise of warrants and we received proceeds of $3,428 representing the aggregate exercise price of such warrants.

The offers, sales and issuances of the securities described above were deemed to be exempt from registration under the Securities Act of 1933, as amended, in reliance on Rule 506 of Regulation D in that each issuance of securities was to an accredited investor under Rule 501 of Regulation D and did not involve a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and where appropriate, legends were affixed to the securities issued in these transactions.

Issuer Repurchases of Equity Securities

None.

Irish Law Matters

See Irish Law Matters included in Item 1 of Part I of this Annual Report on Form 10-K.

Item 6. Selected Financial Data

The selected statement of comprehensive (loss) income data and selected statement of cash flows data for the years ended December 31, 2016, 2015 and 2014, and the balance sheet data as of December 31, 2016 and 2015 have been derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. The selected statements of comprehensive loss data and selected statement of cash flows data for the years ended December 31, 2013 and 2012, and the balance sheet data as of December 31, 2014, 2013 and 2012 have been derived from audited financial statements which are not included in this Annual Report on Form 10-K.

Our historical results are not necessarily indicative of future results. The selected financial data should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes included elsewhere in this Annual Report on Form 10-K. The selected financial data for periods prior to the year ended December 31, 2014 is that of Horizon Pharma, Inc., our predecessor, while the selected financial data for the years ended December 31, 2016, 2015 and 2014 is that of Horizon Pharma plc.

	As of December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Selected Balance Sheet Data					
Cash and cash equivalents	$509,055	$859,616	$218,807	$80,480	$104,087
Working capital	440,430	748,595	106,024	67,455	79,983
Total assets (1)	4,292,059	3,058,588	1,102,842	246,328	190,789
Total debt, net (1)	1,807,493	1,136,756	334,012	104,494	45,606
Accumulated deficit	(848,021)	(681,187)	(720,719)	(457,116)	(308,111)
Total shareholders' equity (deficit)	1,263,779	1,313,145	540,204	(49,082)	105,978

	For the Years Ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands, except per share data)				
Selected Statement of Comprehensive (Loss) Income Data					
Net sales	$981,120	$757,044	$296,955	$74,016	$18,844
Cost of goods sold	393,272	219,502	78,753	14,625	11,875
Gross profit	587,848	537,542	218,202	59,391	6,969
Loss before benefit for income taxes	(228,085)	(132,712)	(269,687)	(150,126)	(92,965)
Net (loss) income	(166,834)	39,532	(263,603)	(149,005)	(87,794)
Net (loss) income per ordinary share - basic	(1.04)	0.27	(3.15)	(2.34)	(2.26)
Net (loss) income per ordinary share - diluted	(1.04)	0.25	(3.15)	(2.34)	(2.26)
Selected Statement of Cash Flows Data					
Net cash provided by (used in) operating activities	$369,456	$194,166	$27,549	$(54,287)	$(76,641)
Net cash used in investing activities	(1,375,881)	(995,048)	(227,720)	(36,135)	(1,386)
Net cash provided by financing activities	657,074	1,442,481	338,285	66,716	164,308
Payments for acquisitions, net of cash acquired	(1,356,271)	(1,022,361)	(224,220)	(35,000)	—
Net proceeds from the issuance of common stock	4,884	500,454	41,934	6,637	128,518
Net proceeds from the issuance of debt	656,190	1,241,027	286,966	143,598	55,578
Repayment of debt	(4,000)	(299,000)	—	(64,884)	(19,788)

(1) In 2016, we retrospectively adopted Accounting Standards Update No. 2015-03, Interest-Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs, simplifying the presentation of debt issuance costs. As a result, deferred financing costs of $11.5 million, $6.3 million and $3.2 million that were classified within “total assets” at December 31, 2014, December 31, 2013 and December 31, 2012, respectively, were reclassified to “total debt, net” in the above table to conform prior-period classifications as a result of the new guidance.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

The discussion below contains "forward-looking statements," as defined in Section 21E of the Securities Exchange Act of 1934, as amended, that reflect our current expectations regarding our future growth, results of operations, cash flows, performance and business prospects and opportunities, as well as assumptions made by, and information currently available to, our management. We have tried to identify forward-looking statements by using words such as "anticipate," "believe," "plan," "expect," "intend," "will," and similar expressions, but these words are not the exclusive means identifying forward-looking statements. These statements are based on information currently available to us and are subject to various risks, uncertainties, and other factors, including, but not limited to, those matters discussed in Item 1A. "Risk Factors" in Part I of this Annual Report on Form 10-K, that could cause our actual growth, results of operations, cash flows, performance and business prospects and opportunities to differ materially from those expressed in, or implied by, these statements. Except as expressly required by the federal securities laws, we undertake no obligation to update such factors or to publicly announce the results of any of the forward-looking statements contained herein to reflect future events, developments, or changed circumstances, or for any other reason.

OVERVIEW

Unless otherwise indicated or the context otherwise requires, references to the "Company", "we", "us" and "our" refer to Horizon Pharma plc and its consolidated subsidiaries, including its predecessor, Horizon Pharma, Inc., or HPI. All references to "Vidara" are references to Horizon Pharma plc (formerly known as Vidara Therapeutics International Public Limited Company) and its consolidated subsidiaries prior to the effective time of the merger of the businesses of HPI and Vidara on September 19, 2014, or the Vidara Merger. The disclosures in this report relating to the pre-Vidara Merger business of Horizon Pharma plc, unless noted as being the business of Vidara prior to the Vidara Merger, pertain to the business of HPI prior to the Vidara Merger.

Our Business

We are a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. We market eleven medicines through our orphan, rheumatology and primary care business units. Our marketed medicines are ACTIMMUNE® (interferon gamma-1b), BUPHENYL® (sodium phenylbutyrate) Tablets and Powder, DUEXIS® (ibuprofen/famotidine), KRYSTEXXA® (pegloticase), MIGERGOT® (ergotamine tartrate & caffeine suppositories), PENNSAID® (diclofenac sodium topical solution) 2% w/w, or PENNSAID 2%, PROCYSBI® (cysteamine bitartrate) delayed-release capsules, QUINSAIR™ (aerosolized form of levofloxacin), RAVICTI® (glycerol phenylbutyrate) Oral Liquid, RAYOS® (prednisone) delayed-release tablets and VIMOVO® (naproxen/esomeprazole magnesium).

We developed DUEXIS and RAYOS, known as LODOTRA® outside the United States, acquired the U.S. rights to VIMOVO from AstraZeneca AB, or AstraZeneca, in November 2013, acquired certain rights to ACTIMMUNE as a result of the Vidara Merger in September 2014, acquired the U.S. rights to PENNSAID 2% from Nuvo Research Inc., or Nuvo, in October 2014, acquired RAVICTI and BUPHENYL, known as AMMONAPS® in certain European countries, as a result of our acquisition of Hyperion Therapeutics Inc., or Hyperion, in May 2015, acquired KRYSTEXXA and the U.S. rights to MIGERGOT as a result of our acquisition of Crealta Holdings LLC., or Crealta,

in January 2016 and acquired PROCYSBI and QUINSAIR as a result of our acquisition of Raptor Pharmaceutical Corp., or Raptor, in October 2016.

On January 13, 2016, we completed our acquisition of Crealta for approximately $539.7 million, including cash acquired of $24.9 million. Following completion of the acquisition, Crealta became our wholly owned subsidiary and was renamed Horizon Pharma Rheumatology LLC.

On May 18, 2016, we entered into a definitive agreement with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim International, to acquire certain rights to interferon gamma-1b, which Boehringer Ingelheim International currently commercializes under the trade names IMUKIN®, IMUKINE®, IMMUKIN® and IMMUKINE® in an estimated thirty countries primarily in Europe and the Middle East. Under the terms of the agreement, we paid Boehringer Ingelheim International €5.0 million ($5.6 million when converted using a Euro-to-Dollar exchange rate at date of payment of 1.1132) upon signing and will pay €20.0 million upon closing, for certain rights for interferon gamma-1b in all territories outside of the United States, Canada and Japan, as we currently hold marketing rights to interferon gamma-1b in these territories. We currently market interferon gamma-1b as ACTIMMUNE in the United States. The transaction is expected to close in 2017 and we are continuing to work with Boehringer Ingelheim International to enable the transfer of applicable marketing authorizations. We recorded an impairment charge of €5.0 million ($5.3 million when converted using a Euro-to-Dollar exchange rate at date of impairment of 1.052) during the three months ended December 31, 2016 to fully write off the value of the initial payment on our consolidated balance sheet, and upon closing we expect to record the additional €20.0 million payment as an expense in our consolidated statement of comprehensive (loss) income. See “Results from Phase 3 Study of ACTIMMUNE (interferon gamma-1b) in Friedreich's Ataxia” section below for further details.

On October 25, 2016, we completed our acquisition of Raptor in which we acquired all of the issued and outstanding shares of Raptor’s common stock for $9.00 per share in cash. The total consideration was $860.8 million, including cash acquired of $24.9 million and $56.0 million to repay Raptor’s outstanding debt. Following completion of the acquisition, Raptor became our wholly owned subsidiary and converted to a limited liability company, changing its name to Horizon Pharmaceutical LLC. We financed the transaction through $300.0 million aggregate principal amount of 8.75% Senior Notes due 2024, or the 2024 Senior Notes, $375.0 million aggregate principal amount of loans pursuant to an amendment to our existing credit agreement and cash on hand.

Part of our commercial strategy for RAYOS and our primary care medicines is to offer physicians the opportunity to have their patients fill prescriptions through pharmacies participating in our HorizonCares patient access program. For commercial patients who are prescribed our primary care medicines or RAYOS, the HorizonCares program offers co-pay assistance when a third-party commercial payer covers a prescription but requires an eligible patient to pay a co-pay or deductible, and offers full subsidization when a third-party commercial payer rejects coverage for an eligible patient. During 2016, we entered into business arrangements with pharmacy benefit managers, or PBMs, and other payers to secure formulary status and reimbursement of our medicines, such as our arrangements with Express Scripts, Inc., or Express Scripts, CVS Caremark and Prime Therapeutics LLC. While we believe that this strategy will result in broader inclusion of certain of our primary care medicines on healthcare plan formularies, and therefore increase payer reimbursement and lower our cost of providing patient access programs, these arrangements generally require us to pay administrative and rebate payments to the PBMs and/or other payers.

We market our medicines in the United States through our field sales force, which numbered approximately 480 representatives as of December 31, 2016. Our strategy is to continue to build a well-balanced, diversified, high-growth biopharmaceutical company. We are executing this through the successful commercialization of our existing medicines, a strong commitment to patient access and support and business development efforts focused on transformative acquisitions to accelerate our rare disease leadership as well as on-market and development-stage medicines to fill out our pipeline.

We are building a sustainable biopharmaceutical company by helping ensure that patients have access to their medicines and support services, and by investing in the further development of medicines for patients with rare or underserved diseases. Our growing business is diversified across three business units: orphan, rheumatology and primary care, and is driven by a successful commercial model that focuses on differentiated, long-life medicines, innovative patient access programs and a disciplined business development strategy.

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Results from Phase 3 Study of ACTIMMUNE (interferon gamma-1b) in Friedreich's Ataxia

On December 8, 2016, we announced that the Phase 3 trial, Safety, Tolerability and Efficacy of ACTIMMUNE Dose Escalation in Friedreich's Ataxia study, or STEADFAST, evaluating ACTIMMUNE for the treatment of Friedreich's ataxia, or FA, did not meet its primary endpoint of a statistically significant change from baseline in the modified Friedreich's Ataxia Rating Scale, or FARS-mNeuro, at twenty-six weeks versus treatment with placebo and that the secondary endpoints did not meet statistical significance, or the FA announcement. No new safety findings were identified on initial review of data other than those already noted in the ACTIMMUNE prescribing information for approved indications. We, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and the Friedreich's Ataxia Research Alliance, or FARA, Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study.

Following the FA announcement, we recorded the following amounts in our consolidated statement of comprehensive loss during the year ended December 31, 2016 (in thousands):

Description	Financial Statement Line Item	Amount Loss/(Gain)	Note
Impairment of in-process research and development	Impairment of in-process research and development	$ 66,000	1
Impairment of non-current asset	General and administrative expenses	5,260	2
Loss on inventory purchase commitments	Cost of goods sold	14,287	3
Remeasurement of contingent royalty liabilities	Cost of goods sold	(2,480)	4
Clinical trial wind-down costs	Research and development expenses	3,966	5
Total		$ 87,033	

Note 1 In-process research and development, or IPR&D, related to the research and development project to evaluate ACTIMMUNE in the treatment of FA, which we acquired in the Vidara Merger. At the time of the Vidara Merger, IPR&D was considered separable from the business as the project could be sold to a third party, and we assigned a fair value of $66.0 million to the intangible asset using an income approach in our purchase accounting. Following the FA announcement, we determined that the IPR&D has no alternative use or economic value, and we recorded an impairment charge during the three months ended December 31, 2016 to fully write off the value of the asset on our consolidated balance sheet.

Note 2 As described above, on May 18, 2016, we entered into a definitive agreement with Boehringer Ingelheim International to acquire certain rights to interferon gamma-1b, and we paid Boehringer Ingelheim International €5.0 million upon signing. The purchase price was determined with the expectation that the STEADFAST study would be successful. Following the FA announcement, we determined that this payment, which was recorded in "other assets" on our consolidated balance sheet was impaired, and we recorded an impairment charge during the three months ended December 31, 2016 to fully write off the value of the asset ($5.3 million when converted using a Euro-to-Dollar exchange rate at date of impairment of 1.052). Upon closing, we will pay Boehringer Ingelheim International an additional €20.0 million and we expect to record this payment as an expense in our consolidated statement of comprehensive (loss) income.

Note 3 During the year ended December 31, 2016, we committed to purchase additional units of ACTIMMUNE from Boehringer Ingelheim RCV GmbH & Co KG, or Boehringer Ingelheim. These additional units of ACTIMMUNE were intended to cover anticipated demand if the results of the STEADFAST study of ACTIMMUNE for the treatment of FA had been successful. Following the FA announcement, we recorded a loss of $14.3 million for firm, non-cancellable and unconditional purchase commitments for quantities in excess of our current forecasts for future demand. During the year ended December 31, 2016, we also committed to incur an additional $14.9 million for

the harmonization of the drug substance manufacturing process with Boehringer Ingelheim. These additional costs have not been included in our consolidated statement of comprehensive loss or our consolidated balance sheet at December 31, 2016.

Note 4 At the time of the Vidara Merger, we assigned a fair value to a contingent liability for royalties potentially payable under previously existing royalty and licensing agreements related to ACTIMMUNE, which included an amount of $2.5 million for estimated future sales of ACTIMMUNE for FA. Following the FA announcement, we recorded an adjustment to reduce the contingent royalty liability for ACTIMMUNE by $2.5 million as we do not anticipate future sales of ACTIMMUNE for FA.

Note 5 Following the FA announcement, we recorded an amount of $4.0 million at December 31, 2016 related to costs anticipated to be incurred to discontinue the STEADFAST study. These costs will be incurred without economic benefit to us, and represent costs to us to wind down the study under U.S. Food and Drug Administration, or FDA, protocol.

RESULTS OF OPERATIONS

Year Ended December 31, 2016 Compared to Year Ended December 31, 2015

	For the Years Ended December 31,		Increase / (Decrease)	Change %
	2016	2015		
	(in thousands)			
Net sales	$981,120	$757,044	$224,076	30 %
Cost of goods sold	393,272	219,502	173,770	79 %
Gross profit	587,848	537,542	50,306	9 %
Operating expenses				
Research and development	60,707	41,865	18,842	45 %
Sales and marketing	320,366	220,444	99,922	45 %
General and administrative	287,942	219,861	68,081	31 %
Impairment of in-process research and development	66,000	—	66,000	*
Total operating expenses	735,015	482,170	252,845	52 %
Operating (loss) income	(147,167)	55,372	(202,539)	(366)%
Other income (expense), net:				
Interest expense, net	(86,610)	(69,900)	(16,710)	24 %
Foreign exchange loss	(1,005)	(1,237)	232	(19)%
Loss on induced conversion of debt and debt extinguishment	—	(77,624)	77,624	*
Loss on sale of long-term investments	—	(29,032)	29,032	*
Other income (expense), net	6,697	(10,291)	16,988	(165)%
Total other expense, net	(80,918)	(188,084)	107,166	(57)%
Loss before benefit for income taxes	(228,085)	(132,712)	(95,373)	72 %
Benefit for income taxes	(61,251)	(172,244)	110,993	(64)%
Net (loss) income	$(166,834)	$39,532	$(206,366)	(522)%

*Percentage change is not meaningful.

Net sales. Net sales increased $224.1 million, or 30%, to $981.1 million during the year ended December 31, 2016, from $757.0 million during the year ended December 31, 2015.

The following table presents a summary of total net sales attributed to geographic sources for the years ended December 31, 2016 and 2015 (in thousands):

Year Ended December 31, 2016 Year Ended December 31, 2015

		% of Total Net Sales			% of Total Net Sales	
	Amount			Amount		
United States	$ 964,041	98	%	$ 744,036	98	%
Rest of world	17,079	2	%	13,008	2	%
Total net sales	$ 981,120			$ 757,044		

The following table reflects the components of net sales for the years ended December 31, 2016 and 2015 (in thousands):

	Year Ended December 31,		Change	Change
	2016	2015	$	%
PENNSAID 2%	$304,433	$147,010	$157,423	107 %
DUEXIS	173,728	190,357	(16,629)	-9 %
RAVICTI	151,532	86,875	64,657	74 %
VIMOVO	121,315	166,672	(45,357)	-27 %
ACTIMMUNE	104,624	107,444	(2,820)	-3 %
KRYSTEXXA	91,102	—	91,102	*
RAYOS	47,356	40,329	7,027	17 %
PROCYSBI	25,268	—	25,268	*
BUPHENYL	16,879	13,458	3,421	25 %
MIGERGOT	4,651	—	4,651	*
LODOTRA	4,193	4,899	(706)	-14 %
QUINSAIR	1,039	—	1,039	*
Litigation settlement	(65,000)	—	(65,000)	*
Total net sales	$981,120	$757,044	$224,076	30 %

*Percentage change is not meaningful.

The increase in net sales during the year ended December 31, 2016 was primarily due to the growth in net sales of PENNSAID 2%, the full-period recognition of RAVICTI sales in 2016, compared to a partial period recognition in 2015 following the acquisition of Hyperion in May 2015, the recognition of KRYSTEXXA sales following the acquisition of Crealta in January 2016 and the recognition of PROCYSBI sales following the acquisition of Raptor in October 2016, offset by the $65.0 million litigation settlement with Express Scripts along with lower net sales of VIMOVO and DUEXIS.

PENNSAID 2%. Net sales increased $157.4 million, or 107%, to $304.4 million during the year ended December 31, 2016, from $147.0 million during the year ended December 31, 2015. Net sales increased by approximately $87.5 million due to higher net pricing and $69.9 million resulting from prescription volume growth.

DUEXIS. Net sales decreased $16.6 million, or 9%, to $173.7 million during the year ended December 31, 2016, from $190.3 million during the year ended December 31, 2015. Net sales decreased by approximately $50.4 million due to lower net pricing resulting from higher co-pay and other patient assistance, offset by an increase of approximately $33.8 million resulting from prescription volume growth.

RAVICTI. Net sales increased $64.7 million, or 74%, to $151.5 million during the year ended December 31, 2016, from $86.8 million during the year ended December 31, 2015. Net sales increased by approximately $55.7 million resulting from prescription volume growth and $9.0 million due to higher net pricing. We began recognizing RAVICTI sales following the acquisition of Hyperion in May 2015, therefore only a partial period of RAVICTI sales were recognized during the year ended December 31, 2015, compared with full-period recognition of sales during the year ended December 31, 2016.

VIMOVO. Net sales decreased $45.4 million, or 27%, to $121.3 million during the year ended December 31, 2016, from $166.7 million during the year ended December 31, 2015. Net sales decreased by approximately $35.9 million due to lower net pricing resulting from higher co-pay and other patient assistance and approximately $9.5 million

resulting from lower prescription volumes.

ACTIMMUNE. Net sales decreased $2.8 million, or 3%, to $104.6 million during the year ended December 31, 2016, from $107.4 million during the year ended December 31, 2015. Net sales decreased by approximately $8.8 million resulting from prescription volume decreases, offset by an increase of approximately $6.0 million due to higher net pricing.

KRYSTEXXA. Net sales were $91.1 million during the year ended December 31, 2016. We began recognizing KRYSTEXXA sales following the acquisition of Crealta in January 2016.

RAYOS. Net sales increased $7.0 million, or 17%, to $47.4 million during the year ended December 31, 2016, from $40.4 million during the year ended December 31, 2015. Net sales increased by approximately $8.4 million resulting from prescription volume growth, offset by a decrease of approximately $1.4 million due to lower net pricing.

PROCYSBI. Net sales were $25.3 million during the year ended December 31, 2016. We began recognizing PROCYSBI sales following the acquisition of Raptor in October 2016.

BUPHENYL. Net sales increased $3.4 million, or 25%, to $16.9 million during the year ended December 31, 2016, from $13.5 million during the year ended December 31, 2015. We began recognizing BUPHENYL sales following the acquisition of Hyperion in May 2015, therefore only a partial period of BUPHENYL sales were recognized during the year ended December 31, 2015, compared with full-period recognition of sales during the year ended December 31, 2016.

MIGERGOT. Net sales were $4.7 million during the year ended December 31, 2016. We began recognizing MIGERGOT sales following the acquisition of Crealta in January 2016.

LODOTRA. Net sales decreased $0.7 million, or 14%, to $4.2 million during the year ended December 31, 2016, from $4.9 million during the year ended December 31, 2015. The decrease was due to fewer shipments to our European distribution partner, Mundipharma International Corporation Limited, or Mundipharma. LODOTRA sales to Mundipharma occur at the time we ship, based on Mundipharma's estimated requirements. Accordingly, LODOTRA sales are not linear or directly tied to Mundipharma's in-market sales and can therefore fluctuate significantly.

QUINSAIR. Net sales were $1.0 million during the year ended December 31, 2016. We began recognizing QUINSAIR sales following the acquisition of Raptor in October 2016.

In September 2016, we entered into a settlement agreement and mutual release with Express Scripts pursuant to which we and Express Scripts were released from any and all claims relating to our then ongoing litigation without admitting any fault or wrongdoing and we agreed to pay Express Scripts $65.0 million. This settlement has been accounted for as a reduction of "net sales" in the consolidated statement of comprehensive loss for the year ended December 31, 2016.

The table below reconciles our gross sales to net sales for the years ended December 31, 2016 and 2015 (in millions):

	Year Ended December 31, 2016		Year Ended December 31, 2015	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Gross sales	$3,234.2	100.0%	$2,057.3	100.0%
Adjustments to gross sales:				
Prompt pay discounts	(64.0)	(2.0)%	(41.3)	(2.0)%
Medicine returns	(17.1)	(0.5)%	(14.4)	(0.7)%
Co-pay and other patient assistance	(1,701.3)	(52.6)%	(1,020.2)	(49.6)%
Wholesaler fees and commercial rebates	(133.7)	(4.2)%	(66.1)	(3.2)%
Government rebates and chargebacks	(272.0)	(8.4)%	(158.3)	(7.7)%
Litigation settlement	(65.0)	(2.0)%	—	—

Total adjustments	(2,253.1)	(69.7)%	(1,300.3)	(63.2)%
Net sales	$981.1	30.3 %	$757.0	36.8 %

During the year ended December 31, 2016, co-pay and other patient assistance, as a percentage of gross sales, increased to 52.6% from 49.6% during the year ended December 31, 2015. The increase was primarily due to the expansion of our HorizonCares program during 2016.

On a quarter-to-quarter basis, our net sales have traditionally been lower in first half of the year, particularly in the first quarter, with the second half of the year representing a greater share of overall net sales each year. This is due to annual managed care plan changes and the re-setting of patient deductibles at the beginning of each year, resulting in higher co-pay and other patient assistance costs as patients meet their annual deductibles during the first and second quarters, and higher net sales in the second half of the year after patients meet their deductibles and healthcare plans reimburse a greater portion of the total cost of our medicines.

Cost of Goods Sold. Cost of goods sold increased $173.8 million to $393.3 million during the year ended December 31, 2016, from $219.5 million during the year ended December 31, 2015. As a percentage of net sales, cost of goods sold was 40.0% during the year ended December 31, 2016, compared to 29.0% during the year ended December 31, 2015. The large increase in costs of goods sold as a percentage of net sales was due to the one-time reduction in net sales in the year ended December 31, 2016 as a result of the litigation settlement with Express Scripts and an increase in cost of goods sold in the year ended December 31, 2016. The increase in cost of goods sold was primarily a result of higher intangible amortization expense of $84.0 million and increased inventory step-up expense of $59.6 million. Other factors that caused cost of goods sold to increase during the year included a $14.3 million expense related to a loss on inventory purchase commitments, higher royalty accretion expense of $20.5 million and a $16.2 million increase in direct and indirect costs associated with higher sales, offset by a $20.8 million decrease in charges relating to the remeasurement of contingent royalty liabilities.

The increase in intangible amortization of $84.0 million during the year ended December 31, 2016 compared to the prior year was due to a $33.9 million increase in amortization expense related to RAVICTI and BUPHENYL intangible assets (acquired in May 2015), $35.9 million amortization of developed technology related to KRYSTEXXA and MIGERGOT (acquired in January 2016), $14.0 million amortization of developed technology related to PROCYSBI (acquired in October 2016) and $0.2 million increase in amortization related to ACTIMMUNE.

Because inventory step-up expense is acquisition-related, will not continue indefinitely and has a significant effect on our gross profit, gross margin percentage and net income (loss) for all affected periods, we disclose balance sheet and income statement amounts related to inventory step-up within the notes to the consolidated financial statements. The increase in inventory step-up expense of $59.6 million during the year ended December 31, 2016 compared to the prior year was due to $48.8 million recorded during the year ended December 31, 2016 related to KRYSTEXXA and MIGERGOT inventory step-up (acquired in January 2016) and $22.4 million related to PROCYSBI and QUINSAIR inventory step-up (acquired in October 2016), compared to $8.4 million recorded during the year ended December 31, 2015 related to RAVICTI and BUPHENYL inventory step-up (acquired in May 2015) and $3.2 million related to ACTIMMUNE inventory step-up (acquired in September 2014).

Research and Development Expenses. Research and development expenses increased $18.8 million to $60.7 million during the year ended December 31, 2016, from $41.9 million during the year ended December 31, 2015. The increase in research and development expenses during the year ended December 31, 2016 was primarily attributable to $2.8 million of higher share-based compensation, an increase of $5.5 million in other employee costs resulting from growth in our headcount following the Hyperion, Crealta and Raptor acquisitions, $4.0 million related to costs to be incurred in the winding down of the STEADFAST study, an increase of $3.0 million in general research and development costs, a $2.0 million upfront fee paid for a license of a patent and an increase of $1.5 million in regulatory submission fees.

Sales and Marketing Expenses. Sales and marketing expenses increased $99.9 million to $320.4 million during the year ended December 31, 2016, from $220.5 million during the year ended December 31, 2015. The increase in sales and marketing expenses was in line with the significant growth in gross sales and an increase in the number of sales representatives over the same period, which primarily contributed to an increase of $52.2 million in employee costs resulting from increased staffing of our field sales force and an increase of $47.7 million in marketing and commercialization expenses following the Hyperion, Crealta and Raptor acquisitions.

General and Administrative Expenses. General and administrative expenses increased $68.1 million to $287.9 million during the year ended December 31, 2016, from $219.8 million during the year ended December 31, 2015. The increase was attributable to $22.4 million of higher share-based compensation, $10.2 million in other employee costs resulting from growth in our headcount following the Hyperion, Crealta and Raptor acquisitions, an increase of $36.8 million in costs following the Hyperion, Crealta and Raptor acquisitions and $5.3 million due to the impairment of the initial amount paid to Boehringer Ingelheim International for certain rights to interferon gamma-1b, offset by a decrease of $6.6 million in acquisition-related general and administrative expenses.

Impairment of In-Process Research and Development. At the time of the Vidara Merger, IPR&D was considered separable from the business as the project could be sold to a third party, and we assigned a fair value of $66.0 million to the intangible asset. Following the FA announcement, we determined that the IPR&D has no alternative use or economic value, and we recorded an impairment charge during the three months ended December 31, 2016 to fully write off the value of the asset on our consolidated balance sheet.

Interest Expense, Net. Interest expense, net, increased $16.7 million to $86.6 million during the year ended December 31, 2016, from $69.9 million during the year ended December 31, 2015. The increased interest expense, net, was primarily due to full-period recognition during the year ended December 31, 2016 of the interest on higher borrowings to fund the acquisition of Hyperion in May 2015, including our $475.0 million aggregate principal amount of 6.625% Senior Notes due 2023, or the 2023 Senior Notes, six-year $400.0 million term loan facility, or the 2015 Term Loan Facility, and $400.0 million aggregate principal amount of 2.50% Exchangeable Senior Notes due 2022, or the Exchangeable Senior Notes, as compared to partial period recognition of the interest on these borrowings during the year ended December 31, 2015 and our lower prior year borrowings under our prior five-year $300.0 million term loan facility, or 2014 Term Loan Facility. We also incurred additional interest expense following our borrowings to fund the acquisition of Raptor in October 2016, including our additional $375.0 million additional borrowings under the 2015 Term Loan Facility, or the 2016 Incremental Loan Facility, and the 2024 Senior Notes.

Foreign Exchange Loss. During the year ended December 31, 2016, we reported a foreign exchange loss of $1.0 million.

Loss on Induced Conversion of Debt and Debt Extinguishment. The loss on induced conversion of debt and debt extinguishment during the year ended December 31, 2015 of $77.6 million was composed of $20.7 million related to the induced conversions of our 5.00% Convertible Senior Notes due 2018, or Convertible Senior Notes, including $10.0 million for cash inducement payments, a $10.1 million charge for the extinguishment of debt and $0.6 million of expenses, and $56.9 million related to the extinguishment of the 2014 Term Loan Facility, consisting of a $45.4 million early redemption premium and a $11.5 million charge for the extinguishment of debt. The number of shares issued equaled the number of shares based on the underlying conversion option. The aggregate cash payments to the holders for additional exchange consideration were recorded as part of the extinguishment loss. There were no induced conversions in 2016.

Loss on Sale of Long-Term Investments. The loss on sale of long-term investments during the year ended December 31, 2015 was $29.0 million. During the third quarter of 2015, we purchased 2,250,000 shares of common stock of Depomed, Inc., or Depomed, representing 3.75% of Depomed's then outstanding common stock. The shares were acquired at a cost of $71.8 million. During the fourth quarter of 2015, following our decision to withdraw our offer to acquire Depomed, we sold all of our shares in Depomed, receiving sales proceeds of $42.8 million and recognized a realized loss of $29.0 million. There were no sales of long-term investments in 2016.

Other Income (Expense) net. Other income, net during the year ended December 31, 2016 was primarily related to the release of a contingent liability of $6.9 million which was assumed as part of the Crealta acquisition. In December 2015, Crealta considered it probable that the manufacture of the active pharmaceutical ingredient, or API, for KRYSTEXXA would be moved out of Israel based on a notice of termination provided by its contract manufacturer, therefore triggering a repayment obligation to Israel's Office of the Chief Scientist. As a result, Crealta established a $6.9 million contingent liability reserve in its December 31, 2015 financial statements. As of the date of our acquisition of Crealta, the $6.9 million repayment obligation was still probable. Therefore, it was recorded as an assumed liability in "other long-term liabilities" as part of the acquisition accounting for Crealta. During the third quarter of 2016, Horizon management negotiated a new amendment to the manufacturing agreement and it was determined that the manufacture of the KRYSTEXXA API would not be moved outside of Israel and thus the repayment of the $6.9 million would not be triggered. The contingent liability was released to "other income (expense)" during the year ended December 31, 2016 as it was a reversal of an assumed liability and therefore did not represent income from operations. Other expense, net, during the year ended December 31, 2015 totaled $10.3 million, which primarily included the fees related to the Hyperion acquisition financing commitment.

Benefit for Income Taxes. During the year ended December 31, 2016, we recorded an income tax benefit of $61.3 million compared to $172.2 million during the year ended December 31, 2015. The recognition of income tax benefit during the year ended December 31, 2016 was primarily attributable to the mix of income and losses amongst jurisdictions, a notional interest deduction and the change in our U.S. state effective tax rate. The recognition of an

income tax benefit during the year ended December 31, 2015 was primarily attributable to the release of $103.1 million in valuation allowances in the U.S. tax consolidation group due to the recognition of significant deferred tax liabilities as a result of the Hyperion acquisition as well as the ability to recognize a tax benefit on losses incurred in the United States.

Year Ended December 31, 2015 Compared to Year Ended December 31, 2014

	For the Years Ended December 31,		Increase / (Decrease)	Change %
	2015	2014		
	(in thousands)			
Net sales	$757,044	$296,955	$460,089	155 %
Cost of goods sold	219,502	78,753	140,749	179 %
Gross profit	537,542	218,202	319,340	146 %
Operating expenses				
Research and development	41,865	17,460	24,405	140 %
Sales and marketing	220,444	120,276	100,168	83 %
General and administrative	219,861	88,957	130,904	147 %
Total operating expenses	482,170	226,693	255,477	113 %
Operating income (loss)	55,372	(8,491)	63,863	752 %
Other income (expense), net:				
Interest expense, net	(69,900)	(23,826)	46,074	193 %
Foreign exchange loss	(1,237)	(3,905)	(2,668)	(68)%
Loss on derivative fair value	—	(214,995)	(214,995)	(100)%
Loss on induced conversion and debt extinguishment	(77,624)	(29,390)	48,234	164 %
Loss on sale of long-term investments	(29,032)	—	29,032	100 %
Bargain purchase gain	—	22,171	22,171	100 %
Other expense	(10,291)	(11,251)	(960)	(9)%
Total other expense, net	(188,084)	(261,196)	(73,112)	28 %
Loss before benefit for income taxes	(132,712)	(269,687)	(136,975)	(51)%
Benefit for income taxes	(172,244)	(6,084)	166,160	2,731 %
Net income (loss)	$39,532	$(263,603)	$303,135	115 %

Net sales. Net sales increased $460.1 million, or 155%, to $757.0 million during the year ended December 31, 2015, from $296.9 million during the year ended December 31, 2014.

The following table presents a summary of total net sales attributed to geographic sources for the years ended December 31, 2015 and 2014 (in thousands):

	Year Ended December 31, 2015		Year Ended December 31, 2014	
	Amount	% of Total Net Sales	Amount	% of Total Net Sales
United States	$ 744,036	98 %	$ 290,396	98 %
Rest of world	13,008	2 %	6,559	2 %
Total net sales	$ 757,044		$ 296,955	

The following table reflects the components of net sales for the years ended December 31, 2015 and 2014:

	Year Ended December 31,		Change	Change
	2015	2014	$	%
	(in thousands)			
DUEXIS	$190,357	$83,243	$107,114	129 %
VIMOVO	166,672	162,954	3,718	2 %
PENNSAID 2%	147,010	-	147,010	*
ACTIMMUNE	107,444	25,251	82,193	326 %
RAVICTI	86,875	-	86,875	*
RAYOS	40,329	19,020	21,309	112 %
BUPHENYL	13,458	-	13,458	*
LODOTRA	4,899	6,487	(1,588)	(25 %)
Total net sales	$757,044	$296,955	$460,089	155 %

*Percentage change is not meaningful.

The increase in net sales during the year ended December 31, 2015 was primarily due to the recognition of PENNSAID 2% sales beginning in January 2015 following our acquisition of the U.S. rights to PENNSAID 2% from Nuvo in October 2014, the growth in sales of DUEXIS, the recognition of RAVICTI and BUPHENYL sales following the acquisition of Hyperion in May 2015, full-period recognition of ACTIMMUNE sales during the year ended December 31, 2015 compared with partial-period recognition during the year ended December 31, 2014, following the Vidara Merger on September 19, 2014, and the growth of RAYOS sales.

DUEXIS. Net sales increased $107.1 million, or 129%, to $190.4 million during the year ended December 31, 2015, from $83.3 million during the year ended December 31, 2014. DUEXIS net sales increased $58.0 million as a result of prescription volume growth driven by the expansion of our field sales force and increased $49.1 million due to higher net pricing resulting from wholesale acquisition cost, or WAC, price increases partially offset by additional patient co-pay reimbursements.

VIMOVO. Net sales increased $3.7 million, or 2%, to $166.7 million during the year ended December 31, 2015, from $163.0 million during the year ended December 31, 2014. VIMOVO net sales increased by $23.5 million resulting from prescription volume growth, offset by a decrease of $19.8 million due to lower net pricing. While we have increased the WAC price for VIMOVO over the last 12 months, the increases were more than offset by additional patient co-pay reimbursements.

PENNSAID 2%. Net sales were $147.0 million during the year ended December 31, 2015. We began recognizing PENNSAID 2% sales in January 2015 following our acquisition of the U.S. rights to PENNSAID 2% from Nuvo in October 2014.

ACTIMMUNE. Net sales increased $82.2 million, or 326%, to $107.5 million during the year ended December 31, 2015, from $25.3 million during the year ended December 31, 2014. Net sales increased by approximately $47.1 million resulting from prescription volume growth and $35.1 million due to higher net pricing. We began recognizing ACTIMMUNE sales following the closing of the Vidara Merger on September 19, 2014, therefore only a partial period of ACTIMMUNE sales were recognized during the year ended December 31, 2014, compared with full-period recognition of sales during the year ended December 31, 2015.

RAVICTI. Net sales were $86.9 million during the year ended December 31, 2015. We began recognizing RAVICTI sales following the acquisition of Hyperion in May 2015.

RAYOS. Net sales increased $21.3 million, or 112%, to $40.3 million during the year ended December 31, 2015, from $19.0 million during the year ended December 31, 2014. The increase was primarily due to prescription growth and net price increases resulting in higher net sales of approximately $20.2 million and $1.1 million, respectively.

BUPHENYL. Net sales were $13.5 million during the year ended December 31, 2015. We began recognizing BUPHENYL sales following the acquisition of Hyperion in May 2015.

LODOTRA. Net sales decreased $1.6 million, or 25%, to $4.9 million during the year ended December 31, 2015, from $6.5 million during the year ended December 31, 2014. The decrease was due to fewer shipments to our European distribution partner, Mundipharma. LODOTRA sales to Mundipharma occur at the time we ship, based on Mundipharma’s estimated requirements. Accordingly, LODOTRA sales are not linear or directly tied to Mundipharma’s in-market sales and can therefore fluctuate significantly.

The table below reconciles our gross sales to net sales for the years ended December 31, 2015 and 2014 (in millions):

	Year Ended December 31, 2015		Year Ended December 31, 2014	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Gross sales	$2,057.3	100.0%	$600.8	100.0%
Adjustments to gross sales:				
Prompt pay discounts	(41.3)	(2.0)%	(11.0)	(1.8)%
Medicine returns	(14.4)	(0.7)%	(7.2)	(1.2)%
Co-pay and other patient assistance	(1,020.2)	(49.6)%	(138.3)	(23.1)%
Wholesaler fees and commercial rebates	(66.1)	(3.2)%	(102.0)	(17.0)%
Government rebates and chargebacks	(158.3)	(7.7)%	(45.3)	(7.5)%
Total adjustments	(1,300.3)	(63.2)%	(303.8)	(50.6)%
Net sales	$757.0	36.8 %	$297.0	49.4 %

During the year ended December 31, 2015, co-pay and other patient assistance, as a percentage of gross sales, increased to 49.6% from 23.1% during the year ended December 31, 2014. The increase was primarily due to the rollout of our HorizonCares program to all sales territories during 2015 which helped ensure patient access to our medicines in the face of exclusionary actions by certain PBMs. During the year ended December 31, 2015, wholesaler fees and commercial rebates, as a percentage of gross sales, decreased to 3.2% from 17.0% during the year ended December 31, 2014, primarily due to a decrease in our managed care rebates following the termination of our agreements with CVS Caremark and Express Scripts in 2014.

Effective January 1, 2015, two significant PBMs placed DUEXIS and VIMOVO on their exclusion lists, which resulted in a loss of reimbursement for patients whose healthcare plans have adopted these PBM exclusion lists. However, this action did not negatively impact sales volume for either medicine. In fact, with successful adoption of our HorizonCares program by physicians, we saw increases in sales volume for both medicines. During the year ended December 31, 2015, DUEXIS sales volumes increased by 70% and VIMOVO sales volumes increased by 14%, each, when compared to the year ended December 31, 2014.

Cost of Goods Sold. Cost of goods sold increased $140.7 million to $219.5 million during the year ended December 31, 2015, from $78.8 million during the year ended December 31, 2014. As a percentage of net sales, cost of goods sold was 29.0% during the year ended December 31, 2015 compared to 26.5% during the year ended December 31, 2014. The increase in cost of goods sold was primarily attributable to an increase in intangible amortization expense of $100.0 million, a $19.1 million increase in medicine costs associated with higher sales, higher royalty accretion expense of $11.1 million and a $10.5 million increase in charges relating to the remeasurement of contingent royalty liabilities.

The increase in intangible amortization of $100.0 million during the year ended December 31, 2015 compared to the prior year was primarily due to increases in intangible amortization expense of $62.2 million in relation to RAVICTI and BUPHENYL (acquired on May 7, 2015), $31.1 million relating to ACTIMMUNE developed technology (acquired on September 19, 2014) and $7.3 million relating to PENNSAID 2% (U.S. rights acquired in October 2014).

Research and Development Expenses. Research and development expenses increased $24.4 million to $41.9 million during the year ended December 31, 2015, from $17.5 million during the year ended December 31, 2014. The increase in research and development expenses during the year ended December 31, 2015 was primarily associated with $17.1 million in research and development expenses for ACTIMMUNE, RAVICTI and BUPHENYL, which included $4.0 million related to the STEADFAST study. We also recorded an increase of $5.1 million in share-based compensation expense during the year ended December 31, 2015 compared to the year ended December 31, 2014 as a result of the increase in the number of employees involved in research and development activities following the Vidara Merger and Hyperion acquisition.

Sales and Marketing Expenses. Sales and marketing expenses increased $100.1 million to $220.4 million during the year ended December 31, 2015, from $120.3 million during the year ended December 31, 2014. The increase in sales and marketing expenses reflects the growth in revenue and increase in the number of sales representatives over the same period, and was primarily attributable to an increase of $58.5 million in employee costs, including $18.9 million related to share-based compensation, resulting from the increased staffing of our field sales force and the expansion of our HorizonCares support team. We also recorded an increase of $22.0 million in marketing and commercialization expenses and an increase of $6.8 million in medicine samples distributed.

General and Administrative Expenses. General and administrative expenses increased $130.9 million to $219.9 million during the year ended December 31, 2015, from $89.0 million during the year ended December 31, 2014. The increase in general and administrative expenses was primarily attributable to an increase of $48.6 million in share-based compensation expense, $18.4 million in acquisition-related general and administrative expenses, and $63.9 million related to our growth in headcount, facilities, finance fees, legal fees and information technology expenses following the Vidara Merger and Hyperion acquisition.

Interest Expense, Net. Interest expense, net, increased $46.1 million to $69.9 million during the year ended December 31, 2015, from $23.8 million during the year ended December 31, 2014. The increased interest expense, net, was due to a full year of interest expense in 2015 on borrowings to fund the Vidara Merger in September 2014 and interest on additional borrowings to partially fund the acquisition of Hyperion in May 2015, including the 2023 Senior Notes, the 2015 Term Loan Facility, and the Exchangeable Senior Notes, as compared to our prior year borrowings under the Convertible Senior Notes and 2014 Term Loan Facility.

Foreign Exchange Loss. During the year ended December 31, 2015, we reported a foreign exchange loss of $1.2 million.

Loss on Derivative Revaluation. During the year ended December 31, 2014, we recorded a $215.0 million non-cash charge related to the increase in the fair value of the embedded derivative associated with our Convertible Senior Notes. The loss on the derivative revaluation was primarily due to an increase in the market value of HPI’s common stock during the period from January 1, 2014 until June 27, 2014, the date HPI’s stockholders approved the issuance of in excess of 13,164,951 shares of HPI’s common stock upon conversion of the Convertible Senior Notes. The derivative liability was re-measured to a final fair value and the entire fair value of the derivative liability of $324.4 million was reclassified to additional paid-in capital. As such, there was no derivative revaluation subsequent to June 2014.

Loss on Induced Conversion of Debt and Debt Extinguishment. The loss on induced conversion of debt and debt extinguishment during the year ended December 31, 2015 of $77.6 million was composed of $20.7 million related to the induced conversions of Convertible Senior Notes, including $10.0 million for cash inducement payments, a $10.1 million charge for the extinguishment of debt and $0.6 million of expenses, and $56.9 million related to the extinguishment of the 2014 Term Loan Facility, consisting of a $45.4 million early redemption premium and a $11.5 million charge for the extinguishment of debt. The loss on induced conversion and debt extinguishment during the year ended December 31, 2014 of $29.4 million was a result of the Convertible Senior Notes induced conversions in the fourth quarter of 2014, which consisted of $16.7 million of loss on induced conversion for cash inducement payments, a $11.7 million charge for the extinguishment of debt and $1.0 million of expenses related to the induced debt conversions. The number of shares issued equaled the number of shares based on the underlying conversion option. The aggregate cash payments to the holders for additional exchange consideration were recorded as part of the extinguishment loss.

Loss on Sale of Long-Term Investments. The loss on sale of long-term investments during the year ended December 31, 2015 was $29.0 million. During the third quarter of 2015, we purchased 2,250,000 shares of common stock of Depomed, representing 3.75% of Depomed’s then outstanding common stock. The shares were acquired at a cost of $71.8 million. During the fourth quarter of 2015, following our decision to withdraw our offer to acquire Depomed, we sold all of our shares in Depomed, receiving sales proceeds of $42.8 million and recognized a realized loss of $29.0 million in the consolidated statement of comprehensive income.

Bargain Purchase Gain. During the year ended December 31, 2014, we recorded a bargain purchase gain of $22.2 million in connection with the Vidara Merger, representing the excess of the estimated fair values of net assets acquired over the acquisition consideration paid.

Other Expense, net. Other expense, net, during the year ended December 31, 2015 totaled $10.3 million, which primarily included the fees related to the Hyperion acquisition financing commitment. Other expense during the year ended December 31, 2014 totaled $11.3 million, representing $5.0 million of commitment fees incurred on the bridge financing in place prior to executing the 2014 Term Loan Facility in June 2014, $3.2 million of commitment fees incurred on the 2014 Term Loan Facility prior to its funding on September 19, 2014 and $2.9 million secondary offering expense fees incurred in the November 2014 underwritten public offering.

Benefit for Income Taxes. During the year ended December 31, 2015, we recorded an income tax benefit of $172.2 million compared to $6.1 million during the year ended December 31, 2014. The recognition of income tax benefit during the year ended December 31, 2015 was primarily attributable to the release of $103.1 million in valuation allowances in the U.S. tax consolidation group due to the recognition of significant deferred tax liabilities as a result of the Hyperion acquisition as well as the ability to recognize a tax benefit on losses incurred in the United States.

Non-GAAP Financial Measures

EBITDA, or earnings before interest, taxes, depreciation and amortization, and adjusted EBITDA are used and provided by us as non-GAAP financial measures. We provide certain other financial measures such as non-GAAP adjusted net sales, non-GAAP net income and non-GAAP earnings per share which include adjustments to GAAP figures. The exclusion of the $65.0 million litigation settlement from GAAP net sales is the only adjustment reflected in non-GAAP adjusted net sales for the year ended December 31, 2016. Adjusted EBITDA and non-GAAP net income are intended to provide additional information on our performance, operations and profitability. Adjustments to our GAAP figures as well as EBITDA exclude acquisition-related expenses, charges related to the discontinuation of ACTIMMUNE development for FA, an upfront fee for a license of a patent, the Express Scripts litigation settlement amount, loss on debt extinguishment and loss on sale of long-term investments, as well as non-cash items such as share-based compensation, inventory step-up expense, depreciation and amortization, remeasurement of royalties for medicines acquired through business combinations, royalty accretion, non-cash interest expense, the reversal of a pre-acquisition reserve upon the signing of a contract, intangible and other non-current asset impairment charges and other non-cash adjustments. Certain other special items or substantive events may also be included in the non-GAAP adjustments periodically when their magnitude is significant within the periods incurred. We maintain an established non-GAAP cost policy that guides the determination of what costs will be excluded in non-GAAP measures. We believe that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of our financial and operating performance. The non-GAAP financial measures are included with the intent of providing investors with a more complete understanding of our historical financial results and trends and to facilitate comparisons between periods and with respect to projected information. In addition, these non-GAAP financial measures are among the indicators our management uses for planning and forecasting purposes and measuring our performance. For example, adjusted EBITDA is used by us as one measure of management performance under certain incentive compensation arrangements. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, financial measures calculated in accordance with GAAP. The non-GAAP financial measures used by us may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies.

Beginning in the second quarter of 2016, we modified the method of calculating non-GAAP income tax expense to align with guidance issued by the Securities and Exchange Commission on May 17, 2016. The new methodology calculates the income tax component of non-GAAP net income for each period by adjusting the GAAP tax expense (benefit) for the estimated tax impact of each non-GAAP adjustment based on the statutory income tax rate of the applicable jurisdictions for each non-GAAP adjustment. This new methodology does not reflect any use of net operating loss carryforwards that we potentially may have been able to use if our actual earnings for these periods had been the non-GAAP net income. Previously, we had calculated the income tax component of non-GAAP net income by using the estimated cash taxes that we expected to pay for the period. The non-GAAP net income and diluted net income per share amounts shown in the GAAP to non-GAAP reconciliation tables below are based on the new methodology.

Reconciliations of reported GAAP net sales to non-GAAP adjusted net sales, reported GAAP net (loss) income to EBITDA, adjusted EBITDA and non-GAAP net income, and the related per share amounts, are as follows (in thousands, except share and per share amounts):

	For the Years Ended December 31,		
	2016	2015	2014
GAAP Net Sales	$981,120	$757,044	$296,955
Litigation settlement	65,000	-	-
Non-GAAP Adjusted Net Sales	$1,046,120	$757,044	$296,955

	For the Years Ended December 31,		
	2016	2015	2014
GAAP Net (Loss) Income	$(166,834)	$39,532	$(263,603)
Non-GAAP adjustments:			
Remeasurement of royalties for medicines acquired through business combinations (1)	386	21,151	10,660
Acquisition-related costs	52,874	72,221	48,835
Upfront fee for license of global patent	2,000	—	—
Loss on sale of long-term investments	—	29,032	—
Loss on derivative revaluation	—	—	214,995
Loss on induced conversion of debt and debt extinguishment	—	77,624	29,390
Bargain purchase gain	—	—	(22,171)
Secondary offering costs	—	—	2,857
Amortization, accretion and step-up:			
Intangible amortization expense	216,875	132,923	32,306
Amortization of debt discount and deferred financing costs	18,546	18,810	9,273
Accretion of royalty liabilities	40,616	20,088	9,020
Inventory step-up expense	71,137	11,495	11,065
Share-based compensation	114,144	85,786	13,198
Depreciation expense	4,962	5,420	1,702
Litigation settlement	65,000	—	—
Reversal of pre-acquisition reserve upon signing of contract	(6,900)	—	—
Impairment of in-process research and development	66,000	—	—
Charges relating to discontinuation of Friedreich's ataxia program (2)	23,513	—	—
Royalties for medicines acquired through business combinations (1)	(37,593)	(29,834)	(18,264)
Total of pre-tax non-GAAP adjustments	631,560	444,716	342,866
Income tax effect of pre-tax non-GAAP adjustments (3)	(110,290)	(122,214)	(76)
Other non-GAAP income tax adjustments (4)	—	(105,133)	—
Total of non-GAAP adjustments	521,270	217,369	342,790
Non-GAAP Net Income	354,436	256,901	79,187
Non-GAAP Earnings Per Share:			
Weighted average ordinary shares – Basic	160,699,543	148,788,020	83,751,129
Non-GAAP Earnings Per Share – Basic			
GAAP (loss) earnings per share - Basic	$(1.04)	$0.27	$(3.15)
Non-GAAP adjustments	3.25	1.46	4.10
Non-GAAP earnings per share – Basic	$2.21	$1.73	$0.95
Weighted average ordinary shares – Diluted			
Weighted average ordinary shares – Basic	160,699,543	148,788,020	83,751,129
Ordinary share equivalents	3,626,570	7,135,231	20,737,726
Weighted average ordinary shares – Diluted	164,326,113	155,923,251	104,488,855
Non-GAAP Earnings Per Share – Diluted			
GAAP (loss) earnings per share – Diluted	$(1.04)	$0.25	(3.15)

Non-GAAP adjustments	3.25	1.40	4.10
Diluted earnings per share effect of ordinary share equivalents	(0.05)	—	(0.19)
Non-GAAP earnings per share – Diluted	$2.16	$1.65	$0.76

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	For the Years Ended December 31,		
	2016	2015	2014
GAAP Net (Loss) Income	$(166,834)	$39,532	$(263,603)
Depreciation	4,962	5,420	1,702
Amortization, accretion and step-up:			
Intangible amortization expense	216,875	132,923	32,306
Amortization of deferred revenue	(836)	(962)	(644)
Accretion of royalty liabilities	40,616	20,088	9,020
Inventory step-up expense	71,137	11,495	11,065
Interest expense, net (including amortization of debt discount and deferred financing costs)	86,610	69,900	23,826
Benefit for income taxes	(61,251)	(172,244)	(6,084)
EBITDA	191,279	106,152	(192,412)
Non-GAAP adjustments:			
Remeasurement of royalties for medicines acquired through business combinations (1)	386	21,151	10,660
Acquisition-related costs	52,874	72,221	48,835
Upfront fee for license of global patent	2,000	—	—
Impairment of in-process research and development	66,000	—	—
Charges relating to discontinuation of Friedreich's ataxia program (2)	23,513	—	—
Share-based compensation	114,144	85,786	13,198
Royalties for medicines acquired through business combinations (1)	(37,593)	(29,834)	(18,264)
Litigation settlement	65,000	—	—
Reversal of pre-acquisition reserve upon signing of contract	(6,900)	—	—
Loss on sale of long-term investments	—	29,032	—
Loss on derivative revaluation	—	—	214,995
Loss on induced conversion of debt and debt extinguishment	—	77,624	29,390
Bargain purchase gain	—	—	(22,171)
Secondary offering costs	—	—	2,857
Total of non-GAAP adjustments	279,424	255,980	279,500
Adjusted EBITDA	$470,703	$362,132	$87,088

(1) Royalties for medicines acquired through business combinations relate to ACTIMMUNE, BUPHENYL, KRYSTEXXA, MIGERGOT, PROCYSBI, RAVICTI and VIMOVO.

(2) Charges relating to the discontinuation of the STEADFAST program include a $14.3 million loss on inventory purchase commitments, a $5.3 million impairment of a non-current asset and $4.0 million of clinical trial wind-down costs.

(3) Adjustment to the GAAP tax (benefit) expense for the estimated tax impact of each non-GAAP adjustment based on the statutory tax rate of the applicable jurisdictions for each non-GAAP adjustment.

(4) Other non-GAAP income tax adjustments in the year ended December 31, 2015 of $105.1 million related to the release of certain valuation allowances in connection with the Hyperion acquisition.

Liquidity, Financial Position and Capital Resources

We have incurred losses since our inception in June 2005 and, as of December 31, 2016, we had an accumulated deficit of $848.0 million. We expect that our sales and marketing expenses will continue to increase as a result of our commercialization of our medicines, but we believe these cost increases will be more than offset by higher net sales and gross profits. We incurred an operating loss in 2016 primarily as a result of significant charges following the FA announcement in the fourth quarter of 2016, the litigation settlement with Express Scripts in September 2016 and costs incurred in connection with our acquisitions of Crealta and Raptor during the year. We expect our current operations to achieve operating profitability in 2017, absent unusual or non-recurring items.

We have financed our operations to date through equity financings, debt financings and the issuance of convertible notes, along with cash flows from operations during past three years. As of December 31, 2016, we had $509.1 million in cash and cash equivalents and total debt with a book value of $1,807.5 million and face value of $1,944.0 million. We believe our existing cash and cash equivalents and our expected cash flows from our operations will be sufficient to fund our business needs for the foreseeable future. Part of our strategy is to expand and leverage our commercial capabilities by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. To the extent we enter into transactions to acquire medicines or businesses in the future, we will most likely need to finance a significant portion of those acquisitions through additional debt, equity or convertible debt financings.

In March 2015, April 2015 and June 2015, we entered into separate, privately negotiated conversion agreements with certain holders of the Convertible Senior Notes which were on substantially the same terms as prior conversion agreements entered into by us. Under these conversion agreements, the applicable holders agreed to convert an aggregate principal amount of $61.0 million of Convertible Senior Notes held by them and we agreed to settle such conversions by issuing an aggregate of 11,368,921 ordinary shares. In addition, pursuant to such conversion agreements, we made an aggregate cash payment of $10.0 million to the applicable holders for additional exchange consideration and $0.9 million for accrued and unpaid interest. Following these conversions, there were no Convertible Senior Notes remaining outstanding. The number of shares issued equaled the number of shares based on the underlying conversion option. The aggregate cash payments to the holders for additional exchange consideration were recorded as part of the extinguishment loss.

On March 13, 2015, Horizon Pharma Investment Limited, a wholly owned subsidiary of Horizon Pharma plc, or Horizon Investment, completed a private placement of $400.0 million aggregate principal amount of Exchangeable Senior Notes to several investment banks acting as initial purchasers who subsequently resold the Exchangeable Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act of 1933, as amended, or the Securities Act. The net proceeds from the offering of the Exchangeable Senior Notes were approximately $387.2 million, after deducting the initial purchasers' discount and offering expenses payable by Horizon Investment.

We have fully and unconditionally guaranteed the Exchangeable Senior Notes on a senior unsecured basis, referred to as the Guarantee. The Exchangeable Senior Notes and the Guarantee are Horizon Investment's and our senior unsecured obligations. The Exchangeable Senior Notes accrue interest at an annual rate of 2.50% payable semiannually in arrears on March 15 and September 15 of each year, beginning on September 15, 2015. The Exchangeable Senior Notes will mature on March 15, 2022, unless earlier exchanged, repurchased or redeemed. The initial exchange rate is 34.8979 of our ordinary shares per $1,000 principal amount of the Exchangeable Senior Notes (equivalent to an initial exchange price of approximately $28.66 per ordinary share).

On April 21, 2015, we closed an underwritten public offering of 17,652,500 of our ordinary shares at a price to the public of $28.25 per share, referred to as the 2015 Offering. The net proceeds to us from the 2015 Offering were approximately $475.7 million, after deducting underwriting discounts and other offering expenses payable by us.

On April 29, 2015, Horizon Pharma Financing Inc., our then wholly owned subsidiary, or Horizon Financing, completed a private placement of $475.0 million aggregate principal amount of 2023 Senior Notes to certain investment banks acting as initial purchasers who subsequently resold the 2023 Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act and in offshore transactions to non-U.S. Persons in reliance on Regulation S under the Securities Act. The net proceeds from the 2023 Senior Notes were approximately $462.3 million.

In connection with the closing of the Hyperion acquisition on May 7, 2015, Horizon Financing merged with and into HPI and, as a result, the 2023 Senior Notes became HPI's general unsecured senior obligations and we and all of our direct and indirect subsidiaries that are guarantors under the 2015 Senior Secured Credit Facility (as described below) fully and unconditionally guaranteed on a senior unsecured basis HPI's obligations under the 2023 Senior Notes.

The 2023 Senior Notes accrue interest at an annual rate of 6.625% payable semiannually in arrears on May 1 and November 1 of each year, beginning on November 1, 2015. The 2023 Senior Notes will mature on May 1, 2023, unless earlier exchanged, repurchased or redeemed.

Except as described below, the 2023 Senior Notes may not be redeemed before May 1, 2018. Thereafter, some or all of the 2023 Senior Notes may be redeemed at any time at specified redemption prices, plus accrued and unpaid interest to the redemption date. At any time prior to May 1, 2018, some or all of the 2023 Senior Notes may be redeemed at a price equal to 100% of the aggregate principal amount thereof, plus a make-whole premium and accrued and unpaid interest to, but not including the redemption date. Also prior to May 1, 2018, up to 35% of the aggregate principal amount of the 2023 Senior Notes may be redeemed at a redemption price of 106.625% of the aggregate principal amount thereof, plus accrued and unpaid interest, with the net proceeds of certain equity offerings; provided that: (1) at least 65% of the aggregate principal amount of notes originally issued under the indenture (excluding notes held by the parent and its subsidiaries) remains outstanding immediately after the occurrence of such redemption; and (2) the redemption occurs with 180 days of the date of closing such equity offering. In addition, the 2023 Senior Notes may be redeemed in whole but not in part at a redemption price equal to 100% of the principal amount plus accrued and unpaid interest and additional amounts, if any, to, but excluding, the redemption date, if on the next date on which any amount would be payable in respect of the 2023 Senior Notes, HPI or any guarantor is or would be required to pay additional amounts as a result of certain tax related events.

If we undergo a change of control, HPI will be required to make an offer to purchase all of the 2023 Senior Notes at a price in cash equal to 101% of the aggregate principal amount thereof plus accrued and unpaid interest to, but not including, the repurchase date. If we or certain of our subsidiaries engage in certain asset sales, HPI will be required under certain circumstances to make an offer to purchase the 2023 Senior Notes at 100% of the principal amount thereof, plus accrued and unpaid interest to the repurchase date.

On May 7, 2015, we, HPI, and certain of our subsidiaries entered into a credit agreement with Citibank N.A., as administrative agent and collateral agent, and the lenders from time to time party thereto, or, as amended, the credit agreement, providing for (i) the six-year $400.0 million 2015 Term Loan Facility; (ii) an uncommitted accordion facility subject to the satisfaction of certain financial and other conditions; and (iii) one or more uncommitted refinancing loan facilities with respect to loans thereunder. This is referred to as the 2015 Senior Secured Credit Facility. The initial borrower under the 2015 Term Loan Facility is HPI. The credit agreement allows for us and certain of our other subsidiaries to become borrowers under the accordion or refinancing facilities. Loans under the 2015 Term Loan Facility bear interest, at each borrower's option, at a rate equal to either the London Inter-Bank Offer Rate, or LIBOR, plus an applicable margin of 4.0% per year (subject to a 1.0% LIBOR floor), or the adjusted base rate plus 3.0%. The adjusted base rate is defined as the greater of (a) LIBOR (using one-month interest period) plus 1.0%, (b) prime rate, (c) fed funds plus ½ of 1% and (d) 2.0%. We borrowed the full $400.0 million available under the 2015 Term Loan Facility on May 7, 2015 as a LIBOR-based borrowing. The net proceeds from the 2015 Term Loan Facility were approximately $391.5 million.

The obligations under the credit agreement and any swap obligations and cash management obligations owing to a lender (or an affiliate of a lender) thereunder are and will be guaranteed by our and each of our existing and subsequently acquired or organized direct and indirect subsidiaries (other than certain immaterial subsidiaries, subsidiaries whose guarantee would result in material adverse tax consequences and subsidiaries whose guarantee is prohibited by applicable law). The obligations under the credit agreement and any such swap and cash management obligations are secured, subject to customary permitted liens and other agreed upon exceptions, by a perfected security interest in (i) all tangible and intangible assets of the borrowers and the guarantors, except for certain customary excluded assets, and (ii) all of the capital stock owned by the borrowers and guarantors thereunder (limited, in the case of the stock of certain non-U.S. subsidiaries of the borrowers, to 65% of the capital stock of such subsidiaries).

We are permitted to make voluntary prepayments at any time without payment of a premium. We are required to make mandatory prepayments of loans under the 2015 Term Loan Facility (without payment of a premium) with (a) net cash proceeds from certain non-ordinary course asset sales (subject to reinvestment rights and other exceptions), (b) casualty proceeds and condemnation awards (subject to reinvestment rights and other exceptions), (c) net cash proceeds from issuances of debt (other than certain permitted debt), and (d) beginning with the fiscal year ending December 31, 2016, 50% of our excess cash flow (subject to decrease to 25% or 0% if our first lien leverage

ratio is less than 2.25:1 and 1.75:1, respectively). The loans under the 2015 Term Loan Facility will amortize in equal quarterly installments in an aggregate annual amount equal to 1% of the original principal amount thereof, with any remaining balance payable on the final maturity date of the loans under the 2015 Term Loan Facility.

We used the net proceeds from the 2015 Offering, the offering of the 2023 Senior Notes, borrowings under the 2015 Term Loan Facility and existing cash to fund our acquisition of Hyperion, repay the $300.0 million outstanding amounts under the 2014 Term Loan Facility plus the related $45.4 million make-whole fee, and pay prepayment premiums, fees and expenses in connection with the foregoing.

On October 25, 2016, HPI and Horizon Pharma USA, Inc., our wholly owned subsidiary, or HPUSA, and, together with HPI, the 2024 Issuers, completed a private placement of $300.0 million aggregate principal amount of 2024 Senior Notes to certain investment banks acting as initial purchasers who subsequently resold the 2024 Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act.

The 2024 Senior Notes are the 2024 Issuers' general unsecured senior obligations and we and all of our direct and indirect subsidiaries that are guarantors under the 2015 Senior Secured Credit Facility and the 2016 Incremental Loan Facility fully and unconditionally guaranteed on a senior unsecured basis the 2024 Issuers' obligations under the 2024 Senior Notes.

The 2024 Senior Notes accrue interest at an annual rate of 8.75% payable semiannually in arrears on May 1 and November 1 of each year, beginning on May 1, 2017. The 2024 Senior Notes will mature on November 1, 2024, unless earlier exchanged, repurchased or redeemed.

Except as described below, the 2024 Senior Notes may not be redeemed before November 1, 2019. Thereafter, some or all of the 2024 Senior Notes may be redeemed at any time at specified redemption prices, plus accrued and unpaid interest to the redemption date. At any time prior to November 1, 2019, some or all of the 2024 Senior Notes may be redeemed at a price equal to 100% of the aggregate principal amount thereof, plus a make-whole premium and accrued and unpaid interest to the redemption date. Also prior to November 1, 2019, up to 35% of the aggregate principal amount of the 2024 Senior Notes may be redeemed at a redemption price of 108.75% of the aggregate principal amount thereof, plus accrued and unpaid interest, with the net proceeds of certain equity offerings. In addition, the 2024 Senior Notes may be redeemed in whole but not in part at a redemption price equal to 100% of the principal amount plus accrued and unpaid interest and additional amounts, if any, to, but excluding, the redemption date, if on the next date on which any amount would be payable in respect of the 2024 Senior Notes, the 2024 Issuers or any guarantor is or would be required to pay additional amounts as a result of certain tax-related events.

If we undergo a change of control, the 2024 Issuers will be required to make an offer to purchase all of the 2024 Senior Notes at a price in cash equal to 101% of the aggregate principal amount thereof plus accrued and unpaid interest to, but not including, the repurchase date. If we or certain of our subsidiaries engage in certain asset sales, the 2024 Issuers will be required under certain circumstances to make an offer to purchase the 2024 Senior Notes at 100% of the principal amount thereof, plus accrued and unpaid interest to the repurchase date.

On October 25, 2016, HPI and HPUSA, together, in such capacity, the Incremental Borrowers, entered into an amendment to the credit agreement, or the 2016 Amendment, with Citibank, N.A., as administrative and collateral agent, and Bank of America, N.A., as the incremental B-1 lender thereunder, pursuant to which the Incremental Borrowers borrowed $375.0 million aggregate principal amount of loans under the 2016 Incremental Loan Facility. The 2016 Incremental Loan Facility was incurred as a separate class of term loans under the credit agreement with the same terms of loans under the 2015 Term Loan Facility, except as described below.

Loans under the 2016 Incremental Loan Facility bear interest, at each Incremental Borrowers' option, at a rate equal to either LIBOR plus an applicable margin of 4.50% per year (subject to a LIBOR floor of 1.0%), or the adjusted base rate plus 3.50%. The terms of the loans under the 2015 Term Loan Facility, or the 2015 Loans, provided for an amendment such that the effective yield of the 2015 Loans would not be less than the effective yield of the loans under the 2016 Incremental Loan Facility, or the 2016 Incremental Loans, minus 0.50%. Consequently, the issuance of the 2016 Incremental Loans resulted in an increase of the interest rate applicable to the 2015 Loans, as of October 25, 2016, to LIBOR plus 4.00%, subject to a LIBOR floor of 1.0% (an initial interest rate of 5.00%). Borrowers under the credit agreement are permitted to make voluntary prepayments of the loans under the credit agreement at any time without payment of a premium, except that with respect to the 2016 Incremental Loans, a 1% premium will apply to a repayment of the 2016 Incremental Loans in connection with a re-pricing of, or any amendment to the credit

agreement in a re-pricing of, such loans effected on or prior to the date that is twelve months following October 25, 2016.

We used the net proceeds of the offering of the 2024 Senior Notes, borrowings under the 2016 Incremental Loan Facility and existing cash to fund our acquisition of Raptor, plus the related fees and expenses in connection with the foregoing.

We have a significant amount of debt outstanding on a consolidated basis. This substantial level of debt could have important consequences to our business, including, but not limited to: making it more difficult for us to satisfy our obligations; requiring a substantial portion of our cash flows from operations to be dedicated to the payment of principal and interest on our indebtedness, therefore reducing our ability to use our cash flows to fund acquisitions, capital expenditures, and future business opportunities; limiting our ability to obtain additional financing, including borrowing additional funds; increasing our vulnerability to, and reducing our flexibility to respond to, general adverse economic and industry conditions; limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; and placing us at a disadvantage as compared to our competitors, to the extent that they are not as highly leveraged. We may not be able to generate sufficient cash to service all of our indebtedness and may be forced to take other actions to satisfy our obligations under our indebtedness.

In addition, the indentures governing the 2024 Senior Notes and 2023 Senior Notes and the credit agreement related to the 2015 Senior Secured Credit Facility and 2016 Incremental Loan Facility impose various covenants that limit our ability and/or our restricted subsidiaries' ability to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales or merger transactions, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries; and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to us.

During the year ended December 31, 2016, we issued an aggregate of:

- 666,984 ordinary shares in net settlement of vested restricted stock units;
- 581,840 ordinary shares in connection with the exercise of stock options and received $3.9 million in proceeds;
- 513,659 ordinary shares pursuant to employee stock purchase plans and received $6.5 million in proceeds; and
- 13,584 ordinary shares in net settlement of vested performance stock units.

During the year ended December 31, 2016, we issued an aggregate of 1,750 ordinary shares upon the cash exercise of warrants and we received proceeds of $8,000 representing the aggregate exercise price for such warrants. In addition, warrants to purchase an aggregate of 207,110 of our ordinary shares were exercised in cashless exercises, resulting in the issuance of 161,259 ordinary shares. As of December 31, 2016, there were outstanding warrants to purchase 1,372,660 of our ordinary shares.

During the year ended December 31, 2016, we made payments of $5.5 million for employee withholding taxes relating to share-based awards.

In May 2016, our board of directors authorized a share repurchase program pursuant to which we may repurchase up to 5,000,000 of our ordinary shares. The timing and amount of repurchases, including whether we decide to repurchase any shares pursuant to the authorization, will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, our cash resources, restrictions under our credit agreement, and market conditions. As of December 31, 2016, we had not purchased any of our ordinary shares under this repurchase program.

Sources and Uses of Cash

The following table provides a summary of our cash position and cash flows for the years ended December 31, 2016, 2015 and 2014 (in thousands):

	For the Years Ended December 31,		
	2016	2015	2014
Cash and cash equivalents	$509,055	$859,616	$218,807

Cash provided by (used in):			
Operating activities	369,456	194,166	27,549
Investing activities	(1,375,881)	(995,048)	(227,720)
Financing activities	657,074	1,442,481	338,285

Net Cash Provided by Operating Activities

During the years ended December 31, 2016, 2015 and 2014, net cash provided by operating activities was $369.5 million, $194.2 million and $27.5 million, respectively.

The increase in net cash provided by operating activities during 2016 was primarily attributable to higher cash collections from accounts receivable balances as a result of an increase in sales of medicines, partially offset by cash outlays for patient access programs, contractual allowances and government rebates and chargebacks and $32.5 million outlay for fifty percent of the litigation settlement amount with Express Scripts. Net cash provided by operating activities was also negatively impacted during the year ended December 31, 2016 due to cash payments of $48.9 million for acquisition-related expenses and $60.8 million for interest payments made on our 2015 Term Loan Facility, 2016 Incremental Loan Facility, 2023 Senior Notes and Exchangeable Senior Notes.

Net cash provided by operating activities during 2015 was primarily attributable to cash collections from net sales. Cash provided by operating activities was negatively impacted during the year ended December 31, 2015 due to cash payments of $68.2 million for acquisition-related expenses, including the payment in April 2015 of approximately $11.2 million of employee and director excise taxes due to the Vidara Merger. Cash payments during the year ended December 31, 2015 also included a $45.4 million early redemption premium related to the 2014 Term Loan Facility, $42.0 million of interest payments made on our 2014 Term Loan Facility, 2015 Term Loan Facility, 2023 Senior Notes and Exchangeable Senior Notes, and $10.0 million of cash payments related to induced debt conversions.

Net cash provided by operating activities during 2014 was primarily attributable to cash collections from net sales, partially offset by cash outlays for related expenses. Cash provided by operating activities during 2014 was negatively impacted by $48.9 million in transaction costs related to the Vidara Merger, $2.9 million relating to the secondary offering of ordinary shares by certain stockholders in November 2014, and $16.7 million of cash payments related to induced debt conversions.

Net Cash Used in Investing Activities

During the years ended December 31, 2016, 2015 and 2014, net cash used in investing activities was $1,375.9 million, $995.0 million and $227.7 million, respectively.

Net cash used in investing activities during 2016 was primarily related to $835.9 million of payments for the acquisition of Raptor, net of cash acquired, $514.8 million of payments for the acquisition of Crealta, net of cash acquired, a $5.6 million (€5.0 million) initial payment for certain non-U.S. intellectual property rights to interferon gamma-1b and $15.7 million of payments for purchases of property and equipment.

Net cash used in investing activities during 2015 was primarily associated with $1,022.4 million of payments for the acquisition of Hyperion, net of cash acquired, and payments of $71.8 million made in relation to the purchase of 2,250,000 shares of common stock of Depomed. This was offset by proceeds of $42.8 million from the sale of such Depomed shares and proceeds from the liquidation of available-for-sale investments of $64.6 million.

Net cash used in investing activities during 2014 was primarily associated with the net cash paid for the Vidara Merger of $179.2 million and the acquisition of PENNSAID 2% of $45.0 million.

Net Cash Provided by Financing Activities

During the years ended December 31, 2016, 2015 and 2014, net cash provided by financing activities was $657.1 million, $1,442.5 million and $338.3 million, respectively.

Net cash provided by financing activities during 2016 was primarily related to $364.3 million of net proceeds received from borrowings under our 2016 Incremental Loan Facility and $291.9 million of net proceeds received from borrowings under our 2024 Senior Notes.

Net cash provided by financing activities during 2015 was primarily attributable to $387.2 million of net proceeds received from borrowings under the Exchangeable Senior Notes, $391.5 million net proceeds from the 2015 Term Loan Facility, $462.3 million net proceeds from the 2023 Senior Notes and $475.7 million of net proceeds from the issuance of 17,652,500 ordinary shares in the 2015 Offering, partially offset by the repayment of the 2014 Term Loan Facility and a partial repayment of the 2015 Term Loan Facility, which resulted in a financing outflow of $299.0 million.

Net cash provided by financing activities during 2014 was primarily attributable to $287.0 million of net proceeds received under our prior $300.0 million five-year senior secured credit facility in connection with the Vidara Merger in September 2014. In addition, during 2014, we received proceeds of $38.5 million in connection with the exercise of warrants to purchase 8,990,120 ordinary shares, and received $9.4 million of cash proceeds from the settlement of the capped call termination in September 2014.

Financial Condition as of December 31, 2016 compared to December 31, 2015

Accounts receivable, net. Accounts receivable, net, increased $95.3 million, from $210.4 million as of December 31, 2015 to $305.7 million as of December 31, 2016. The increase is due to growth in gross sales of our medicines, from 2015 to 2016. There has not been a material change to the ageing of our accounts receivable balances.

Inventories, net. Inventories, net, increased $156.4 million, from $18.4 million as of December 31, 2015 to $174.8 million as of December 31, 2016. This increase is primarily due to $95.3 million of stepped-up KRYSTEXXA and MIGERGOT inventory at December 31, 2016 recorded as a result of the Crealta acquisition in January 2016 and $44.0 million of stepped-up PROCYSBI and QUINSAIR inventory at December 31, 2016 recorded as a result of the Raptor acquisition in October 2016.

Prepaid expenses and other current assets. Prepaid expenses and other current assets increased $33.7 million, from $15.9 million as of December 31, 2015 to $49.6 million as of December 31, 2016. The increase is primarily due to $9.2 million of quarterly estimated income tax installments prepaid as of December 31, 2016, a $7.8 million deferred charge for taxes on intra-group profit, an increase of $5.5 million in medicine samples inventory, an increase of $3.4 million in value added tax receivable and an additional $2.3 million of rabbi trust assets held at December 31, 2016.

Developed technology, net. Developed technology, net, increased $1,158.1 million, from $1,609.1 million as of December 31, 2015 to $2,767.2 million as of December 31, 2016. The increase is due to $428.2 million of KRYSTEXXA and MIGERGOT developed technology acquired in the Crealta acquisition in January 2016 and $946.0 million of PROCYSBI developed technology acquired in the Raptor acquisition, offset by $216.1 million of amortization of developed technology during the year ended December 31, 2016.

In-process research and development. In-process research and development decreased $66.0 million, from $66.0 million as of December 31, 2015 to a zero balance as of December 31, 2016. Following the decision to discontinue the STEADFAST program, we determined that the IPR&D has no alternative use or economic value, and we recorded an impairment charge during the three months ended December 31, 2016 to fully write off the value of the asset on our consolidated balance sheet.

Goodwill. Goodwill increased $191.8 million, from $253.8 million as of December 31, 2015 to $445.6 million as of December 31, 2016. The increase is due to $189.1 million of goodwill recognized upon the acquisition of Raptor in October 2016 and $9.9 million of goodwill recognized upon the acquisition of Crealta in January 2016, offset by an adjustment related to deferred tax liabilities of Hyperion which resulted in a decrease to goodwill of $7.2 million during the year ended December 31, 2016.

Accounts payable. Accounts payable increased $35.9 million, from $16.6 million as of December 31, 2015 to $52.5 million as of December 31, 2016. This increase is primarily due to $16.8 million of trade discounts and rebates

included within accounts payable as of December 31, 2016 and increased expenses and payments following our acquisitions of Crealta and Raptor during the year.

Accrued expenses. Accrued expenses increased $82.8 million, from $100.0 million as of December 31, 2015 to $182.8 million as of December 31, 2016. This is primarily due to a $32.5 million unpaid litigation settlement amount as of December 31, 2016, following the litigation settlement with Express Scripts in September 2016, an increase of $16.5 million in consulting and professional services fee accruals, an increase in payroll-related accrued expenses of $14.5 million, $9.5 million related to a loss on inventory purchase commitments and an increase of $8.3 million in accrued interest as a result of our increased borrowings to fund the acquisition of Raptor in October 2016.

Accrued trade discounts and rebates. Accrued trade discounts and rebates increased $113.8 million, from $183.8 million as of December 31, 2015 to $297.6 million as of December 31, 2016. This is due to a $74.3 million increase in accrued co-pay and other patient assistance, a $26.4 million increase in accrued wholesaler fees and commercial rebates, and a $13.1 million increase in accrued government rebates and chargebacks. These increases are in line with the increase in gross sales during the period.

Long-term debt, net, net of current. Long-term debt, net, net of current, increased $651.8 million, from $849.9 million as of December 31, 2015 to $1,501.7 million as of December 31, 2016. This increase is due to our increased borrowings to fund the acquisition of Raptor in October 2016 including the $371.3 million non-current portion of our 2016 Incremental Loan Facility and the $300.0 million 2024 Senior Notes, offset by a $15.5 million net increase in debt discount and deferred financing fees and $4.0 million reclassified to long-term debt, current portion, during the year relating to the 2015 Term Loan Facility.

Accrued royalties, net of current. Accrued royalties, net of current, increased $148.8 million, from $123.5 million as of December 31, 2015 to $272.3 million as of December 31, 2016. This increase is primarily due to KRYSTEXXA and MIGERGOT contingent royalties of $65.8 million at December 31, 2016 as a result of the Crealta acquisition in January 2016 and PROCYSBI contingent royalties of $94.9 million at December 31, 2016 as a result of the Raptor acquisition in October 2016.

Deferred tax liabilities, net. Deferred tax liabilities, net, increased $183.5 million, from $113.4 million as of December 31, 2015 to $296.6 million as of December 31, 2016. The increase is primarily due to the recording of $237.2 million of deferred tax liabilities in connection with the acquisition of Raptor on October 25, 2016 and $20.1 million of deferred tax liabilities in connection with the acquisition of Crealta on January 13, 2016. This was offset by the reduction of $9.2 million in acquired deferred tax liabilities as a result of a change in our U.S. state effective tax rate after our acquisition of Raptor on October 25, 2016 and a reduction of $8.1 million in the deferred tax liabilities of the U.S. group of companies following an the overall reduction in the U.S. state effective tax rate from December 31, 2015 to December 31, 2016. In addition, other activity during the year ended December 31, 2016 resulting from business operations further reduced the deferred tax liabilities, net by $56.5 million.

Other long-term liabilities. Other long-term liabilities increased $36.7 million, from $9.4 million as of December 31, 2015 to $46.1 million as of December 31, 2016. The increase is primarily due to a $25.5 million assumed contingent liability arising following our acquisition of Raptor in October 2016, a $4.8 million liability related to the non-current portion of the loss on purchase commitments for inventory which is in excess of our current forecasts for future demand and a $2.3 million increase in long-term deferred compensation plan liabilities.

Contractual Obligations

As of December 31, 2016, minimum future cash payments due under contractual obligations, including, among others, our debt agreements, minimum purchase agreements and non-cancelable operating lease agreements, were as follows (in thousands):

2022 &

	2017	2018	2019	2020	2021	Thereafter	Total
Debt agreements – principal (1)	$7,750	$7,750	$7,750	$7,750	$738,000	$1,175,000	$1,944,000
Debt agreements - interest (1)	108,951	108,114	107,901	107,163	86,844	130,953	649,926
Purchase commitments (2)	46,940	13,000	9,717	9,570	6,180	46,981	132,388
Operating lease obligations (3)	7,716	7,611	6,753	5,968	5,316	15,856	49,220
Total contractual cash obligations	$171,357	$136,475	$132,121	$130,451	$836,340	$1,368,790	$2,775,534

(1) Represents the minimum contractual obligation due under the following debt agreements:

- $775.0 million under the 2015 Senior Secured Credit Facility and the 2016 Incremental Loan Facility, which includes quarterly interest payments and quarterly payments of 0.25% of the principal, and repayment of the remaining principal in May 2021.

- $475.0 million 2023 Senior Notes, which includes bi-annual interest payments and repayment of the principal in May 2023.
- $400.0 million Exchangeable Senior Notes, which includes bi-annual interest payments and repayment of the principal in March 2022.
- $300.0 million 2024 Senior Notes, which includes bi-annual interest payments and repayment of the principal in November 2024.

(2) These amounts reflect the following purchase commitments with our third-party manufacturers:

- Minimum annual order quantities required to be placed with Boehringer Ingelheim for final packaged ACTIMMUNE through July 2020 and additional units we also committed to purchase which were intended to cover anticipated demand if the results of the STEADFAST study of ACTIMMUNE for the treatment of FA had been successful. Following the FA announcement, we recorded a loss of $14.3 million in our consolidated statement of comprehensive loss for excess inventories.
- A commitment to spend $14.9 million with Boehringer Ingelheim related to the harmonization of the manufacturing process for ACTIMMUNE drug substance.
- Minimum purchase commitment for RAYOS/LODOTRA tablets from Jagotec AG through December 2023 (the end of the minimum term), which is the firm commitment term under the contract.
- Purchase commitment for final packaged DUEXIS tablets from Sanofi-Aventis U.S. through March 2017.
- Minimum purchase commitment for VIMOVO tablets from Patheon Pharmaceuticals Inc. through March 2017.
- Purchase commitment for final packaged PENNSAID 2% from Nuvo through March 2017.
- Purchase commitment for RAVICTI and BUPHENYL through 2017.
- Minimum purchase commitment for KRYSTEXXA through 2030.
- Purchase commitment for PROCYSBI and QUINSAIR through 2017.

(3) These amounts reflect payments due under our operating leases, which are principally for our facilities. For further details regarding these properties, see Item 2 of Part I, Properties, of this Annual Report on Form 10-K.

As of December 31, 2016, our contingent liability for uncertain tax positions amounted to $17.7 million (excluding interest and penalties). Due to the nature and timing of the ultimate outcome of these uncertain tax positions, we cannot make a reasonably reliable estimate of the amount and period of related future payments, if any. Therefore, our contingent liability has been excluded from the above contractual obligations table. We do not expect a significant tax payment related to these obligations within the next year.

In addition to the obligations set out in the above table, we have assumed material obligations to make royalty and milestone payments to certain third parties on net sales of certain of our medicines as outlined below.

Under the license agreement with Aralez Pharmaceuticals Inc., or Aralez, we are required to pay Aralez a flat 10% royalty on net sales of VIMOVO and such other medicines sold by us, our affiliates or sublicensees during the royalty term, subject to minimum annual royalty obligations of $5.0 million in 2014 and $7.5 million each year thereafter, which minimum royalty obligations will continue for each year during which one of Aralez's patents covers such medicines in the United States and there are no competing medicines in the United States. The royalty rate may be reduced to a mid-single digit royalty rate as a result of loss of market share to competing medicines. Our obligation to pay royalties to Aralez will expire upon the later of (a) expiration of the last-to-expire of certain patents covering such medicines in the United States, and (b) ten years after the first commercial sale of such medicines in the United States. In addition, we are obligated to reimburse Aralez for costs, including attorneys' fees, incurred by Aralez in connection with VIMOVO patent litigation moving forward, subject to agreed caps.

Under a letter agreement among AstraZeneca, Aralez and us, we and AstraZeneca agreed to pay Aralez milestone payments upon the achievement by us and AstraZeneca, collectively, of certain annual aggregate global net sales thresholds ranging from $550.0 million to $1.25 billion with respect to VIMOVO. The aggregate milestone payment amount that may be owed by AstraZeneca and us, collectively, under the letter agreement is $260.0 million, with the amount payable by each of us and AstraZeneca with respect to each milestone to be based upon the proportional sales achieved by each of us and AstraZeneca, respectively, in the applicable year.

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Under the terms of a license agreement, as amended, with Genentech Inc., or Genentech, who was the original developer of ACTIMMUNE, we are or were obligated to pay royalties to Genentech on our net sales of ACTIMMUNE as follows:

- For the period from November 26, 2014 through May 5, 2018, the royalty payments are in the 20% to 30% range for the first $3.7 million in net sales achieved in any calendar year, and in the 1% to 9% range for all additional net sales in any year; and
- From May 6, 2018 and for so long as we continue to commercially sell ACTIMMUNE, we will be obligated to pay an annual royalty in the low single digits as a percentage of annual net sales.

Under the terms of an assignment and option agreement with Connetics Corporation (which was the predecessor parent company to InterMune Pharmaceuticals Inc. and is now part of GlaxoSmithKline), or Connetics, we are obligated to pay royalties to Connetics on our net sales of ACTIMMUNE as follows:

- Low-single digits as a percentage of net sales of ACTIMMUNE in the United States.

Under the terms of an asset purchase agreement with Ucyclyd Pharma, Inc., or Ucyclyd, we are obligated to pay to Ucyclyd tiered mid to high single-digit royalties on our global net sales of RAVICTI.

Under the terms of an amended and restated collaboration agreement with Ucyclyd, we are obligated to pay to Ucyclyd tiered mid to high single-digit royalties on our net sales in the United States of BUPHENYL to UCD patients outside of the FDA approved labeled age range for RAVICTI.

Under the terms of a license agreement with Saul W. Brusilow, M.D. and Brusilow Enterprises, Inc., or Brusilow, we are obligated to pay low single-digit royalties to Brusilow on net sales of RAVICTI that are covered by a valid claim of a licensed patent.

Under the terms of a license agreement with Duke University, or Duke, and Mountain View Pharmaceuticals, or MVP, we are obligated to pay Duke a mid-single digit royalty on our global net sales of KRYSTEXXA and a low-double digit royalty on any global sublicense revenue. We are also obligated to pay MVP a mid-single digit royalty on our net sales of KRYSTEXXA outside of the United States and a low-double digit to royalty on any sublicense revenue outside of the United States.

Under the terms of a license agreement with The Regents of the University of California, San Diego, or UCSD, we are obligated to pay to UCSD tiered low to mid single-digit royalties on our net sales of PROCYSBI.

On November 8, 2016, we entered into a collaboration and option agreement with a privately held life-science entity. Under the terms of the agreement, the privately held life-science entity will conduct certain research and pre-clinical and clinical development activities. Upon execution of the agreement, we paid $0.1 million for the option to acquire certain of the privately held life-science entity's assets for $25.0 million, which is exercisable on specified key dates. Under the collaboration and option agreement, we will be required to pay up to $9.8 million upon the attainment of various milestones, primarily to fund clinical development costs for the medicine.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, including the use of structured finance, special purpose entities or variable interest entities, other than the indemnification agreements discussed in Note 15 in the notes to our consolidated financial statements included in this report.

Critical Accounting Policies and Significant Judgments and Estimates

The methods, estimates and judgments that we use in applying our critical accounting policies have a significant impact on the results that we report in our financial statements. Some of our accounting policies require us to make

difficult and subjective judgments, often as a result of the need to make estimates regarding matters that are inherently uncertain.

We have identified the accounting policies and estimates listed below as those that we believe require management's most subjective and complex judgments in estimating the effect of inherent uncertainties. This section should also be read in conjunction with Note 2 in the notes to our consolidated financial statements included in this report, which includes a discussion of these and other significant accounting policies.

Revenue Recognition

Revenue is recognized when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the price is fixed or determinable; and collectability is reasonably assured. Some of our agreements contain multiple elements and in accordance with these agreements, we may be eligible for upfront license fees, marketing or commercial milestones and payment for medicine deliveries.

Revenue From Medicine Deliveries

Revenue from medicine deliveries comprises a significant amount of our gross sales. We recognize revenue from the sale of our medicines when delivery has occurred, title has transferred, the selling price is fixed or determinable, the right of return no longer exists (which is the earlier of medicine being dispensed through patient prescriptions or the expiration of the right of return) or medicine returns can be reasonably estimated, collectability is reasonably assured and we have no further performance obligations. Due to our ability to reasonably estimate and determine allowances for co-pay and other patient assistance, medicine returns, rebates and discounts based on our own internal data for DUEXIS and RAYOS or data relating to prior sales of our acquired medicines which was received in connection with the acquisition of those medicines, we recognize revenue at the point of sale to wholesale pharmaceutical distributors and retail chains for all currently distributed medicines.

Revenue From Upfront License Fees

We recognize revenues from the receipt of non-refundable, upfront license fees. In situations where the licensee is able to obtain stand-alone value from the license and no further performance obligations exist on our part, revenues are recognized on the earlier of when payments are received or collection is assured. Where continuing involvement by us is required in the form of technology transfer, medicine manufacturing or technical support, revenues are deferred and recognized over the term of the agreement.

Revenue From Milestone Receipts

Milestone payments are recognized as revenue based on achievement of the associated milestones, as defined in the relevant agreements. Revenue from a milestone achievement is recognized when earned, as evidenced by acknowledgment from our partner, provided that (1) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, (2) the milestone represents the culmination of an earnings process and (3) the milestone payment is non-refundable. If any of these criteria are not met, revenue from the milestone achievement is recognized over the remaining minimum period of our performance obligations under the agreement.

Medicine Sales Discounts and Allowances

We record allowances for medicine returns, rebates and discounts at the time of sale to wholesale pharmaceutical distributors and retail chains. We are also required to make significant judgments and estimates in determining some of these allowances. If actual results differ from our estimates, we will be required to make adjustments to these allowances in the future.

Commercial Rebates

We participate in certain commercial rebate programs. Under these rebate programs, we pay a rebate to the commercial entity or third-party administrator of the program. We accrue estimated rebates based on contract prices, estimated percentages of medicine sold to qualified patients and estimated levels of inventory in the distribution channel and record the rebate as a reduction of revenue. Accrued commercial rebates are included in “accrued trade discounts and rebates” on the consolidated balance sheet.

Distribution Service Fees

We include distribution service fees paid to our wholesalers for distribution and inventory management services as a reduction to revenue. We accrue estimated distribution fees based on contractually determined amounts, typically as a percentage of revenue, and record the fees as a reduction of revenue. Accrued distribution service fees are included in "accrued trade discounts and rebates" on the consolidated balance sheet.

Patient Access Programs

We offer discount card and other programs such as our HorizonCares program to patients under which the patient receives a discount on his or her prescription. In certain circumstances when a patient's prescription is rejected by a managed care vendor, we will pay for the full cost of the prescription. We reimburse pharmacies for this discount through third-party vendors. We reduce gross sales by the amount of actual co-pay and other patient assistance in the period based on the invoices received. We also record an accrual to reduce gross sales for estimated co-pay and other patient assistance on units sold to distributors that have not yet been prescribed/dispensed to a patient. The estimate is based on contract prices, estimated percentages of medicine that will be prescribed to qualified patients, average assistance paid based on reporting from the third-party vendors and estimated levels of inventory in the distribution channel. Accrued co-pay and other patient assistance fees are included in "accrued trade discounts and rebates" on the consolidated balance sheet. Patient assistance programs include both co-pay assistance and fully bought down prescriptions.

Sales Returns

Consistent with industry practice, we maintain a return policy that allows customers to return medicine within a specified period prior to and subsequent to the medicine expiration date. Generally, medicine may be returned for a period beginning six months prior to its expiration date and up to one year after its expiration date. The right of return expires on the earlier of one year after the medicine expiration date or the time that the medicine is dispensed to the patient. The majority of our medicine returns are the result of medicine dating, which falls within the range set by our policy, and are settled through the issuance of a credit to the customer. Our estimate of the provision for returns is based upon our historical experience with actual returns, which is applied to the level of sales for the period that corresponds to the period during which our customer may return medicine. This period is known to us based on the shelf lives of our medicines at the time of shipment. We record sales returns as an allowance against accounts receivable and a reduction of revenue.

Prompt Pay Discounts

As an incentive for prompt payment, we offer a 2% cash discount to customers. We expect that all customers will comply with the contractual terms to earn the discount. We record the discount as an allowance against accounts receivable and a reduction of revenue.

Government Rebates

We participate in certain federal government rebate programs, such as Medicare and Medicaid. We accrue estimated rebates based on estimated percentages of medicine sold to qualified patients, estimated rebate percentages and estimated levels of inventory in the distribution channel that will be sold to qualified patients and record the rebates as a reduction of revenue. Accrued government rebates are included in "accrued trade discounts and rebates" on the consolidated balance sheet.

Government Chargebacks

We provide discounts to federal government qualified entities with whom we have contracted. These federal entities purchase medicines from the wholesale pharmaceutical distributors at a discounted price, and the wholesale pharmaceutical distributors then charge back to us the difference between the current retail price and the contracted price that the federal entities paid for the medicine. We accrue estimated chargebacks based on contract prices and sell-through sales data obtained from third-party information and record the chargeback as a reduction of revenue. Accrued government chargebacks are included in “accrued trade discounts and rebates” on the consolidated balance sheet.

Cost of Goods Sold

We recognize cost of goods sold in connection with our sales of each of our distributed medicines. Cost of goods sold includes all costs directly related to the acquisition of our medicines from our third-party manufacturers, including freight charges and other direct expenses such as insurance and supply chain costs. Cost of goods sold also includes amortization of intellectual property as described in the intangible assets and goodwill accounting policy below, inventory step-up expense, royalty payments to third parties, royalty accretion expense, changes in estimates associated with the contingent royalty liability as described in the accrued contingent royalty accounting policy below and loss on inventory purchase commitments.

Intangible Assets

Definite-lived intangible assets are amortized over their estimated useful lives. We review our intangible assets when events or circumstances may indicate that the carrying value of these assets exceeds their fair value. We measure fair value based on the estimated future discounted cash flows associated with our assets in addition to other assumptions and projections that we deem to be reasonable and supportable. The total estimated useful lives, from the date of acquisition, for all identified intangible assets that are subject to amortization are as follows:

Intangible Asset	Estimated Useful Life
ACTIMMUNE developed technology	13 years
BUPHENYL developed technology	7 years
Customer relationships	10 years
KRYSTEXXA developed technology	12 years
LODOTRA and RAYOS developed technology	12 years
MIGERGOT developed technology	10 years
PENNSAID 2% developed technology	6 years
PROCYSBI developed technology (ex-U.S. rights)	9 years
PROCYSBI developed technology (U.S. rights)	13 years
RAVICTI developed technology	11 years
VIMOVO developed technology	5 years

We determined that no impairment of the above intangible assets existed as of December 31, 2016.

Indefinite-lived intangible assets consist of capitalized IPR&D. IPR&D assets represent capitalized incomplete research projects that we acquired through business combinations. Such assets are initially measured at their acquisition date fair values and are tested for impairment, until completion or abandonment of research and development efforts associated with the projects. An IPR&D asset is considered abandoned when research and development efforts associated with the asset have ceased, and there are no plans to sell or license the asset or derive value from the asset. At that point, the asset is considered to be disposed of and is written off. Upon successful completion of each project, we will make a determination about the then remaining useful life of the intangible asset and begin amortization. We test our indefinite-lived intangibles, including IPR&D assets, for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired.

IPR&D as of December 31, 2015 related to the research and development project to evaluate ACTIMMUNE in the treatment of FA, which we acquired in the Vidara Merger. At the time of the Vidara Merger, IPR&D was considered separable from the business as the project could be sold to a third party, and we assigned a fair value of $66.0 million to the intangible asset using an income approach in our purchase accounting. On December 8, 2016, we announced

that the Phase 3 trial, STEADFAST, evaluating ACTIMMUNE for the treatment of FA did not meet its primary endpoint of a statistically significant change from baseline in the modified FARS-mNeuro at twenty-six weeks versus treatment with placebo. In addition, the secondary endpoints did not meet statistical significance. No new safety findings were identified on initial review of data other than those already noted in the ACTIMMUNE prescribing information for approved indications. We, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and FARA, Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study. The IPR&D has no alternative use or economic value as a result of the cancellation of the project, and we recorded an impairment charge of $66.0 million during the three months ended December 31, 2016 to fully write off the value of the asset on our consolidated balance sheet.

Goodwill

Goodwill represents the excess of the purchase price of acquired businesses over the estimated fair value of the identifiable net assets acquired. Goodwill is not amortized but is tested for impairment at least annually at the reporting unit level or more frequently if events or changes in circumstances indicate that the asset might be impaired. Impairment loss, if any, is recognized based on a comparison of the fair value of the asset to its carrying value, without consideration of any recoverability. We test goodwill for impairment annually during the fourth quarter and whenever indicators of impairment exist by first assessing qualitative factors to determine whether it is more likely than not that the fair value is less than its carrying amount. If we conclude it is more likely than not that the fair value of a reporting unit is less than its carrying amount, a quantitative impairment test is performed. If we conclude that goodwill is impaired, we will record an impairment charge in our consolidated statement of comprehensive (loss) income. Based upon our most recent annual impairment test performed in the fourth quarter of 2016, we concluded goodwill was not impaired.

Business Combinations

We account for business combinations in accordance with the pronouncement guidance in ASC 805, Business Combinations, in which acquired assets and liabilities are measured at their respective estimated fair values as of the acquisition date. We may be required, as in the case of intangible assets or contingent royalties, to determine the fair value associated with these amounts by estimating the fair value using an income approach under the discounted cash flow method, which may include revenue projections and other assumptions made by us to determine the fair value. During the year ended December 31, 2014, we recorded a bargain purchase gain of $22.2 million in connection with the Vidara Merger, representing the excess of the estimated fair value of net assets acquired over the acquisition consideration paid. During the year ended December 31, 2015, we recorded goodwill of $253.8 million in connection with the acquisition of Hyperion, and we recorded an adjustment of $7.2 million to this amount during the year ended December 31, 2016. During the year ended December 31, 2016 we recorded goodwill of $9.9 million and $189.1 million in connection with our acquisitions of Crealta and Raptor, respectively.

Provision for Income Taxes

We account for income taxes based upon an asset and liability approach. Deferred tax assets and liabilities represent the future tax consequences of the differences between the financial statement carrying amounts of assets and liabilities versus the tax basis of assets and liabilities. Under this method, deferred tax assets are recognized for deductible temporary differences, and operating loss and tax credit carryforwards. Deferred tax liabilities are recognized for taxable temporary differences. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The impact of tax rate changes on deferred tax assets and liabilities is recognized in the year that the change is enacted. We also account for the uncertainty in income taxes by utilizing a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of any uncertain tax positions that have been taken or are expected to be taken on an income tax return. Deferred tax assets and deferred tax liabilities are netted by jurisdiction on our consolidated balance sheets.

Share-Based Compensation

We account for employee share-based compensation by measuring and recognizing compensation expense for all share-based payments based on estimated grant date fair values. We use the straight-line method to allocate compensation cost to reporting periods over each awardee’s requisite service period, which is generally the vesting period.

Accrued Contingent Royalties

Our accrued contingent royalties consist of the contingent royalty obligations assumed by us related to our acquisitions of rights to ACTIMMUNE, BUPHENYL, KRYSTEXXA, MIGERGOT, PROCYSBI, RAVICTI and VIMOVO. At the time of each acquisition, we assigned a fair value to the liability for royalties. The royalty liability was based on anticipated revenue streams utilizing the income approach under the discounted cash flow method. The estimated liability for royalties is increased or decreased over time to reflect the change in its present value, and accretion expense is recorded as part of cost of goods sold. We evaluate the adequacy of the estimated contingent royalty liability at least annually in the fourth quarter, or whenever events or changes in circumstances indicate that an evaluation of the estimate is necessary. As part of our evaluation, we adjust the carrying value of the liability to the present value of the revised estimated cash flows using the original discount rate.

Any adjustment to the liability is recorded as an increase or reduction in cost of goods sold. The royalty liability is included in current and long-term accrued royalties on the consolidated balance sheets.

During the year ended December 31, 2016, based on higher sales of KRYSTEXXA and RAVICTI versus our previous expectations and estimates for future sales of these medicines, we recorded a total charge of $24.6 million to cost of goods sold ($15.4 million related to KRYSTEXXA and $9.2 million related to RAVICTI). We also recorded a reduction of $24.2 million to cost of goods sold related to ACTIMMUNE and VIMOVO as a result of updated estimates of future sales of these medicines ($8.7 million related to ACTIMMUNE, including $2.5 million in connection with FA, and $15.5 million related to VIMOVO).

Fair Value of Financial Instruments

The carrying amounts of our financial instruments, including cash and cash equivalents, restricted cash, accounts receivable, accounts payable and accrued expenses, approximate their fair values due to their short maturities.

At December 31, 2013 and at the final measurement on June 27, 2014, the estimated fair value of our derivative liability related to the convertible portion of our Convertible Senior Notes was derived utilizing the binomial lattice approach for the valuation of convertible instruments. Assumptions used in the calculation included, among others, determining the appropriate credit spread using benchmarking analysis and solving for the implied credit spread, calculating the fair value of the stock component using a discounted risk free rate and borrowing cost and calculating the fair value of the note component using a discounted credit adjusted discount rate. Based on the assumptions used to determine the fair value of the derivative liability associated with the Convertible Senior Notes, we concluded that these inputs were Level 3 inputs.

New Accounting Pronouncements Impacting Critical Accounting Policies

Refer to Note 2 in the notes to our consolidated financial statements included in this report, which includes a discussion of the new accounting pronouncements impacting critical accounting policies.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to various market risks, which include potential losses arising from adverse changes in market rates and prices, such as interest rates and foreign exchange fluctuations. We do not enter into derivatives or other financial instruments for trading or speculative purposes.

Interest Rate Risk. We are subject to interest rate fluctuation exposure through our borrowings under the 2015 Term Loan Facility and our investment in money market accounts which bear a variable interest rate. The terms of the 2015 Term Loan Facility provided for an amendment such that the effective yield of the 2015 Term Loan Facility would not be less than the effective yield of the 2016 Incremental Loans minus 0.50%. Consequently, the issuance of the 2016 Incremental Loans resulted in an increase of the interest rate applicable to the 2015 Term Loan Facility, as of October 25, 2016, to LIBOR plus 4.00%, subject to a LIBOR floor of 1.0% (an initial interest rate of 5.00%). Thus, loans under the 2015 Term Loan Facility bear interest, at our option, at a rate equal to either the LIBOR rate, plus an applicable margin of 4.00% per annum (subject to a 1.00% LIBOR floor), or the adjusted base rate plus 3.00%. The adjusted base rate is defined as the greater of (a) LIBOR (using one-month interest period) plus 1%, (b) prime rate, (c) fed funds plus ½ of 1% and (d) 2%. Since drawing the full $400.0 million available in May 2015, our borrowings had been based on LIBOR. Since current LIBOR rates are below the 1.0% LIBOR floor, the interest rate on our borrowings is currently 5.00% per annum for the 2015 Term Loan Facility and 5.5% per annum for the 2016

Incremental Loans. An increase in the LIBOR of 100 basis points above the 1.0% LIBOR floor would increase our interest expense by $7.9 million per year.

The primary goals of our investment policy are the preservation of capital, fulfillment of liquidity needs and fiduciary control of cash. To achieve our secondary goal of maximizing income without assuming significant market risk, we maintain our excess cash and cash equivalents in money market funds and bank deposits. Because of the short-term maturities of our cash equivalents, we do not believe that a decrease in interest rates would have any material negative impact on the fair value of our cash equivalents.

Foreign Currency Risk. Our purchase cost of ACTIMMUNE under our contract with Boehringer Ingelheim as well as sales contracts relating to LODOTRA, QUINSAIR and sales of PROCYSBI outside the United States are principally denominated in Euros and are subject to foreign currency risk. We also incur certain operating expenses in currencies other than the U.S. dollar in relation to our Irish operations and foreign subsidiaries, including Horizon Pharma Switzerland GmbH. Following the acquisition of Raptor, we are subject to increased foreign currency risk for our operations in Europe due to an increased level of sales and operating expenses denominated in Euros. To date, we have not entered into any hedging contracts since exchange rate fluctuations have had minimal impact on our results of operations and cash flows.

Inflation Risk. We do not believe that inflation has had a material impact on our business or results of operations during the periods for which the consolidated financial statements are presented in this report.

Credit Risk. Historically, our accounts receivable balances have been highly concentrated with a select number of customers, consisting primarily of large wholesale pharmaceutical distributors who, in turn, sell the medicines to pharmacies, hospitals and other customers. As of December 31, 2016, 2015 and 2014, our top three customers accounted for approximately 78%, 72% and 68%, respectively, of our total outstanding accounts receivable balances.

Item 8. Financial Statements and Supplementary Data

The financial information required by Item 8 is contained in Part IV, Item 15 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our Chief Executive Officer and Chief Financial Officer, after evaluating the effectiveness of our “disclosure controls and procedures” (as defined in Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act), have concluded that, as of December 31, 2016, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer’s management, including its principal executive officer or officers and principal financial officer or officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Management Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control system was designed to provide reasonable assurance to management and our board of directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control – Integrated Framework (2013). Management's assessment included an evaluation of the design of our internal control over financial reporting and testing of the operational effectiveness of our internal control over financial reporting. Based on management's assessment, management believes that, as of December 31, 2016, our internal control over financial reporting was effective based on those criteria.

Management's assessment of internal control over financial reporting as of December 31, 2016 excluded Raptor's internal controls over financial reporting because we acquired Raptor in a purchase business combination in October 2016. Raptor represented less than 1% of our total assets and 3% of our total net sales at and for the year ended December 31, 2016.

The effectiveness of our internal control over financial reporting as of December 31, 2016 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Changes in Internal Control Over Financial Reporting

As discussed above, on October 25, 2016, we completed our acquisition of Raptor and Raptor became our wholly owned subsidiary. As a result of the Raptor acquisition, the internal control over financial reporting utilized by us prior to the acquisition became the internal control over financial reporting of Raptor, and we are currently in the process of evaluating and integrating Raptor's historical internal controls over financial reporting with ours.

During the three months ended December 31, 2016, other than continuing changes to our internal control processes resulting from the Raptor acquisition as discussed above, there have been no material changes to our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f), that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is incorporated herein by reference from our definitive Proxy Statement to be filed in connection with our 2017 Annual General Meeting of Shareholders, or our 2017 Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after December 31, 2016.

We have adopted a written Code of Business Conduct and Ethics, or Ethics Code, that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Ethics Code is available on our website at www.horizonpharma.com. If we make any substantive amendments to the Ethics Code or grant any waiver from a provision of the Ethics Code to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation

The information required by this item is incorporated herein by reference from our 2017 Proxy Statement.

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

The information required by this item is incorporated herein by reference from our 2017 Proxy Statement.

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

The information required by this item is incorporated herein by reference from our 2017 Proxy Statement.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated herein by reference from our 2017 Proxy Statement.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this report.

1. Financial Statements
The financial statements listed on the Index to Financial Statements F-1 to F-70 are filed as part of this Annual Report on Form 10-K.

2. Financial Statement Schedules
Schedule II – Valuation and Qualifying Accounts and Reserves for each of the three fiscal years ended December 31, 2016, 2015 and 2014. Other financial statement schedules have been omitted because the required information is included in the consolidated financial statements or notes thereto or because they are not applicable or not required.

3. Exhibits
The exhibits listed on the Index to Exhibits are filed as part of this Annual Report on Form 10-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

HORIZON PHARMA PLC

Dated: February 27, 2017 By: /s/ Timothy P. Walbert
Timothy P. Walbert

President, Chief Executive Officer and

Chairman of the Board

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Timothy P. Walbert and Paul W. Hoelscher, and each of them, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

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

SIGNATURE	TITLE	DATE
/s/ TIMOTHY P. WALBERT Timothy P. Walbert	President, Chief Executive Officer and Chairman of the Board (Principal Executive Officer)	February 27, 2017
/s/ PAUL W. HOELSCHER Paul W. Hoelscher	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 27, 2017
/s/ MILES W. MCHUGH Miles W. McHugh	Senior Vice President and Chief Accounting Officer (Principal Accounting Officer)	February 27, 2017
/s/ MICHAEL GREY Michael Grey	Director	February 27, 2017
/s/ LIAM DANIEL Liam Daniel	Director	February 27, 2017

/s/ JEFF HIMAWAN Jeff Himawan, Ph.D.	Director	February 27, 2017
/s/ VIRINDER NOHRIA Virinder Nohria, M.D., Ph.D.	Director	February 27, 2017
/s/ RONALD PAULI Ronald Pauli	Director	February 27, 2017
/s/ GINO SANTINI Gino Santini	Director	February 27, 2017
/s/ H. THOMAS WATKINS H. Thomas Watkins	Director	February 27, 2017

HORIZON PHARMA PLC

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Horizon Pharma plc

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of comprehensive (loss) income, shareholders' equity (deficit), and cash flows present fairly, in all material respects, the financial position of Horizon Pharma plc and its subsidiaries at December 31, 2016 and 2015, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2016 in conformity with accounting principles generally accepted in the United States of America. In addition, in our opinion, the financial statement schedule listed in the index appearing under Item 15(a)(2) presents fairly, in all material respects, the information set forth therein when read in conjunction with the related consolidated financial statements. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements and financial statement schedule, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements, on the financial statement schedule, and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

As described in Management's Report on Internal Control over Financial Reporting, management has excluded Raptor Pharmaceutical Corp. ("Raptor") from its assessment of internal control over financial reporting as of December 31, 2016 because it was acquired by the Company in a purchase business combination during 2016. We have also

excluded Raptor from our audit of internal control over financial reporting. Raptor is a wholly-owned subsidiary whose total assets and total revenues represent less than 1% and 3%, respectively, of the related consolidated financial statement amounts as of and for the year ended December 31, 2016.

/s/ PricewaterhouseCoopers LLP

Chicago, Illinois
February 27, 2017

HORIZON PHARMA PLC

CONSOLIDATED BALANCE SHEETS

(In thousands, except share data)

	As of December 31, 2016	As of December 31, 2015
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$509,055	$859,616
Restricted cash	7,095	1,860
Accounts receivable, net	305,725	210,437
Inventories, net	174,788	18,376
Prepaid expenses and other current assets	49,619	15,858
Total current assets	1,046,282	1,106,147
Property and equipment, net	23,484	14,020
Developed technology, net	2,767,184	1,609,049
In-process research and development	—	66,000
Other intangible assets, net	6,251	7,061
Goodwill	445,579	253,811
Deferred tax assets, net	911	2,278
Other assets	2,368	222
TOTAL ASSETS	$4,292,059	$3,058,588
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Long-term debt—current portion	$7,750	$4,000
Accounts payable	52,479	16,590
Accrued expenses	182,765	100,046
Accrued trade discounts and rebates	297,556	183,769
Accrued royalties—current portion	61,981	51,700
Deferred revenues—current portion	3,321	1,447
Total current liabilities	605,852	357,552
LONG-TERM LIABILITIES:		
Exchangeable notes, net	298,002	282,889
Long-term debt, net, net of current	1,501,741	849,867
Accrued royalties, net of current	272,293	123,519
Deferred revenues, net of current	7,763	8,785
Deferred tax liabilities, net	296,568	113,400
Other long-term liabilities	46,061	9,431
Total long-term liabilities	2,422,428	1,387,891
COMMITMENTS AND CONTINGENCIES		
SHAREHOLDERS' EQUITY:		
Ordinary shares, $0.0001 nominal value; 300,000,000 shares authorized;	16	16
162,004,956 and 160,069,067 shares issued at December 31, 2016 and		

December 31, 2015, respectively, and 161,620,590 and 159,684,701 shares outstanding at December 31, 2016 and December 31, 2015, respectively		
Treasury stock, 384,366 ordinary shares at December 31, 2016 and December 31, 2015	(4,585)	(4,585)
Additional paid-in capital	2,119,455	2,001,552
Accumulated other comprehensive loss	(3,086)	(2,651)
Accumulated deficit	(848,021)	(681,187)
Total shareholders' equity	1,263,779	1,313,145
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$4,292,059	$3,058,588

The accompanying notes are an integral part of these consolidated financial statements.

HORIZON PHARMA PLC

CONSOLIDATED STATEMENTS OF COMPREHENSIVE (LOSS) INCOME

(In thousands, except share and per share data)

	For the Years Ended December 31,		
	2016	2015	2014
Net sales	$981,120	$757,044	$296,955
Cost of goods sold	393,272	219,502	78,753
Gross profit	587,848	537,542	218,202
OPERATING EXPENSES:			
Research and development	60,707	41,865	17,460
Sales and marketing	320,366	220,444	120,276
General and administrative	287,942	219,861	88,957
Impairment of in-process research and development	66,000	—	—
Total operating expenses	735,015	482,170	226,693
Operating (loss) income	(147,167)	55,372	(8,491)
OTHER (EXPENSE) INCOME, NET:			
Interest expense, net	(86,610)	(69,900)	(23,826)
Foreign exchange loss	(1,005)	(1,237)	(3,905)
Loss on induced conversion of debt and debt extinguishment	—	(77,624)	(29,390)
Loss on sale of long-term investments	—	(29,032)	—
Bargain purchase gain	—	—	22,171
Loss on derivative fair value	—	—	(214,995)
Other income (expense), net	6,697	(10,291)	(11,251)
Total other (expense) income, net	(80,918)	(188,084)	(261,196)
Loss before benefit for income taxes	(228,085)	(132,712)	(269,687)
BENEFIT FOR INCOME TAXES	(61,251)	(172,244)	(6,084)
NET (LOSS) INCOME	$(166,834)	$39,532	$(263,603)
NET (LOSS) INCOME PER ORDINARY SHARE—Basic	$(1.04)	$0.27	$(3.15)
WEIGHTED AVERAGE ORDINARY SHARES OUTSTANDING—Basic	160,699,543	148,788,020	83,751,129
NET (LOSS) INCOME PER ORDINARY SHARE—Diluted	(1.04)	0.25	(3.15)
WEIGHTED AVERAGE ORDINARY SHARES OUTSTANDING—Diluted	160,699,543	155,923,251	83,751,129
OTHER COMPREHENSIVE (LOSS) INCOME, NET OF TAX			
Foreign currency translation adjustments	(302)	1,712	(1,960)
Pension remeasurements	(133)	—	—
Other comprehensive (loss) income	(435)	1,712	(1,960)
COMPREHENSIVE (LOSS) INCOME	$(167,269)	$41,244	$(265,563)

The accompanying notes are an integral part of these consolidated financial statements.

HORIZON PHARMA PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY (DEFICIT)

(In thousands, except share data)

	Ordinary Shares		Treasury Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balances at December 31, 2013	66,097,417	$ 7	—	$—	$410,430	$ (2,403)	$ (457,116)	$ (49,082)
Issuance of ordinary shares in connection with Vidara merger	31,350,000	3	—	—	387,796	—	—	387,799
Issuance of ordinary shares in conjunction with inducement of convertible notes (net of the reacquisition of the equity component of $129,776)	16,594,793	2	—	—	78,437	—	—	78,439
Reclassification of derivative liability	—	—	—	—	324,405	—	—	324,405
Issuance of ordinary shares in conjunction with vesting of restricted stock units and stock option exercises	864,780	—	—	—	2,506	—	—	2,506
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(894)	—	—	(894)
Issuance of ordinary shares in conjunction with ESPP purchases	536,543	—	—	—	1,674	—	—	1,674
Share-based compensation	—	—	—	—	13,197	—	—	13,197
	8,990,120	1	—	—	38,460	—	—	38,461

Issuance of ordinary shares in conjunction with warrant exercises								
Proceeds from capped call transactions	—	—	384,366	(4,585)	13,970	—	—	9,385
Treasury stock purchase	—	—	7,800	(123)	—	—	—	(123)
Treasury stock retirement	(7,800)	—	(7,800)	123	(123)	—	—	—
Currency translation adjustment	—	—	—	—	—	(1,960)	—	(1,960)
Net loss	—	—	—	—	—	—	(263,603)	(263,603)
Balances at December 31, 2014	124,425,853	$ 13	384,366	$(4,585)	$1,269,858	$ (4,363)	$(720,719)	$540,204
Issuance of ordinary shares	17,652,500	2	—	—	475,683	—	—	475,685
Issuance of ordinary shares in conjunction with vesting of restricted stock units and stock option exercises	1,157,807	—	—	—	5,217	—	—	5,217
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(3,024)	—	—	(3,024)
Issuance of ordinary shares in conjunction with inducement of convertible notes (net of the reacquisition of the equity component of $243,984)	11,368,921	1	—	—	57,543	—	—	57,544
Issuance of ordinary shares in conjunction with ESPP purchases	591,277	—	—	—	4,452	—	—	4,452
Share-based compensation	—	—	—	—	83,553	—	—	83,553
Issuance of ordinary shares in	4,872,709	—	—	—	18,124	—	—	18,124

conjunction with warrant exercises								
Issuance of Exchangeable Senior Notes	—	—	—	—	119,080	—	—	119,080
Deferred tax on Exchangeable Senior Notes	—	—	—	—	(29,770)	—	—	(29,770)
Deferred tax on capped call transactions	—	—	—	—	836	—	—	836
Currency translation adjustment	—	—	—	—	—	1,712	—	1,712
Net income	—	—	—	—	—	—	39,532	39,532
Balances at December 31, 2015	160,069,067	$ 16	384,366	$(4,585)	$2,001,552	$ (2,651)	$(681,187)	$1,313,145
Issuance of ordinary shares in conjunction with vesting of restricted stock units and stock option exercises	1,245,637	—	—	—	3,875	—	—	3,875
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(5,539)	—	—	(5,539)
Issuance of ordinary shares in conjunction with ESPP purchases	513,659	—	—	—	6,540	—	—	6,540
Issuance of ordinary shares in conjunction with PSU vesting	13,584	—	—	—	—	—	—	—
Share-based compensation	—	—	—	—	113,019	—	—	113,019
Issuance of ordinary shares in conjunction with warrant exercises	163,009	—	—	—	8	—	—	8
Currency translation adjustment	—	—	—	—	—	(302)	—	(302)
Pension remeasurements	—	—	—	—	—	(133)	—	(133)
Net loss	—	—	—	—	—	—	(166,834)	(166,834)

Balances at December 31, 2016	162,004,956	$ 16	384,366	$(4,585)	$2,119,455	$ (3,086)	$(848,021)	$ 1,263,779

The accompanying notes are an integral part of these consolidated financial statements.

HORIZON PHARMA PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	For the Years Ended December 31,		
	2016	2015	2014
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net (loss) income	$(166,834)	$39,532	$(263,603)
Adjustments to reconcile net (loss) income to net cash provided by operating activities:			
Depreciation and amortization expense	221,837	138,343	34,009
Equity-settled share-based compensation	113,019	83,553	13,198
Royalty accretion	40,616	20,088	9,020
Royalty liability remeasurement	386	21,151	10,660
Impairment of in-process research and development	66,000	—	—
Impairment of non-current asset	5,260	—	—
Loss on induced conversions of debt and debt extinguishment	—	21,581	11,709
Amortization of debt discount and deferred financing costs	18,546	18,810	9,273
Loss on sale of long-term investments	—	29,032	—
Loss on derivative revaluation	—	—	214,995
Bargain purchase gain	—	—	(22,171)
Deferred income taxes	(65,561)	(180,549)	(7,516)
Foreign exchange loss and other adjustments	420	1,495	3,916
Changes in operating assets and liabilities:			
Accounts receivable	(67,496)	(124,766)	(46,183)
Inventories	67,633	12,216	7,173
Prepaid expenses and other current assets	(28,239)	1,014	(9,208)
Accounts payable	32,065	(8,362)	9,383
Accrued trade discounts and rebates	112,381	94,046	54,090
Accrued expenses and accrued royalties	13,854	20,169	(1,270)
Deferred revenues	1,114	1,693	(562)
Payment of original issue discount upon repayment of 2014 Term Loan Facility	—	(3,000)	—
Other non-current assets and liabilities	4,455	8,120	636
Net cash provided by operating activities	369,456	194,166	27,549
CASH FLOWS FROM INVESTING ACTIVITIES:			
Payments for acquisitions, net of cash acquired	(1,356,271)	(1,022,361)	(224,220)
Proceeds from liquidation of available-for-sale investments	—	64,623	—
Purchases of long-term investments	—	(71,813)	—
Proceeds from sale of long-term investments	—	42,781	—
Purchases of property and equipment	(15,731)	(7,156)	(3,500)
Change in restricted cash	(3,879)	(1,122)	—
Net cash used in investing activities	(1,375,881)	(995,048)	(227,720)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Net proceeds from the Incremental Loan Facility	364,297	—	—
Net proceeds from issuance of 2024 Senior Notes	291,893	—	—

Net proceeds from issuance of Exchangeable Senior Notes	—	387,181	—
Net proceeds from issuance of 2023 Senior Notes	—	462,340	—
Net proceeds from the 2015 Term Loan Facility	—	391,506	—
Repayment of the 2015 Term Loan Facility	(4,000)	(2,000)	—
Net proceeds from issuance of ordinary shares	—	475,685	—
Proceeds from the settlement of capped call transactions	—	—	9,385
Proceeds from the issuance of ordinary shares in connection with warrant exercises	8	18,124	38,461
Proceeds from the issuance of ordinary shares through ESPP programs	6,540	4,452	1,674
Proceeds from the issuance of ordinary shares in connection with stock option exercises	3,875	5,217	2,693
Payment of employee withholding taxes relating to share-based awards	(5,539)	(3,024)	(894)
Net proceeds from the 2014 Term Loan Facility	—	—	286,966
Repayment of the 2014 Term Loan Facility	—	(297,000)	—
Net cash provided by financing activities	657,074	1,442,481	338,285
Effect of foreign exchange rate changes on cash	(1,210)	(790)	213
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	(350,561)	640,809	138,327
CASH AND CASH EQUIVALENTS, beginning of the year	859,616	218,807	80,480
CASH AND CASH EQUIVALENTS, end of the year	$509,055	$859,616	$218,807

HORIZON PHARMA PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS (CONTINUED)

(In thousands)

	For the Years Ended December 31,		
	2016	2015	2014
Supplemental cash flow information:			
Cash paid for interest	$60,817	$42,021	$14,109
Cash paid for income taxes	22,339	1,880	37
Fees paid for debt commitments	—	9,000	8,222
Cash paid for induced conversions	—	10,005	16,690
Cash paid for debt extinguishment	—	45,367	—
Supplemental non-cash flow information:			
Conversion of Convertible Senior Notes to ordinary shares	—	60,985	89,015
Purchases of property and equipment included in accounts payable and accrued expenses	700	4,940	1,463

The accompanying notes are an integral part of these consolidated financial statements.

HORIZON PHARMA PLC

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

December 31, 2016, 2015 and 2014

NOTE 1 – BASIS OF PRESENTATION

On September 19, 2014, the businesses of Horizon Pharma, Inc. ("HPI") and Vidara Therapeutics International Public Limited Company ("Vidara") were combined in a merger transaction (the "Vidara Merger"), accounted for as a reverse acquisition under the acquisition method of accounting for business combinations, with HPI treated as the acquiring company in the Vidara Merger for accounting purposes. As part of the Vidara Merger, a wholly owned subsidiary of Vidara merged with and into HPI, with HPI surviving the Vidara Merger as a wholly owned subsidiary of Vidara. Prior to the Vidara Merger, Vidara changed its name to Horizon Pharma plc (or the "Company"). Upon the consummation of the Vidara Merger, the historical financial statements of HPI became the Company's historical financial statements. Accordingly, the historical financial statements of HPI are included in the comparative prior periods. The consolidated financial statements presented herein include the accounts of the Company and its wholly owned subsidiaries. All inter-company transactions and balances have been eliminated.

Unless otherwise indicated or the context otherwise requires, references to the "Company", "we", "us" and "our" refer to Horizon Pharma plc and its consolidated subsidiaries, including its predecessor, HPI. All references to "Vidara" are references to Horizon Pharma plc (formerly known as Vidara Therapeutics International Public Limited Company) and its consolidated subsidiaries prior to the effective time of the Vidara Merger on September 19, 2014. The disclosures in this report relating to the pre-Vidara Merger business of Horizon Pharma plc, unless noted as being the business of Vidara prior to the Vidara Merger, pertain to the business of HPI prior to the Vidara Merger.

On October 17, 2014, the Company acquired the U.S. rights to PENNSAID 2% from Nuvo Research Inc. ("Nuvo") for $45.0 million in cash.

On May 7, 2015, the Company completed its acquisition of Hyperion Therapeutics Inc. ("Hyperion") in which the Company acquired all of the issued and outstanding shares of Hyperion's common stock for $46.00 per share in cash or approximately $1.1 billion on a fully-diluted basis. Following the completion of the acquisition, Hyperion became a wholly owned subsidiary of the Company and was renamed as Horizon Therapeutics, Inc. (which subsequently converted to a limited liability company, Horizon Therapeutics, LLC).

On January 13, 2016, the Company completed its acquisition of Crealta Holdings LLC ("Crealta") for approximately $539.7 million, including cash acquired of $24.9 million. Following completion of the acquisition, Crealta became a wholly owned subsidiary of the Company and was renamed as Horizon Pharma Rheumatology LLC.

On October 25, 2016, the Company completed its acquisition of Raptor Pharmaceutical Corp. ("Raptor") in which the Company acquired all of the issued and outstanding shares of Raptor's common stock for $9.00 per share in cash. The total consideration was $860.8 million, including cash acquired of $24.9 million and $56.0 million to repay Raptor's outstanding debt. Following completion of the acquisition, Raptor became a wholly owned subsidiary of the Company and converted to a limited liability company, changing its name to Horizon Pharmaceutical LLC. The Company financed the transaction through $300.0 million aggregate principal amount of 8.75% Senior Notes due 2024 (the "2024 Senior Notes"), $375.0 million aggregate principal amount of loans pursuant to an amendment to the Company's existing credit agreement and cash on hand.

The consolidated financial statements presented herein include the results of operations of the acquired Vidara, Hyperion, Crealta and Raptor businesses from the applicable dates of acquisition. See Note 4 for further details of business acquisitions.

Overview

The Company is a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. The Company markets eleven medicines through its orphan, rheumatology and primary care business units. The Company's marketed medicines are ACTIMMUNE® (interferon gamma-1b), BUPHENYL® (sodium phenylbutyrate) Tablets and Powder, DUEXIS® (ibuprofen/famotidine), KRYSTEXXA® (pegloticase), MIGERGOT® (ergotamine tartrate & caffeine suppositories), PENNSAID® (diclofenac sodium topical solution) 2% w/w ("PENNSAID 2%"), PROCYSBI® (cysteamine bitartrate) delayed-release capsules, QUINSAIR™ (aerosolized form of levofloxacin), RAVICTI® (glycerol phenylbutyrate) Oral Liquid, RAYOS® (prednisone) delayed-release tablets and VIMOVO® (naproxen/esomeprazole magnesium).

On May 18, 2016, the Company entered into a definitive agreement with Boehringer Ingelheim International GmbH ("Boehringer Ingelheim International") to acquire certain rights to interferon gamma-1b, which Boehringer Ingelheim International currently commercializes under the trade names IMUKIN®, IMUKINE®, IMMUKIN® and IMMUKINE® in an estimated thirty countries, primarily in Europe and the Middle East. Under the terms of the agreement, the Company paid Boehringer Ingelheim International €5.0 million ($5.6 million when converted using a Euro-to-Dollar exchange rate at date of payment of 1.1132) upon signing and will pay €20.0 million upon closing, for certain rights for interferon gamma-1b in all territories outside of the United States, Canada and Japan, as the Company currently holds marketing rights to interferon gamma-1b in these territories. The Company currently markets interferon gamma-1b as ACTIMMUNE® in the United States. The transaction is expected to close in 2017 and the Company is continuing to work with Boehringer Ingelheim International to enable the transfer of applicable marketing authorizations.

On December 8, 2016, the Company announced that the Phase 3 trial, Safety, Tolerability and Efficacy of ACTIMMUNE Dose Escalation in Friedreich's Ataxia study ("STEADFAST") evaluating ACTIMMUNE for the treatment of Friedreich's ataxia ("FA") did not meet its primary endpoint of a statistically significant change from baseline in the modified Friedreich's Ataxia Rating Scale ("FARS-mNeuro"), at twenty-six weeks versus treatment with placebo. In addition, the secondary endpoints did not meet statistical significance. No new safety findings were identified on initial review of data other than those already noted in the ACTIMMUNE prescribing information for approved indications. The Company, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and the Friedreich's Ataxia Research Alliance ("FARA") Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study. Following this announcement, the Company recorded in "general and administrative expenses" an impairment charge to fully write off the carrying value of the €5.0 million initial payment ($5.3 million when converted using a Euro-to-Dollar exchange rate at date of impairment of 1.052) for the acquisition of certain rights to interferon gamma-1b, as described above, in the Company's consolidated statement of comprehensive loss for the three months ended December 31, 2016. Upon closing, the Company expects to record the additional €20.0 million payment, as described above, as an expense in its consolidated statement of comprehensive (loss) income.

The Company

The Company is a public limited company formed under the laws of Ireland. The Company operates through a number of international and U.S. subsidiaries with principal business purposes to either perform research and development or manufacturing operations, serve as distributors of the Company's medicines, hold intellectual property assets or provide services and financial support to the Company.

Part of the Company's commercial strategy for RAYOS and its primary care medicines is to offer physicians the opportunity to have their patients fill prescriptions through pharmacies participating in the Company's HorizonCares patient access program. For commercial patients who are prescribed the Company's primary care medicines or

RAYOS, the HorizonCares program offers co-pay assistance when a third-party commercial payer covers a prescription but requires an eligible patient to pay a co-pay or deductible, and offers full subsidization when a third-party commercial payer rejects coverage for an eligible patient. During 2016, the Company entered into business arrangements with pharmacy benefit managers ("PBMs") and other payers to secure formulary status and reimbursement of the Company's medicines, such as the Company's arrangements with Express Scripts, Inc. ("Express Scripts"), CVS Caremark and Prime Therapeutics LLC. While the Company believes that this strategy will result in broader inclusion of certain of the Company's primary care medicines on healthcare plan formularies, and therefore increase payer reimbursement and lower the Company's cost of providing patient access programs, these arrangements generally require the Company to pay administrative and rebate payments to the PBMs and/or other payers.

The Company has a comprehensive compliance program in place to address adherence with various laws and regulations relating to the selling, marketing and manufacturing of the Company's medicines, as well as certain third-party relationships, including pharmacies. Specifically with respect to pharmacies, the compliance program utilizes a variety of methods and tools to monitor and audit pharmacies, including those that participate in the Company's patient access programs, to confirm their activities, adjudication and practices are consistent with the Company's compliance policies and guidance.

The Company markets its medicines in the United States through a combined field sales force, which numbered approximately 480 representatives as of December 31, 2016. The Company's strategy is to continue to build a well-balanced, diversified, high-growth biopharmaceutical company, and is executing this strategy through the successful commercialization of its existing medicines, a strong commitment to patient access and support and business development efforts focused on transformative acquisitions to accelerate its rare disease leadership as well as on-market and development-stage medicines to fill out its pipeline. The Company is building a sustainable biopharmaceutical company by helping ensure that patients have access to their medicines and support services, and by investing in the further development of medicines for patients with rare or underserved diseases. The Company's growing business is diversified across three business units: orphan, rheumatology and primary care, and is driven by a successful commercial model that focuses on differentiated, long-life medicines, innovative patient access programs and a disciplined business development strategy.

NOTE 2 – SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with the accounting principles generally accepted in the United States of America ("GAAP") and in accordance with the instructions for Form 10-K and Article 3 of Regulation S-X.

Principles of Consolidation

The consolidated financial statements include the Company's accounts and those of its wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated. Additionally, certain reclassifications have been made to prior-period financial statements to conform to the 2016 presentation.

Segment Information

The Company operates as one segment. Management does not segment its business for internal reporting.

Use of Estimates

The preparation of the accompanying consolidated financial statements in conformity with GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Foreign Currency Translation and Transactions

The reporting currency of the Company and its subsidiaries is the U.S. dollar.

The U.S. dollar is the functional currency for the Company's U.S. based businesses and the majority of its subsidiaries. Other foreign subsidiaries have the following functional currencies: Euro, Canadian Dollar, Israeli New Shekel and the British Pound. Foreign currency-denominated assets and liabilities of these subsidiaries are translated into U.S. dollars based on exchange rates prevailing at the end of the period, revenues and expenses are translated at average exchange rates prevailing during the corresponding period, and shareholders' equity (deficit) accounts are translated at historical exchange rates as of the date of any equity transaction. The effects of foreign exchange gains and losses arising from the translation of assets and liabilities of those entities where the functional currency is not the U.S. dollar are included as a component of accumulated other comprehensive (loss) income.

Gains and losses resulting from foreign currency transactions are reflected within the Company's results of operations. During the years ended December 31, 2016, 2015 and 2014, the Company recorded a foreign exchange loss of $1.0 million, $1.2 million and $3.9 million, respectively. The Company does not currently utilize and has not in the past utilized any foreign currency hedging strategies to mitigate the effect of its foreign currency exposure.

Revenue Recognition

Revenue is recognized when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the price is fixed or determinable; and collectability is reasonably assured. Some of the Company's agreements contain multiple elements and in accordance with these agreements, the Company may be eligible for upfront license fees, marketing or commercial milestones and payment for medicine deliveries.

Revenue From Medicine Deliveries

Revenue from medicine deliveries comprises a significant amount of the Company's gross sales. The Company recognizes revenue from the sale of its medicines when delivery has occurred, title has transferred, the selling price is fixed or determinable, collectability is reasonably assured and the Company has no further performance obligations. In addition, revenue is only recognized when the right of return no longer exists (which is the earlier of the medicine being dispensed through patient prescriptions or the expiration of the right of return) or when medicine returns can be reasonably estimated. Due to the Company's ability to reasonably estimate and determine allowances for co-pay and other patient assistance, medicine returns, rebates and discounts based on its own internal data for DUEXIS and RAYOS or data relating to prior sales of its acquired medicines which was received in connection with the acquisition of those medicines, the Company recognizes revenue at the point of sale to wholesale pharmaceutical distributors and retail chains for all currently distributed medicines.

Revenue From Upfront License Fees

The Company recognizes revenues from the receipt of non-refundable, upfront license fees. In situations where the licensee is able to obtain stand-alone value from the license and no further performance obligations exist on the Company's part, revenues are recognized on the earlier of when payments are received or collection is reasonably assured. Where continuing involvement by the Company is required in the form of technology transfer, medicine manufacturing or technical support, revenues are deferred and recognized over the term of the agreement.

Revenue From Milestone Receipts

Milestone payments are recognized as revenue based on achievement of the associated milestones, as defined in the relevant agreements. Revenue from a milestone achievement is recognized when earned, as evidenced by acknowledgment from the Company's partner, provided that (1) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, (2) the milestone represents the culmination of an earnings process and (3) the milestone payment is non-refundable. If any of these criteria are not met, revenue from the milestone achievement is recognized over the remaining minimum period of the Company's performance obligations under the agreement.

As of December 31, 2016 and 2015, deferred revenues related to milestone and upfront payments received were $11.1 million and $10.2 million, respectively.

Medicine Sales Discounts and Allowances

The Company records allowances for medicine returns, rebates and discounts at the time of sale to wholesale pharmaceutical distributors and retail chains. The Company is required to make significant judgments and estimates in

determining some of these allowances. If actual results differ from its estimates, the Company will be required to make adjustments to these allowances in the future.

Commercial Rebates

The Company participates in certain commercial rebate programs. Under these rebate programs, the Company pays a rebate to the commercial entity or third-party administrator of the program. The Company accrues estimated rebates based on contract prices, estimated percentages of medicine sold to qualified patients and estimated levels of inventory in the distribution channel and records the rebate as a reduction of revenue. Accrued commercial rebates are included in “accrued trade discounts and rebates” on the consolidated balance sheet.

Distribution Service Fees

The Company includes distribution service fees paid to its wholesalers for distribution and inventory management services as a reduction to revenue. The Company accrues estimated distribution fees based on contractually determined amounts, typically as a percentage of revenue, and records the fees as a reduction of revenue. Accrued distribution service fees are included in “accrued trade discounts and rebates” on the consolidated balance sheet.

Patient Access Programs

The Company offers discount card and other programs such as its HorizonCares program to patients under which the patient receives a discount on his or her prescription. In certain circumstances when a patient’s prescription is rejected by a managed care vendor, the Company will pay for the full cost of the prescription. The Company reimburses pharmacies for this discount through third-party vendors. The Company reduces gross sales by the amount of actual co-pay and other patient assistance in the period based on the invoices received. The Company also records an accrual to reduce gross sales for estimated co-pay and other patient assistance on units sold to distributors that have not yet been prescribed/dispensed to a patient. The estimate is based on contract prices, estimated percentages of medicine that will be prescribed to qualified patients, average assistance paid based on reporting from the third-party vendors and estimated levels of inventory in the distribution channel. Accrued co-pay and other patient assistance fees are included in “accrued trade discounts and rebates” on the consolidated balance sheet. Patient assistance programs include both co-pay assistance and fully bought down prescriptions.

Sales Returns

Consistent with industry practice, the Company maintains a return policy that allows customers to return medicine within a specified period prior to and subsequent to the medicine expiration date. Generally, medicine may be returned for a period beginning six months prior to its expiration date and up to one year after its expiration date. The right of return expires on the earlier of one year after the medicine expiration date or the time that the medicine is dispensed to the patient. The majority of medicine returns result from medicine dating, which falls within the range set by the Company’s policy, and are settled through the issuance of a credit to the customer. The estimate of the provision for returns is based upon the Company’s historical experience with actual returns, which is applied to the level of sales for the period that corresponds to the period during which the customer may return medicines. This period is known to the Company based on the shelf life of medicines at the time of shipment. The Company records sales returns as an allowance against accounts receivable and a reduction of revenue.

Prompt Pay Discounts

As an incentive for prompt payment, the Company offers a 2% cash discount to customers. The Company expects that all customers will comply with the contractual terms to earn the discount. The Company records the discount as an allowance against accounts receivable and a reduction of revenue.

Government Rebates

The Company participates in certain federal government rebate programs, such as Medicare and Medicaid. The Company accrues estimated rebates based on percentages of medicine sold to qualified patients, estimated rebate percentages and estimated levels of inventory in the distribution channel that will be sold to qualified patients and records the rebates as a reduction of revenue. Accrued government rebates are included in “accrued trade discounts and rebates” on the consolidated balance sheet.

Government Chargebacks

The Company provides discounts to federal government qualified entities with whom the Company has contracted. These federal entities purchase medicines from the wholesale pharmaceutical distributors at a discounted price, and the wholesale pharmaceutical distributors then charge back to the Company the difference between the current retail price and the contracted price that the federal entities paid for the medicines. The Company accrues estimated chargebacks based on contract prices and sell-through sales data obtained from third-party information and records the chargeback as a reduction of revenue. Accrued government chargebacks are included in “accrued trade discounts and rebates” on the consolidated balance sheet.

Bad Debt Expense

The Company's medicines are sold to wholesale pharmaceutical distributors and retail chains. The Company monitors its accounts receivable balances to determine the impact, if any, of such factors as changes in customer concentration, credit risk and the realizability of its accounts receivable, and records a bad debt reserve when applicable. The Company has established an immaterial reserve for bad debt expense and recorded an immaterial amount of bad debt expense for the years ended December 31, 2016 and 2015.

Inventories

Inventories are stated at the lower of cost or market value, using the first-in, first-out convention. Inventories consist of raw materials, work-in-process and finished goods. The Company has entered into manufacturing and supply agreements for the manufacture or purchase of raw materials and production supplies. The Company's inventories include the direct purchase cost of materials and supplies and manufacturing overhead costs. The Company reviews its inventory balance and purchase obligations to assess if it has obsolete or excess inventory, and records a charge to "cost of goods sold" when applicable.

Inventories acquired in business combinations are recorded at their estimated fair values. "Step-up" represents the write-up of inventory from the lower of cost or market value (the historical book value as previously recorded on the acquired company's balance sheet) to fair market value at the acquisition date. Inventory step-up expense is recorded in the consolidated statement of comprehensive (loss) income based on actual sales, or usage, using the first-in, first-out convention.

Inventories exclude medicine sample inventory, which is included in other current assets and is expensed as a component of sales and marketing expense when shipped to sales representatives. As of December 31, 2016 and 2015, the Company had medicine sample inventory of $10.2 million and $4.7 million, respectively.

Cost of Goods Sold

The Company recognizes cost of goods sold in connection with its sales of each of its distributed medicines. Cost of goods sold includes all costs directly related to the acquisition of the Company's medicines from its third-party manufacturers, including freight charges and other direct expenses such as insurance and supply chain costs. Cost of goods sold also includes amortization of intellectual property as described in the intangible assets and goodwill accounting policy below, inventory step-up expense, royalty payments to third parties, royalty accretion expense, changes in estimates associated with the contingent royalty liability as described in the accrued contingent royalty accounting policy below and loss on inventory purchase commitments.

Preclinical Studies and Clinical Trial Accruals

The Company's preclinical studies and clinical trials have historically been conducted by third-party contract research organizations and other vendors. Preclinical study and clinical trial expenses are based on the services received from these contract research organizations and vendors. Payments depend on factors such as the milestones accomplished, successful enrollment of certain numbers of patients and site initiation. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts the accrual accordingly. To date, the Company has had no significant adjustments to accrued clinical expenses. As of December 31, 2016 and December 31, 2015, the Company had preclinical study and clinical trial accruals of $11.0 million and $4.7 million, respectively.

Net (Loss) Income Per Share

Basic net (loss) income per share is computed by dividing net (loss) income by the weighted-average number of ordinary shares outstanding during the period. Diluted earnings per share ("EPS") reflects the potential dilution beyond shares for basic EPS that could occur if securities or other contracts to issue ordinary shares were exercised, converted into ordinary shares, or resulted in the issuance of ordinary shares that would have shared in the Company's earnings.

Cash and Cash Equivalents

We consider all highly liquid investments, readily convertible to cash, that mature within three months or less from date of purchase to be cash equivalents. Cash and cash equivalents primarily consist of cash balances and money market funds. Cash and cash equivalents were $509.1 million and $859.6 million as of December 31, 2016 and 2015, respectively. The Company generally invests excess cash in money market funds and other financial instruments with short-term durations, based upon operating requirements.

Restricted Cash

Restricted cash consists primarily of balances in interest-bearing money market accounts required by a vendor for the Company's sponsored employee business credit card program and collateral for a letter of credit. As of December 31, 2016 and 2015, the Company had restricted cash of $7.1 million and $1.9 million, respectively.

Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, including cash and cash equivalents, restricted cash, accounts receivable, accounts payable and accrued expenses, approximate their fair values due to their short maturities.

At December 31, 2013 and at the final measurement date of June 27, 2014, the estimated fair value of the Company's derivative liability related to the convertible portion of the 5.00% Convertible Senior Notes due 2018 (the "Convertible Senior Notes") was derived utilizing the binomial lattice approach for the valuation of convertible instruments. Assumptions used in the calculation included, among others, determining the appropriate credit spread using benchmarking analysis and solving for the implied credit spread, calculating the fair value of the stock component using a discounted risk free rate and borrowing cost and calculating the fair value of the note component using a discounted credit adjusted discount rate. Based on the assumptions used to determine the fair value of the derivative liability associated with the Convertible Senior Notes, the Company concluded that these inputs were Level 3 inputs.

Business Combinations

The Company accounts for business combinations in accordance with the guidance in ASC 805, Business Combinations, in which acquired assets and liabilities are measured at their respective estimated fair values as of the acquisition date. The Company may be required, as in the case of intangible assets, contingent royalties or derivatives, to determine the fair value associated with these amounts by estimating the fair value using an income approach under the discounted cash flow method, which may include revenue projections and other assumptions made by the Company to determine the fair value. As further described in the "Recent Accounting Pronouncements" section below, the Company plans to adopt Accounting Standards Update ("ASU") No. 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business in the first quarter of 2017. The adoption is not expected to have a material impact on the consolidated financial statements.

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation. Depreciation is recognized using the straight-line method over the estimated useful lives of the related assets for financial reporting purposes and an accelerated method for income tax reporting purposes. Upon retirement or sale of an asset, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in operations. Repair and maintenance costs are charged to expenses as incurred and improvements are capitalized.

Leasehold improvements are amortized on a straight-line basis over the term of the applicable lease, or the useful life of the assets, whichever is shorter.

Depreciation and amortization periods for the Company's property and equipment are as follows:

Machinery and equipment	5 to 7 years
Furniture and fixtures	3 to 5 years
Computer equipment	3 years
Software	3 years
Trade show equipment	3 years

The Company capitalizes software development costs associated with internal use software, including external direct costs of materials and services and payroll costs for employees devoting time to a software project. Costs incurred during the preliminary project stage, as well as costs for maintenance and training, are expensed as incurred.

Software includes internal-use software acquired and modified to meet the Company's internal requirements. Amortization commences when the software is ready for its intended use.

Intangible Assets

Definite-lived intangible assets are amortized over their estimated useful lives. The Company reviews its intangible assets when events or circumstances may indicate that the carrying value of these assets exceeds their fair value. The Company measures fair value based on the estimated future discounted cash flows associated with these assets in addition to other assumptions and projections that the Company deems to be reasonable and supportable. The total estimated useful lives, from the date of acquisition, for all identified intangible assets that are subject to amortization are as follows:

Intangible Asset	Estimated Useful Life
ACTIMMUNE developed technology	13 years
BUPHENYL developed technology	7 years
Customer relationships	10 years
KRYSTEXXA developed technology	12 years
LODOTRA and RAYOS developed technology	12 years
MIGERGOT developed technology	10 years
PENNSAID 2% developed technology	6 years
PROCYSBI developed technology (ex-U.S. rights)	9 years
PROCYSBI developed technology (U.S. rights)	13 years
RAVICTI developed technology	11 years
VIMOVO developed technology	5 years

The Company determined that no impairment of the above definite-lived intangible assets existed as of December 31, 2016.

Indefinite-lived intangible assets consist of capitalized in-process research and development ("IPR&D"). IPR&D assets represent capitalized incomplete research projects that the Company acquired through business combinations. Such assets are initially measured at their acquisition date fair values and are tested for impairment, until completion or abandonment of research and development efforts associated with the projects. An IPR&D asset is considered abandoned when research and development efforts associated with the asset have ceased, and there are no plans to sell or license the asset or derive value from the asset. At that point, the asset is considered to be disposed of and is written off. Upon successful completion of each project, the Company will make a determination about the then remaining useful life of the intangible asset and begin amortization. The Company tests its indefinite-lived intangible assets, including IPR&D assets, for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired.

IPR&D as of December 31, 2015 related to the research and development project to evaluate ACTIMMUNE in the treatment of FA, which the Company acquired in the Vidara Merger. At the time of the Vidara Merger, IPR&D was considered separable from the business as the project could be sold to a third party, and the Company assigned a fair

value of $66.0 million to the intangible asset using an income approach in its purchase accounting. On December 8, 2016, the Company announced that the Phase 3 trial, STEADFAST, evaluating ACTIMMUNE for the treatment of FA did not meet its primary endpoint of a statistically significant change from baseline in the modified FARS-mNeuro at twenty-six weeks versus treatment with placebo. In addition, the secondary endpoints did not meet statistical significance. No new safety findings were identified on initial review of data other than those already noted in the ACTIMMUNE prescribing information for approved indications. The Company, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and FARA, Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study. The IPR&D has no alternative use or economic value as a result of the cancellation of the project, and the Company recorded an impairment charge of $66.0 million during the three months ended December 31, 2016 to fully write off the value of the asset on its consolidated balance sheet.

Goodwill

Goodwill represents the excess of the purchase price of acquired businesses over the estimated fair value of the identifiable net assets acquired. Goodwill is not amortized but is tested for impairment at least annually at the reporting unit level or more frequently if events or changes in circumstances indicate that the asset might be impaired. Impairment loss, if any, is recognized based on a comparison of the fair value of the asset to its carrying value, without consideration of any recoverability. The Company tests goodwill for impairment annually during the fourth quarter and whenever indicators of impairment exist by first assessing qualitative factors to determine whether it is more likely than not that the fair value is less than its carrying amount. If the Company concludes it is more likely than not that the fair value of a reporting unit is less than its carrying amount, a quantitative impairment test is performed. If the Company concludes that goodwill is impaired, it will record an impairment charge in its consolidated statement of comprehensive (loss) income. Based upon the Company's most recent annual impairment test performed in the fourth quarter of 2016, the Company concluded goodwill was not impaired.

Research and Development Expenses

Research and development expenses include, but are not limited to, payroll and other personnel expenses, consultant expenses, expenses incurred under agreements with contract research organizations to conduct clinical trials and expenses incurred to manufacture clinical trial materials.

Sales and Marketing Expenses

Sales and marketing expenses consist principally of payroll of sales representatives and marketing and support staff, travel and other personnel-related expenses, marketing materials and distributed sample inventories. In addition, sales and marketing expenses include the Company's medical affairs expenses, which consist of expenses related to scientific publications, health outcomes, biostatistics, medical education and information, and medical communications.

Deferred Financing Costs

Costs incurred in connection with debt financings have been capitalized to "Long-term debt, net, net of current" and "Exchangeable notes, net" in the Company's consolidated balance sheets as deferred financing costs, and are charged to interest expense using the effective interest method over the terms of the related debt agreements. These costs include document preparation costs, commissions, fees and expenses of investment bankers and underwriters, and accounting and legal fees.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that may potentially subject the Company to significant concentrations of credit risk consist of cash and cash equivalents. The Company's cash and cash equivalents are invested in deposits with various banks in the United States, Ireland, Bermuda, Switzerland, Luxembourg and Germany that management believes are creditworthy. At times, deposits in these banks may exceed the amount of insurance provided on such deposits. To date, the Company has not experienced any losses on its deposits of cash and cash equivalents.

The purchase cost of ACTIMMUNE under a contract with Boehringer Ingelheim RCV GmbH & Co. KG ("Boehringer Ingelheim") as well as sales contracts relating to LODOTRA and QUINSAIR, and sales of PROCYSBI outside the United States are principally denominated in Euros and are subject to foreign currency risk. The Company also incurs certain operating expenses in currencies other than the U.S. dollar in relation to its Ireland operations and other foreign subsidiaries, including Horizon Pharma Switzerland GmbH. Following the acquisition of Raptor, the Company is subject to increased foreign currency risk for its operations in Europe due to an increased level of sales and operating expenses denominated in Euros. The Company does not currently utilize and has not in the past utilized

any foreign currency hedging strategies to mitigate the effect of its foreign currency.

Historically, the Company's accounts receivable balances have been highly concentrated with a select number of customers, consisting primarily of large wholesale pharmaceutical distributors who, in turn, sell the medicines to pharmacies, hospitals and other customers. As of December 31, 2016, 2015 and 2014, the Company's top three customers accounted for approximately 78%, 72% and 68%, respectively, of the Company's total outstanding accounts receivable balances.

The Company depends on single-source suppliers and manufacturers for certain of its medicines, medicine candidates and their active pharmaceutical ingredients.

Comprehensive (Loss) Income

Comprehensive (loss) income is composed of net (loss) income and other comprehensive (loss) income ("OCI"). OCI includes certain changes in shareholders' equity that are excluded from net (loss) income, which consist of foreign currency translation adjustments and pension remeasurements. The Company reports the effect of significant reclassifications out of accumulated OCI on the respective line items in net income if the amount being reclassified is required under GAAP to be reclassified in its entirety to net income. For other amounts that are not required under GAAP to be reclassified in their entirety to net income in the same reporting period, the Company cross-references other disclosures required under GAAP that provide additional detail about those amounts. As of December 31, 2016, 2015 and 2014 accumulated other comprehensive loss was $3.1 million, $2.7 million and $4.4 million, respectively.

Share-Based Compensation

The Company accounts for employee share-based compensation by measuring and recognizing compensation expense for all share-based payments based on estimated grant date fair values. The Company uses the straight-line method to allocate compensation cost to reporting periods over each awardee's requisite service period, which is generally the vesting period.

Accrued Contingent Royalties

The Company's accrued contingent royalties consist of the contingent royalty obligations assumed by the Company related to the Company's acquisitions of rights to ACTIMMUNE, BUPHENYL, KRYSTEXXA, MIGERGOT, PROCYSBI, RAVICTI and VIMOVO. At the time of each acquisition, the Company assigned an estimated fair value to its contingent liability for royalties. The estimated royalty liability is based on anticipated revenue streams utilizing the income approach under the discounted cash flow method. The estimated liability for royalties is increased or decreased over time to reflect the change in its present value and accretion expense is recorded as part of cost of goods sold. The Company evaluates the adequacy of the estimated contingent royalty liability at least annually in the fourth quarter, or whenever events or changes in circumstances indicate that an evaluation of the estimate is necessary. As part of its evaluation, the Company adjusts the carrying value of the liability to the present value of the revised estimated cash flows using the original discount rate. Any adjustment to the liability is recorded as an increase or reduction in cost of goods sold. The royalty liability is included in current and long-term accrued royalties on the consolidated balance sheets.

Contingencies

From time to time, the Company may become involved in claims and other legal matters arising in the ordinary course of business. The Company records accruals for loss contingencies to the extent that it concludes that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. Legal fees and other expenses related to litigation are expensed as incurred and included in selling, general and administrative expenses.

Recent Accounting Pronouncements

From time to time, the Company adopts, as of the specified effective date, new accounting pronouncements issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on the Company's financial position or results of operations upon adoption.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers ("ASC 606"). The new standard aims to achieve a consistent application of revenue recognition within the United States, resulting in a single revenue model to be applied by reporting companies under GAAP. Under the new model, recognition of revenue occurs when a customer obtains control of promised goods or services in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In addition, the new standard requires that reporting companies disclose the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers. The new standard is required to be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying it recognized at the date of initial application. In March 2016, April 2016 and December 2016, the FASB issued ASU No. 2016-08, Revenue From Contracts with Customers (Topic 606): Principal Versus Agent Considerations, ASU No. 2016-10, Revenue From Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, and ASU No. 2016-20, Technical Corrections and Improvements to Topic 606, Revenue From Contracts with Customers, respectively, which further clarify the implementation guidance on principal versus agent considerations contained in ASU No. 2014-09. In May 2016, the FASB issued ASU 2016-12, narrow-scope improvements and practical expedients which provides clarification on assessing the collectability criterion, presentation of sales taxes, measurement date for non-cash consideration and completed contracts at transition. These standards will be effective for the Company beginning in the first quarter of 2018. Early adoption is permitted. The Company expects to elect the modified retrospective method and expects to identify similar performance obligations under ASC 606 as compared with deliverables and separate units of account previously identified. As a result, the Company expects the timing of the majority of its revenue to remain the same. Certain of the Company's contracts for sales outside the United States include contingent amounts of variable consideration that the Company was precluded from recognizing because of the requirement for amounts to be "fixed or determinable". However, the Company anticipates that ASC 606 will require it to estimate these amounts and as a result, the Company expects to recognize the majority of its revenue under such contracts earlier under ASC 606 than it would have recognized under current guidance. Otherwise, the adoption is not expected to have a material impact on the consolidated financial statements and related disclosures.

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements — Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. ASU No. 2014-15 is intended to define management's responsibility to evaluate whether there is substantial doubt about an organization's ability to continue as a going concern and to provide related footnote disclosures. Substantial doubt about an entity's ability to continue as a going concern exists when relevant conditions and events, considered in the aggregate, indicate that it is probable that the entity will be unable to meet its obligations as they become due within one year after the date that the financial statements are issued (or available to be issued). ASU No. 2014-15 provides guidance to an organization's management, with principles and definitions that are intended to reduce diversity in the timing and content of disclosures that are commonly provided by organizations in the financial statement footnotes. ASU No. 2014-15 is effective for annual reporting periods ending after December 15, 2016 and to annual and interim periods thereafter. Early adoption is permitted. The Company adopted ASU No. 2014-15 on April 1, 2016, and the adoption did not have a material impact on the consolidated financial statements and related disclosures.

In April 2015, the FASB issued ASU No. 2015-03, Interest-Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs. The amendments in this ASU require that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. In August 2015, the FASB issued ASU No. 2015-15, Interest-Imputation of Interest (Subtopic 835-30): Presentation and Subsequent Measurement of Debt Issuance Costs Associated with Line-of-Credit Arrangements which further clarifies the implementation guidance of ASU No. 2015-03. The amendments in these ASUs are effective for the financial statements issued for fiscal years beginning after December 15, 2015, and interim periods within those fiscal years. The Company adopted ASU No. 2015-03 on January 1, 2016. The following table summarizes the adjustments made to conform prior-period classifications as a result of the new guidance (in thousands):

	As of December 31, 2015		
	As filed	Reclassification	As adjusted
Other non-current assets	$8,581	$ (8,359)	$222
Exchangeable notes, net	(283,675)	786	(282,889)
Long-term debt, net, net of current	(857,440)	7,573	(849,867)

In April 2015, the FASB issued ASU No. 2015-05: Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Fees Paid in a Cloud Computing Arrangement which provides guidance on a customer's accounting for fees paid in a cloud computing arrangement. Under the new standard, customers apply the same criteria as vendors to determine whether a cloud computing arrangement contains a software license or is solely a service contract. The amendments in this ASU, which may be applied prospectively or retrospectively, are effective for annual and interim periods beginning after December 15, 2015. The Company adopted ASU No. 2015-05 on January 1, 2016. The adoption did not have a material impact on the consolidated financial statements and related disclosures.

In July 2015, the FASB issued ASU No. 2015-11, Inventory (Topic 330): Simplifying the Measurement of Inventory. Under this new guidance, entities that measure inventory using any method other than last-in, first-out or the retail inventory method will be required to measure inventory at the lower of cost and net realizable value. The amendments in this ASU, which should be applied prospectively, are effective for annual and interim periods beginning after December 15, 2016. Early adoption is permitted. The Company adopted ASU No. 2015-11 on April 1, 2016, and the adoption did not have a material impact on the consolidated financial statements and related disclosures.

In September 2015, the FASB issued ASU No. 2015-16, Business Combinations (Topic 805): Simplifying the Accounting for Measurement-Period Adjustments ("ASC 805"). Under this guidance, an acquirer is required to recognize adjustments to provisional amounts that are identified during the measurement period in the reporting period in which the adjustment amounts are determined. The amendments in this ASU require that the acquirer record, in the same period's financial statements, the effect on earnings of changes in depreciation, amortization or other income effects, if any, as a result of the change to the provisional amounts, calculated as if the accounting had been completed at the acquisition date. The amendments in this ASU require an entity to present separately on the face of the income statement or disclose in the notes the portion of the amount recorded in current-period earnings by line item that would have been recorded in previous reporting periods if the adjustment to the provisional amounts had been recognized as of the acquisition date. The amendments in this ASU, which should be applied prospectively, are effective for annual and interim periods beginning after December 15, 2015. The Company adopted ASU No. 2015-16 on January 1, 2016, and the adoption did not have a material impact on the consolidated financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842). Under ASU No. 2016-02, an entity will be required to recognize right-of-use assets and lease liabilities on its balance sheet and disclose key information about leasing arrangements. ASU No. 2016-02 offers specific accounting guidance for a lessee, a lessor and sale and leaseback transactions. Lessees and lessors are required to disclose qualitative and quantitative information about leasing arrangements to enable a user of the financial statements to assess the amount, timing and uncertainty of cash flows arising from leases. ASU No. 2016-02 is effective for annual reporting periods beginning after December 15, 2018, including interim periods within that reporting period, with early adoption permitted. At adoption, this update will be applied using a modified retrospective approach. The Company is currently in the process of evaluating the impact of adoption of ASU No. 2016-02 on its consolidated financial statements and related disclosures.

In March 2016, the FASB issued ASU No. 2016-09, Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The updated guidance will change how companies account for certain aspects of share-based payments to employees. Entities will be required to recognize the income tax effects of awards in the statement of income when the awards vest or are settled. The guidance on accounting for an employee's use of shares to satisfy the statutory income tax withholding obligation and for forfeitures is changing, and the update requires companies to present excess tax benefits as an operating activity on the statement of cash flows rather than as a financing activity. The amendments in this update will be effective for annual periods beginning after December 15, 2016 and interim periods within those annual periods. Early adoption is permitted. The Company is currently in the process of evaluating the impact of adoption of ASU No. 2016-09 on its consolidated financial statements and related disclosures.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows (Topic230): Classification of Certain Cash Receipts and Cash Payments. The amendments in this ASU provide guidance on the following eight specific cash flow classification issues: (1) debt prepayment or debt extinguishment costs; (2) settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing; (3) contingent consideration payments made after a business combination; (4) proceeds from the settlement of insurance claims; (5) proceeds from the settlement of corporate-owned life insurance policies, including bank-owned life insurance policies; (6) distributions received from equity method investees; (7) beneficial interests in securitization transactions; and (8) separately identifiable cash flows and application of the predominance principle. Current GAAP does not include specific guidance on these eight cash flow classification issues. The amendments of this ASU are effective for reporting periods beginning after December 15, 2017, with early adoption permitted. The adoption of ASU No. 2016-15 is not expected to have a material impact on the consolidated financial statements and related disclosures.

In October 2016, the FASB issued ASU No. 2016-16, Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory. ASU No. 2016-16 was issued to improve the accounting for the income tax consequences of intra-entity transfers of assets other than inventory. Current GAAP prohibits the recognition of current and deferred income taxes for an intra-entity asset transfer until the asset has been sold to an outside party which has resulted in diversity in practice and increased complexity within financial reporting. ASU No. 2016-16 would require an entity to recognize the income tax consequences of an intra-entity transfer of an asset other than inventory when the transfer occurs and do not require new disclosure requirements. ASU No. 2016-16 is effective for annual reporting periods beginning after December 15, 2017, and interim periods within those annual periods. Early adoption is permitted and the adoption of ASU No. 2016-16 should be applied on a modified retrospective basis through a cumulative-effect adjustment directly to retained earnings as of the beginning of the period of adoption. The Company is currently in the process of evaluating the impact of adoption of ASU No. 2016-16 on its consolidated financial statements and related disclosures.

In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash, which addresses diversity in practice related to the classification and presentation of changes in restricted cash on the statement of cash flows. ASU No. 2016-18 will require that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU No. 2016-18 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017. Early adoption is permitted. The adoption of ASU No. 2016-18 is not expected to have a material impact on the consolidated financial statements and related disclosures.

In January 2017, the FASB issued ASU No. 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business. The amendments in ASU No. 2017-01 clarify the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The definition of a business affects many areas of accounting including acquisitions, disposals, goodwill, and consolidation. The guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. Early adoption is permitted. The Company plans to adopt ASU No. 2017-01 in the first quarter of 2017. The adoption is not expected to have a material impact on the consolidated financial statements and related disclosures.

In January 2017, the FASB issued ASU No. 2017-04, Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment, to eliminate the second step of the goodwill impairment test. ASU No. 2017-04 requires an entity to measure a goodwill impairment loss as the amount by which the carrying value of a reporting unit exceeds its fair value. Additionally, an entity should include the income tax effects from any tax deductible goodwill on the carrying value of the reporting unit when measuring a goodwill impairment loss, if applicable. ASU No. 2017-04 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2019. Early

adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. The Company does not expect the adoption of ASU No. 2017-04 to have a material impact to its consolidated financial position, results of operations or cash flow.

NOTE 3 – NET (LOSS) INCOME PER SHARE

The following table presents basic net (loss) income per share for the years ended December 31, 2016, 2015 and 2014 (in thousands, except share and per share data):

	For the Years Ended December 31,		
	2016	2015	2014
Basic earnings per share calculation:			
Net (loss) income	$(166,834)	$39,532	$(263,603)
Weighted average of ordinary shares outstanding	160,699,543	148,788,020	83,751,129
Basic net (loss) income per share	$(1.04)	$0.27	$(3.15)

The following table presents diluted net (loss) income per share for the years ended December 31, 2016, 2015 and 2014 (in thousands, except share and per share data):

	For the Years Ended December 31,		
	2016	2015	2014
Diluted earnings per share calculation:			
Net (loss) income	$(166,834)	$39,532	$(263,603)
Weighted average of ordinary shares outstanding	160,699,543	155,923,251	83,751,129
Diluted net (loss) income per share	$(1.04)	$0.25	$(3.15)

Basic net (loss) income per share is computed by dividing net (loss) income by the weighted-average number of ordinary shares outstanding during the period. Diluted EPS reflects the potential dilution beyond shares for basic EPS that could occur if securities or other contracts to issue ordinary shares were exercised, converted into ordinary shares, or resulted in the issuance of ordinary shares that would have shared in the Company's earnings.

The outstanding securities listed in the table below were excluded from the computation of diluted loss per ordinary share for the years ended December 31, 2016, 2015 and 2014 due to being anti-dilutive:

	For the Years Ended December 31,		
	2016	2015	2014
Stock options	7,515,297	2,853,821	7,027,683
Restricted stock units	492,030	817,168	1,618,502
Performance stock units	5,247,987	1,074	—
Employee stock purchase plans	56,805	1,046,275	—
Warrants	1,123,737	2,416,894	6,683,811
Convertible Senior Notes	—	—	11,369,398
	14,435,856	7,135,232	26,699,394

The potentially dilutive impact of the Horizon Pharma Investment Limited ("Horizon Investment"), a wholly owned subsidiary of the Company, March 2015 private placement of $400.0 million aggregate principal amount of 2.50%

Exchangeable Senior Notes due 2022 (the “Exchangeable Senior Notes”) is determined using a method similar to the treasury stock method. Under this method, no numerator or denominator adjustments arise from the principal and interest components of the Exchangeable Senior Notes because the Company has the intent and ability to settle the Exchangeable Senior Notes’ principal and interest in cash. Instead, the Company is required to increase the diluted EPS denominator by the variable number of shares that would be issued upon conversion if it settled the conversion spread obligation with shares. For diluted EPS purposes, the conversion spread obligation is calculated based on whether the average market price of the Company's ordinary shares over the reporting period is in excess of the exchange price of the Exchangeable Senior Notes. There was no calculated spread added to the denominator for the years ended December 31, 2016 and 2015.

NOTE 4 – BUSINESS ACQUISITIONS AND OTHER ARRANGEMENTS

Business acquisitions

Raptor Acquisition

On October 25, 2016, the Company completed its acquisition of Raptor and acquired all of the issued and outstanding shares of Raptor's common stock for $9.00 per share. The acquisition added two medicines, PROCYSBI and QUINSAIR, to the Company's medicine portfolio. Through the acquisition, the Company expects to leverage as well as expand the existing infrastructure of its orphan disease business. Following completion of the acquisition, Raptor became a wholly owned subsidiary of the Company and converted to a limited liability company, changing its name to Horizon Pharmaceutical LLC. The Company financed the transaction through $300.0 million of aggregate principal amount of 2024 Senior Notes, $375.0 million aggregate principal amount of loans pursuant to an amendment to the Company's existing credit agreement, as described in Note 17, and cash on hand. The total consideration for the acquisition was approximately $860.8 million, including cash acquired of $24.9 million and $56.0 million to repay Raptor's outstanding debt, and was composed of the following (in thousands):

Cash	$841,494
Net settlements on the exercise of stock options and restricted stock units	19,268
Total consideration	$860,762

During the year ended December 31, 2016, the Company incurred $38.3 million in Raptor acquisition-related costs including advisory, legal, accounting, valuation, severance, retention bonuses and other professional and consulting fees, which were accounted for as "general and administrative" expenses in the consolidated statements of comprehensive loss.

Pursuant to ASC 805, the Company accounted for the Raptor acquisition as a business combination using the acquisition method of accounting. Identifiable assets and liabilities of Raptor, including identifiable intangible assets, were recorded based on their estimated fair values as of the date of the closing of the acquisition. The excess of the purchase price over the fair value of the net assets acquired was recorded as goodwill. Significant judgment was required in determining the estimated fair values of developed technology intangible assets, inventories and certain other assets and liabilities. Such preliminary valuation required estimates and assumptions including, but not limited to, estimating future cash flows and direct costs in addition to developing the appropriate discount rates and current market profit margins. The Company's management believes the fair values recognized for the assets acquired and the liabilities assumed are based on reasonable estimates and assumptions. Accordingly, the purchase price adjustments are preliminary and are subject to further adjustments as additional information becomes available and as additional analyses are performed, and such further adjustments may be material.

The following table summarizes the preliminary fair values assigned to the assets acquired and the liabilities assumed by the Company, along with the resulting goodwill (in thousands):

(Liabilities assumed) and assets acquired:	Allocation
Accounts payable	$(4,572)
Accrued expenses	(23,773)
Accrued trade discounts and rebates	(6,377)
Deferred tax liabilities	(237,166)
Contingent royalty liability	(102,000)
Accrued royalties	(2,705)
Other non-current liability	(25,500)
Cash and cash equivalents	24,897
Restricted cash	1,350
Accounts receivable, net	17,767
Inventories	74,463
Prepaid expenses and other current assets	4,194
Property and equipment	3,373
Developed technology	946,000
Other non-current assets	1,765
Goodwill	189,046
Fair value of consideration paid	$860,762

Inventories acquired included raw materials, work in process and finished goods for PROCYSBI and QUINSAIR. Inventories were recorded at their preliminary estimated fair values. The fair value of finished goods has been determined based on the estimated selling price, net of selling costs and a margin on the selling costs. The fair value of work in process has been determined based on estimated selling price, net of selling costs and costs to complete the manufacturing, and a margin on the selling and manufacturing costs. The fair value of raw materials was estimated to equal the replacement cost. A step-up in the value of inventory of $67.0 million was recorded in connection with the acquisition. During the three months ended December 31, 2016, the Company recorded inventory step-up expense of $22.4 million related to PROCYSBI and QUINSAIR.

Other tangible assets and liabilities were valued at their respective carrying amounts as management believes that these amounts approximated their acquisition date fair values.

Other non-current liability of $25.5 million represents the fair value of an assumed contingent liability, arising from contingent payments associated with development, regulatory and commercial milestones following Raptor’s acquisition of QUINSAIR.

Identifiable intangible assets and liabilities acquired include developed technology and contingent royalties. The preliminary estimated fair values of the developed technology and contingent royalties represent preliminary valuations performed with the assistance of an independent appraisal firm based on management’s estimates, forecasted financial information and reasonable and supportable assumptions.

Developed technology intangible asset reflects the estimated fair value of Raptor’s rights to its currently marketed medicine, PROCYSBI. The preliminary fair value of developed technology was determined using an income approach. The income approach explicitly recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs for Raptor’s medicines. Indications of value were developed by discounting these benefits to their

acquisition-date worth at a discount rate of 12.5%. The fair value of the PROCYSBI developed technology was capitalized as of the Raptor acquisition date and is subsequently being amortized over approximately thirteen years and nine years for the U.S. rights and ex-U.S. rights, respectively, which are the periods in which over 90% of the estimated cash flows are expected to be realized. The Company assigned no preliminary fair value to QUINSAIR developed technology as projections of future net sales do not exceed the related costs.

The Company has assigned a preliminary fair value of $102.0 million to a contingent liability for royalties potentially payable under previously existing agreements related to PROCYSBI. The royalties for PROCYSBI are payable under the terms of a license agreement with The Regents of the University of California, San Diego ("UCSD"). See Note 15 for details of the percentages of royalties payable under this agreement. The initial fair value of this liability was determined using a discounted cash flow analysis incorporating the estimated future cash flows of royalty payments resulting from future sales. The discount rate used was the same as for the fair value of the developed technology.

Deferred tax assets and liabilities arise from acquisition accounting adjustments where book values of certain assets and liabilities differ from their tax bases. Deferred tax assets and liabilities are recorded at the currently enacted rates which will be in effect at the time when the temporary differences are expected to reverse in the country where the underlying assets and liabilities are located. Raptor's developed technology as of the acquisition date was located primarily in the United States where a U.S. tax rate of 36.6% is being utilized and a significant deferred tax liability is recorded. Goodwill represents the excess of the preliminary acquisition consideration over the estimated fair value of net assets acquired and was recorded in the consolidated balance sheet as of the acquisition date. The Company does not expect any portion of this goodwill to be deductible for tax purposes.

Acquisition of Additional Rights to Interferon Gamma-1b

On May 18, 2016, the Company entered into a definitive agreement with Boehringer Ingelheim International to acquire certain rights to interferon gamma-1b, which Boehringer Ingelheim International currently commercializes under the trade names IMUKIN, IMUKINE, IMMUKIN and IMMUKINE (collectively, "IMUKIN") in an estimated thirty countries primarily in Europe and the Middle East. Under the terms of the agreement, the Company paid Boehringer Ingelheim International €5.0 million ($5.6 million when converted using a Euro-to-Dollar exchange rate at date of payment of 1.1132) upon signing and will pay €20.0 million upon closing, for certain rights for interferon gamma-1b in all territories outside of the United States, Canada and Japan, as the Company currently holds marketing rights to interferon gamma-1b in these territories. The transaction is expected to close in 2017 and the Company is continuing to work with Boehringer Ingelheim International to enable the transfer of applicable marketing authorizations. The Company currently markets interferon gamma-1b as ACTIMMUNE in the United States. The €5.0 million upfront amount paid in May 2016 had been included in "other assets" in the Company's consolidated balance sheet. Following the discontinuation of the STEADFAST program for ACTIMMUNE, as further described in Note 1, the Company recorded an impairment charge of €5.0 million ($5.3 million when converted using a Euro-to-Dollar exchange rate at date of impairment of 1.052) to fully write off the asset on its consolidated balance sheet during the three months ended December 31, 2016 as projections for future net sales of IMUKIN in these territories do not exceed the related costs. Upon closing, the Company expects to record the additional €20.0 million payment as an expense in its consolidated statement of comprehensive (loss) income.

Crealta Acquisition

On January 13, 2016, the Company completed its acquisition of all the membership interests of Crealta. The acquisition added two medicines, KRYSTEXXA and MIGERGOT, to the Company's medicine portfolio. The Crealta acquisition further diversified the Company's portfolio of medicines and aligned with its focus of acquiring value-enhancing, clinically differentiated, long-life medicines that treat orphan diseases. The total consideration for the acquisition was approximately $539.7 million, including cash acquired of $24.9 million, and was composed of the following before and after the measurement period adjustments (in thousands):

	Before	Adjustments	After
Cash	$536,181	$ 25	$536,206
Net settlements on the exercise of stock options and	3,526	—	3,526

unrestricted units			
Total consideration	$539,707	$ 25	$539,732

During the year ended December 31, 2016, the Company incurred $13.0 million in Crealta acquisition-related costs including advisory, legal, accounting, valuation, severance, retention bonuses and other professional and consulting fees, of which $12.4 million was accounted for as “general and administrative” expenses, $0.2 million was accounted for as “research and development” expenses and $0.4 million was accounted for as “costs of goods sold” in the consolidated statements of comprehensive loss.

Pursuant to ASC 805, the Company accounted for the Crealta acquisition as a business combination using the acquisition method of accounting. Identifiable assets and liabilities of Crealta, including identifiable intangible assets, were recorded based on their estimated fair values as of the date of the closing of the acquisition. The excess of the purchase price over the fair value of the net assets acquired was recorded as goodwill. Significant judgment was required in determining the estimated fair values of developed technology intangible assets, inventories and certain other assets and liabilities. Such preliminary valuation required estimates and assumptions including, but not limited to, estimating future cash flows and direct costs in addition to developing the appropriate discount rates and current market profit margins. The Company's management believes the fair values recognized for the assets acquired and the liabilities assumed are based on reasonable estimates and assumptions. Accordingly, the purchase price adjustments are preliminary and are subject to further adjustments as additional information becomes available and as additional analyses are performed, and such further adjustments may be material.

During the year ended December 31, 2016, the Company recorded measurement period adjustments related to developed technology, inventory and deferred tax liabilities, which resulted in a net increase in goodwill of $8.1 million. The measurement period adjustments were the result of an adjustment for inventory that was subsequently discovered to have been damaged and defective as of the acquisition date, a net working capital true-up adjustment and the alignment of Crealta's inventory and obsolescence reserve policy to the Company's policy.

The following table summarizes the preliminary fair values assigned to the assets acquired and the liabilities assumed by the Company, along with the resulting goodwill before and after the measurement period adjustments (in thousands):

(Liabilities assumed) and assets acquired:	Before	Adjustments	After
Accounts payable and accrued expenses	$(4,543)	$ —	$(4,543)
Accrued trade discounts and rebates	(1,424)	—	(1,424)
Deferred tax liabilities	(20,835)	694	(20,141)
Other non-current liabilities	(6,900)	—	(6,900)
Contingent royalty liabilities	(51,300)	—	(51,300)
Cash and cash equivalents	24,893	—	24,893
Accounts receivable	10,014	—	10,014
Inventories	169,054	(19,691)	149,363
Prepaid expenses and other current assets	1,382	—	1,382
Developed technology	417,300	10,900	428,200
Other non-current assets	275	—	275
Goodwill	1,791	8,122	9,913
Fair value of consideration paid	$539,707	$ 25	$539,732

Inventories acquired included raw materials, work in process and finished goods for KRYSTEXXA and MIGERGOT. Inventories were recorded at their preliminary estimated fair values. The fair value of finished goods has been determined based on the estimated selling price, net of selling costs and a margin on the selling costs. The fair value of work in process has been determined based on estimated selling price, net of selling costs and costs to complete the manufacturing, and a margin on the selling and manufacturing costs. The fair value of raw materials was estimated to equal the replacement cost. A step-up in the value of inventory of $163.6 million was originally recorded in connection with the acquisition and this was reduced to $144.3 million following the recording of $19.3 million in measurement period adjustments during the year ended December 31, 2016. During the year ended December 31, 2016, the Company recorded inventory step-up expense of $48.8 million.

Other tangible assets and liabilities were valued at their respective carrying amounts as management believes that these amounts approximated their acquisition date fair values.

Other non-current liabilities represented an assumed $6.9 million probable contingent liability which was released to “other income (expense)” in the consolidated statement of comprehensive loss during the year ended December 31, 2016. See Note 15 for further details.

Identifiable intangible assets and liabilities acquired include developed technology and contingent royalties. The preliminary estimated fair values of the developed technology and contingent royalties represent preliminary valuations performed with the assistance of an independent appraisal firm based on management’s estimates, forecasted financial information and reasonable and supportable assumptions.

Developed technology intangible assets reflect the estimated fair value of Crealta's rights to its currently marketed medicines, KRYSTEXXA and MIGERGOT. The preliminary fair value of developed technology was determined using an income approach. The income approach explicitly recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs for Crealta's medicines. Indications of value were developed by discounting these benefits to their acquisition-date worth at a discount rate of 27% for KRYSTEXXA and 23% for MIGERGOT. The fair value of the KRYSTEXXA and MIGERGOT developed technologies were capitalized as of the Crealta acquisition date and are subsequently being amortized over approximately twelve and ten years, respectively, which are the periods in which over 90% of the estimated cash flows are expected to be realized.

The Company has assigned a preliminary fair value of $51.3 million to a contingent liability for royalties potentially payable under previously existing agreements related to KRYSTEXXA and MIGERGOT. The royalties for KRYSTEXXA are payable under the terms of a license agreement with Duke University ("Duke") and Mountain View Pharmaceuticals ("MVP"). See Note 15 for details of the percentages of royalties payable under such agreements. The initial fair value of this liability was determined using a discounted cash flow analysis incorporating the estimated future cash flows of royalty payments resulting from future sales. The discount rate used was the same as for the fair value of the developed technology.

The preliminary deferred tax liability recorded represents deferred tax liabilities assumed as part of the acquisition, net of deferred tax assets, related to net operating tax loss carryforwards of Crealta.

Goodwill represents the excess of the preliminary acquisition consideration over the estimated fair value of net assets acquired and was recorded in the consolidated balance sheet as of the acquisition date. The Company does not expect any portion of this goodwill to be deductible for tax purposes.

Hyperion Acquisition

On May 7, 2015, the Company completed the acquisition of Hyperion in which it acquired all of the issued and outstanding shares of Hyperion's common stock for $46.00 per share. The acquisition added two important medicines, RAVICTI and BUPHENYL, to the Company's medicine portfolio. Through the acquisition, the Company leveraged as well as expanded the existing infrastructure of its orphan disease business. The total consideration for the acquisition was approximately $1.1 billion and was composed of the following (in thousands, except share and per share data):

Fully diluted equity value (21,425,909 shares at $46.00 per share)	$985,592
Net settlements on the exercise of stock options, restricted stock and performance stock units	89,806
Total consideration	$1,075,398

During the year ended December 31, 2016, the Company recorded a net expense reduction of $0.7 million in Hyperion acquisition-related costs due to a reduction in severance and other payroll-related payments required. Net expense reductions of $0.6 million and $0.4 million were accounted for as "general and administrative" and "other cost of sales", respectively, and a net expense of $0.3 million was recorded as "research and development" expenses in the consolidated statement of comprehensive loss. No further significant acquisition-related costs are expected to be

incurred in relation to the Hyperion acquisition.

During the year ended December 31, 2015, the Company incurred $53.7 million in Hyperion acquisition-related costs including advisory, legal, accounting, valuation, severance, retention bonuses, and other professional and consulting fees, of which $40.6 million, $10.0 million and $3.1 million were accounted for as “general and administrative”, “other, net” and “research and development” expenses, respectively, in the consolidated statement of comprehensive income.

Pursuant to ASC 805, the Company accounted for the Hyperion acquisition as a business combination using the acquisition method of accounting. Identifiable assets and liabilities of Hyperion, including identifiable intangible assets, were recorded based on their estimated fair values as of the date of the closing of the acquisition. The excess of the purchase price over the fair value of the net assets acquired was recorded as goodwill. Significant judgment was required in determining the estimated fair values of developed technology intangible assets and certain other assets and liabilities. Such a valuation required estimates and assumptions including, but not limited to, estimating future cash flows and direct costs in addition to developing the appropriate discount rates and current market profit margins. The Company's management believes the fair values recognized for the assets acquired and the liabilities assumed are based on reasonable estimates and assumptions.

During the year ended December 31, 2016, the Company recorded an adjustment related to deferred tax liabilities which resulted in a decrease to goodwill of $7.2 million. In evaluating whether the Company's previously issued consolidated financial statements were materially misstated, the Company considered the guidance in FASB ASC Topic 250, Accounting Changes and Error Corrections, ASC Topic 250-10-S99-1, Assessing Materiality, and ASC Topic 250-10-S99-2, Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements. The adjustment was the result of a correction of an error in the Hyperion pre-acquisition deferred tax calculation. The Company concluded that this misstatement was not material, individually or in the aggregate, to any of the reporting periods impacted. As such, the correction for this error was made during the year ended December 31, 2016.

The following table summarizes the final fair values assigned to the assets acquired and the liabilities assumed by the Company (in thousands):

(Liabilities assumed) and assets acquired:	As Reported	Adjustment	As Adjusted
Deferred tax liability, net	$(262,732)	$ 7,191	$(255,541)
Accounts payable	(2,439)	—	(2,439)
Accrued trade discounts and rebates	(9,792)	—	(9,792)
Accrued expenses	(7,566)	—	(7,566)
Contingent royalties	(86,800)	—	(86,800)
Cash and cash equivalents	53,037	—	53,037
Short-term investments	39,049	—	39,049
Long-term investments	25,574	—	25,574
Accounts receivable, net	11,858	—	11,858
Inventory	13,498	—	13,498
Prepaid expenses and other current assets	2,533	—	2,533
Property and equipment	1,044	—	1,044
Other non-current assets	123	—	123
Developed technology	1,044,200	—	1,044,200
Goodwill	253,811	(7,191)	246,620
Fair value of consideration paid	$1,075,398	$ —	$1,075,398

Inventories acquired included raw materials and finished goods. Inventories were recorded at their current fair values. The fair value of finished goods has been determined based on the estimated selling price, net of selling costs and a margin on the selling costs. The fair value of raw materials was estimated to equal the replacement cost. A step-up in the value of inventory of $8.7 million was recorded in connection with the acquisition and has subsequently been fully recognized in the consolidated statements of comprehensive (loss) income.

Other tangible assets and liabilities were valued at their respective carrying amounts as management believes that these amounts approximated their acquisition date fair values.

Identifiable intangible assets and liabilities acquired include developed technology and contingent royalties. The fair values of the developed technology and contingent royalties represent valuations performed with the assistance of an independent appraisal firm based on management's estimates, forecasted financial information and reasonable and supportable assumptions.

Developed technology intangible assets reflect the estimated value of Hyperion's rights to its currently marketed medicines, RAVICTI and BUPHENYL. The fair value of developed technology was determined using an income approach. The income approach explicitly recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs for Hyperion's medicines. Indications of value were developed by discounting these benefits to their acquisition-date worth at a discount rate of 8.5% that reflected the then-current return requirements of the market. The fair value of the RAVICTI and BUPHENYL developed technologies were capitalized as of the Hyperion acquisition date and are subsequently being amortized over 11 and 7 years, respectively, which are the periods in which over 90% of the estimated cash flows are expected to be realized.

The Company has assigned a fair value to a contingent liability for royalties potentially payable under previously existing agreements related to RAVICTI and BUPHENYL. The royalties are payable under the terms of an asset purchase agreement and an amended and restated collaboration agreement with Ucyclyd Pharma, Inc. ("Ucyclyd") and a license agreement with Saul W. Brusilow, M.D. and Brusilow Enterprises Inc. ("Brusilow"). See Note 15 for details of the percentages payable under such agreements. The initial fair value of this liability was $86.8 million and was determined using a discounted cash flow analysis incorporating the estimated future cash flows of royalty payments resulting from future sales. The discount rate used was the same as for the fair value of the developed technology. See Note 2 for details of the Company's accounting policies for accrued contingent royalties.

Deferred tax assets and liabilities arise from acquisition accounting adjustments where book values of certain assets and liabilities differ from their tax bases. Deferred tax assets and liabilities are recorded at the currently enacted rates which will be in effect at the time when the temporary differences are expected to reverse in the country where the underlying assets and liabilities are located. Hyperion's developed technology as of the acquisition date was located primarily in the United States where a U.S. tax rate of 39% is being utilized and a significant deferred tax liability is recorded. Upon consummation of the Hyperion acquisition, Hyperion became a member of the Company's U.S. tax consolidation group. As such, its tax assets and liabilities were considered in determining the appropriate amount (if any) of valuation allowances that should be recognized in assessing the realizability of the group's deferred tax assets. The Hyperion acquisition adjustments resulted in the recognition of significant net deferred tax liabilities. Per ASC Topic 740, Accounting for Uncertainty in Income Taxes, ("ASC 740") future reversals of existing taxable temporary differences provide objectively verifiable evidence that should be considered as a source of taxable income to realize a tax benefit for deductible temporary differences and carryforwards. Generally, the existence of sufficient taxable temporary differences will enable the use of the tax benefit of existing deferred tax assets. As of the first quarter of 2015, the Company had significant U.S. federal and state valuation allowances. These valuation allowances were released in the second quarter of 2015 to reflect the recognition of Hyperion's deferred tax liabilities that will provide taxable temporary differences that will be realized within the carryforward period of the Company's U.S. tax consolidation group's available net operating losses and other deferred tax assets. Accordingly, the Company recorded an income tax benefit of $105.1 million in the second quarter of 2015 relating to the release of existing U.S. federal and state valuation allowances.

Short-term and long-term investments included in the table above represent available-for-sale securities that were reported in short-term investments or long-term investments based on maturity dates and whether such assets are reasonably expected to be realized in cash or sold or consumed during the normal cycle of business. Available-for-sale investments were recorded at fair value and were liquidated shortly after the acquisition.

Goodwill represents the excess of the acquisition consideration over the estimated fair value of net assets acquired and was recorded in the consolidated balance sheet as of the acquisition date. The Company does not expect any portion of this goodwill to be deductible for tax purposes.

Other arrangements

On November 8, 2016, the Company entered into a collaboration and option agreement with a privately held life-science entity. Under the terms of the agreement, the privately held life-science entity will conduct certain research and pre-clinical and clinical development activities. Upon execution of the agreement, the Company paid $0.1 million for the option to acquire certain of the privately held life-science entity's assets for $25.0 million, which is exercisable on specified key dates. Under the collaboration and option agreement, the Company will be required to pay up to $9.8 million upon the attainment of various milestones, primarily to fund clinical development costs for the medicine. The Company paid $0.2 million in the fourth quarter of 2016 and a further $0.9 million in the first quarter of 2017. The Company has determined that the privately held life-science entity is a variable interest entity ("VIE") as it does not have enough equity to finance its activities without additional financial support. As the Company does not have the power to direct the activities of the VIE that most significantly affect its economic performance, it is not the primary beneficiary of, and does not consolidate the results of, the VIE. The Company will reassess the appropriate accounting treatment for this arrangement throughout the life of the agreement and modify these accounting conclusions accordingly. The initial upfront amount paid of $0.1 million has been included in "other assets" in the Company's consolidated balance sheet as of December 31, 2016, and the milestone amounts of $1.1 million paid to date were recorded as "research and development" expenses in the consolidated statement of comprehensive loss during the year ended December 31, 2016.

Pro Forma Information

The following table represents consolidated financial information for the Company on a pro forma basis. The 2016 pro forma adjustments assume that the Crealta and Raptor acquisitions occurred as of January 1, 2016, the 2015 pro forma adjustments assume that the Hyperion, Crealta and Raptor acquisitions occurred as of January 1, 2015 and the 2014 pro forma adjustments assume that the Hyperion acquisition and the Vidara Merger occurred as of January 1, 2014.

The results of Raptor from October 25, 2016 to December 31, 2016 and the results of Crealta from January 13, 2016 to December 31, 2016 are included in the 2016 as reported figures, the results of Hyperion from May 7, 2015 to December 31, 2016 are included in the 2015 and 2016 as reported figures and the results of Vidara from September 19, 2014 to December 31, 2016 are included in the 2014, 2015 and 2016 as reported figures.

The historical financial information has been adjusted to give effect to pro forma items that are directly attributable to the Hyperion, Crealta and Raptor acquisitions and the Vidara Merger, and are expected to have a continuing impact on the consolidated results. These items include, among others, adjustments to record the amortization of definite-lived intangible assets, interest expense, debt discount and deferred financing costs associated with the debt in connection with the acquisitions. Additionally, the following table sets forth unaudited financial information and has been compiled from historical financial statements and other information, but is not necessarily indicative of the results that actually would have been achieved had the transactions occurred on the dates indicated or that may be achieved in the future (in thousands, except per share data):

	For the Year Ended December 31,								
	2016			2015			2014		
	As reported	Pro forma adjustments	Pro forma (Unaudited)	As reported	Pro forma adjustments	Pro forma (Unaudited)	As reported	Pro forma adjustments	Pro forma (Unaudited)

		(Unaudited)			(Unaudited)			(Unaudited)	
Net sales	$981,120	$109,298	$1,090,418	$757,044	$200,611	$957,655	$296,955	$164,149	$461,104
Net (loss) income	(166,834)	(201,765)	(368,599)	39,532	(127,801)	(88,269)	(263,603)	(70,803)	(334,406)
Basic net (loss) income per share	$(1.04)	$(1.26)	$(2.30)	$0.27	$(0.86)	$(0.59)	$(3.15)	$(0.15)	$(3.30)
Diluted net (loss) income per share	(1.04)	(1.26)	(2.30)	0.25	(0.86)	(0.59)	(3.15)	(0.15)	(3.30)

The Company's consolidated statements of comprehensive loss for the year ended December 31, 2016 include KRYSTEXXA and MIGERGOT net sales as a result of the acquisition of Crealta in January 2016 of $91.1 million and $4.7 million, respectively, and PROCYSBI and QUINSAIR net sales as a result of the acquisition of Raptor in October 2016 of $25.3 million and $1.0 million, respectively. The Company's consolidated statements of comprehensive income for the year ended December 31, 2015 include RAVICTI and BUPHENYL net sales as a result of the acquisition of Hyperion in May 2015 of $86.9 million and $13.5 million, respectively. The Company's consolidated statements of comprehensive loss for the year ended December 31, 2014 include ACTIMMUNE net sales as a result of the Vidara Merger of $25.3 million.

Vidara, Hyperion, Crealta and Raptor have been fully integrated into the Company's business and as a result of these integration efforts, the Company cannot distinguish between these operations and those of the Company's legacy business.

NOTE 5 – INVENTORIES

Inventories are stated at the lower of cost or market value. Inventories consist of raw materials, work-in-process and finished goods. The Company has entered into manufacturing and supply agreements for the manufacture or purchase of raw materials and production supplies. The Company's inventories include the direct purchase cost of materials and supplies and manufacturing overhead costs.

The components of inventories as of December 31, 2016 and 2015 consisted of the following (in thousands):

	As of December 31,	
	2016	2015
Raw materials	$10,233	$6,232
Work-in-process	85,022	631
Finished goods	79,533	11,513
Inventories, net	$174,788	$18,376

Because inventory step-up expense is acquisition-related, will not continue indefinitely and has a significant effect on the Company's gross profit, gross margin percentage and net income (loss) for all affected periods, the Company discloses balance sheet and income statement amounts related to inventory step-up within the notes to the consolidated financial statements.

Finished goods at December 31, 2016 included $27.7 million of stepped-up KRYSTEXXA and MIGERGOT inventory and $38.1 million of stepped-up PROCYSBI and QUINSAIR inventory. Work-in-process at December 31, 2016 included $67.6 million of stepped-up KRYSTEXXA and MIGERGOT inventory and $5.9 million of stepped-up PROCYSBI and QUINSAIR inventory. The Company recorded $48.8 million of KRYSTEXXA and MIGERGOT inventory step-up expense during the year ended December 31, 2016. The Company recorded $22.4 million of PROCYSBI and QUINSAIR inventory step-up expense during the year ended December 31, 2016.

The Company expects that the KRYSTEXXA and MIGERGOT inventory step-up will be fully expensed by the end of the first quarter of 2018. Following that period, the Company expects the costs of goods sold related to KRYSTEXXA and MIGERGOT to decrease significantly to levels consistent with the historical cost of goods sold of Crealta. The Company expects the PROCYSBI and QUINSAIR inventory step-up will be fully expensed by the end of the third quarter of 2017. Following that period, the Company expects the costs of goods sold related to PROCYSBI and QUINSAIR to decrease significantly to levels consistent with the historical cost of goods sold of Raptor.

During the year ended December 31, 2015, the Company recorded $8.4 million of RAVICTI and BUPHENYL inventory step-up expense and $3.2 million of ACTIMMUNE inventory step-up expense.

During the year ended December 31, 2016, the Company committed to purchase additional units of ACTIMMUNE from Boehringer Ingelheim. These additional units of ACTIMMUNE were intended to cover anticipated demand if the results of the STEADFAST study of ACTIMMUNE for the treatment of FA had been successful. Following the discontinuation of the STEADFAST program, the Company recorded a loss of $14.3 million for firm, non-cancellable and unconditional purchase commitments for quantities in excess of the Company's current forecasts for future demand. Inventories, net at December 31, 2016 does not include an amount related to these additional units of ACTIMMUNE. During the year ended December 31, 2016, the Company also committed to incur an additional $14.9 million for the harmonization of the drug substance manufacturing process with Boehringer Ingelheim. These additional costs have not been included in the Company's consolidated statement of comprehensive loss or the Company's consolidated balance sheet at December 31, 2016.

NOTE 6 – PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets as of December 31, 2016 and 2015 consisted of the following (in thousands):

	As of December 31,	
	2016	2015
Medicine samples inventory	$10,192	4,697
Prepaid income taxes	9,155	4
Deferred charge for taxes on intra-group profit	7,801	—
Rabbi trust assets	3,073	773
Prepaid co-pay expenses	2,070	1,881
Other prepaid expenses	17,328	8,503
Prepaid expenses and other current assets	$49,619	$15,858

NOTE 7 – PROPERTY AND EQUIPMENT

Property and equipment as of December 31, 2016 and 2015 consisted of the following (in thousands):

	As of December 31,	
	2016	2015
Software	$10,876	$1,360
Leasehold improvements	9,184	1,966
Machinery and equipment	4,566	2,946
Computer equipment	3,069	2,514
Other	2,664	276
	30,359	9,062
Less accumulated depreciation	(8,319)	(3,791)
Construction in process	17	3,492
Software implementation in process	1,427	5,257
Property and equipment, net	$23,484	$14,020

The Company capitalizes development costs associated with internal use software, including external direct costs of materials and services and payroll costs for employees devoting time to a software project. Costs incurred during the preliminary project stage, as well as costs for maintenance and training, are expensed as incurred.

Software implementation in process as of December 31, 2016 and December 31, 2015 is related to new enterprise resource planning software being implemented by the Company. The software is being implemented on a phased basis starting January 2016 and depreciation is not recorded on capitalized costs relating to a phase which has not yet entered service. Once a particular phase of the project enters service, associated capitalized costs are moved from “software implementation in process” to “software” in the table above, and depreciation commences.

Depreciation expense for the years ended December 31, 2016, 2015 and 2014 was $5.0 million, $5.4 million and $1.7 million, respectively.

NOTE 8 – GOODWILL AND INTANGIBLE ASSETS

Goodwill

The gross carrying amount of goodwill as of December 31, 2016 was as follows (in thousands):

Balance at December 31, 2014	$—
Goodwill recognized on acquisition of Hyperion	253,811
Balance at December 31, 2015	253,811
Goodwill recognized on acquisition of Crealta	9,913
Goodwill recognized on acquisition of Raptor	189,046
Adjustment relating to the acquisition of Hyperion in the prior year	(7,191)
Balance at December 31, 2016	$445,579

In May 2015, the Company recognized goodwill with a value of $253.8 million in connection with the Hyperion acquisition, which represented the excess of the purchase price over the fair value of the net assets acquired. During the year ended December 31, 2016, the Company recorded an adjustment related to deferred tax liabilities which resulted in a decrease to goodwill of $7.2 million. The adjustment was the result of a correction of an error in the Hyperion pre-acquisition deferred tax calculation. The Company concluded that this misstatement was not material, individually or in the aggregate, to any of the reporting periods impacted. As such, the correction for this error was made during the year ended December 31, 2016.

In January 2016, the Company recognized goodwill with a preliminary value of $1.8 million in connection with the Crealta acquisition, which represented the excess of the purchase price over the fair value of the net assets acquired. During the year ended December 31, 2016, the Company recorded measurement period adjustments related to developed technology, inventory and deferred tax liabilities, which resulted in a net increase in goodwill of $8.1 million, to $9.9 million.

In October 2016, the Company recognized goodwill with a preliminary value of $189.1 million in connection with the Raptor acquisition, which represented the excess of the purchase price over the fair value of the net assets acquired.

As of December 31, 2016, there were no accumulated goodwill impairment losses.

See Note 4 for further details of goodwill acquired in business acquisitions.

Intangible Assets

As of December 31, 2016, the Company’s intangible assets consist of developed technology related to ACTIMMUNE, BUPHENYL, KRYSTEXXA, MIGERGOT, PENNSAID 2%, PROCYSBI, RAVICTI, RAYOS and VIMOVO in the United States, and AMMONAPS, BUPHENYL, LODOTRA and PROCYSBI outside the United States, as well as customer relationships for ACTIMMUNE.

In May 2015, in connection with the acquisition of Hyperion, the Company capitalized $1,021.6 million of developed technology related to RAVICTI and $22.6 million of developed technology related to BUPHENYL.

In January 2016, in connection with the acquisition of Crealta, the Company capitalized $392.7 million of developed technology related to KRYSTEXXA and $24.6 million of developed technology related to MIGERGOT. During the year ended December 31, 2016, the Company recorded measurement period adjustments which increased the cost basis of KRYSTEXXA and MIGERGOT developed technology by $9.5 million to $402.2 million, and $1.4 million to $26.0 million, respectively.

In October 2016, in connection with the acquisition of Raptor, the Company capitalized $946.0 million of developed technology related to PROCYSBI.

See Note 4 for further details of intangible assets acquired in business acquisitions.

IPR&D of $66.0 million was related to one research and development project to evaluate ACTIMMUNE in the treatment of FA. The fair value of the IPR&D was recorded as an indefinite-lived intangible asset and was being tested for impairment annually until completion or abandonment of the research and development efforts associated with the project. On December 8, 2016, the Company announced that the Phase 3 trial, STEADFAST, evaluating ACTIMMUNE for the treatment of FA did not meet its primary endpoint of a statistically significant change from baseline in the FARS-mNeuro at twenty-six weeks versus treatment with placebo. In addition, the secondary endpoints did not meet statistical significance. No new safety findings were identified on initial review of data other

than those already noted in the ACTIMMUNE prescribing information for approved indications. The Company, in conjunction with the independent Data Safety Monitoring Board, the principal investigator and FARA, Collaborative Clinical Research Network in FA, determined that, based on the trial results, the STEADFAST program would be discontinued, including the twenty-six week extension study and the long-term safety study. The IPR&D has no alternative use or economic value as a result of the cancellation of the project, and the Company recorded an impairment charge of $66.0 million to “impairment of in-process research and development” in its consolidated statements of comprehensive loss during the three months ended December 31, 2016 to fully write off the value of the asset on its consolidated balance sheet.

The Company tests its intangible assets for impairment when events or circumstances may indicate that the carrying value of these assets exceeds their fair value. The Company does not believe there have been any circumstances or events that would indicate that the carrying value of any of its intangible assets, except for IPR&D as described above, was impaired at December 31, 2016 or December 31, 2015.

As of December 31, 2016 and December 31, 2015, amortizable intangible assets consisted of the following (in thousands):

	As of December 31, 2016			2015		
	Cost Basis	Accumulated Amortization	Net Book Value	Cost Basis	Accumulated Amortization	Net Book Value
Developed technology	$3,166,695	$ (399,511)	$2,767,184	$1,792,495	$ (183,446)	$1,609,049
Customer relationships	8,100	(1,849)	6,251	8,100	(1,039)	7,061
Amortizable intangible assets	$3,174,795	$ (401,360)	$2,773,435	$1,800,595	$ (184,485)	$1,616,110

Amortization expense for the years ended December 31, 2016, 2015 and 2014 was $216.9 million, $132.9 million and $32.3 million, respectively. As of December 31, 2016, estimated future amortization expense was as follows (in thousands):

2017	$280,088
2018	280,088
2019	267,096
2020	266,879
2021	259,377
Thereafter	1,419,907
Total	$2,773,435

NOTE 9 – ACCRUED TRADE DISCOUNTS AND REBATES

Accrued trade discounts and rebates as of December 31, 2016 and December 31, 2015 consisted of the following (in thousands):

	As of December 31, 2016	2015
Accrued wholesaler fees and commercial rebates	$47,460	$21,112
Accrued co-pay and other patient assistance	188,504	114,201
Accrued government rebates and chargebacks	61,592	48,456
Accrued trade discounts and rebates	$297,556	$183,769
Invoiced wholesaler fees and commercial rebates,	16,830	—

co-pay and other patient assistance, and government rebates and chargebacks in accounts payable		
Total customer-related accruals and allowances	$314,386	$183,769

The following table summarizes changes in the Company's customer-related accruals and allowances from December 31, 2014 to December 31, 2016 (in thousands):

	Wholesaler Fees and Commercial Rebates	Co-Pay and Other Patient Assistance	Government Rebates and Chargebacks	Total
Balance at December 31, 2014	$ 30,852	$ 30,047	$ 20,437	$ 81,336
Current provisions relating to sales in the year ended				
December 31, 2015	67,762	1,020,327	162,157	1,250,246
Adjustments relating to prior year sales	(1,657)	(121)	(3,842)	(5,620)
Payments relating to sales in the year ended				
December 31, 2015	(47,848)	(906,126)	(123,299)	(1,077,273)
Payments relating to sales in prior years	(28,241)	(29,926)	(16,545)	(74,712)
Hyperion acquisition on May 7, 2015	244	—	9,548	9,792
Balance at December 31, 2015	$ 21,112	$ 114,201	$ 48,456	$ 183,769
Current provisions relating to sales in the year ended				
December 31, 2016	133,012	1,701,287	278,877	2,113,176
Adjustments relating to prior year sales	671	—	(6,875)	(6,204)
Payments relating to sales in the year ended				
December 31, 2016	(87,147)	(1,496,240)	(224,343)	(1,807,730)
Payments relating to sales in prior years	(20,644)	(114,201)	(41,581)	(176,426)
Crealta acquisition on January 13, 2016	492	—	932	1,424
Raptor acquisition on October 25, 2016	155	96	6,126	6,377
Balance at December 31, 2016	$ 47,651	$ 205,143	$ 61,592	$ 314,386

NOTE 10 – ACCRUED EXPENSES

Accrued expenses as of December 31, 2016 and 2015 consisted of the following (in thousands):

	As of December 31	
	2016	2015
Payroll-related expenses	$ 61,691	$ 47,205
Consulting and professional services	33,614	17,160
Litigation settlement	32,500	—
Accrued interest	18,938	10,637
Accrued other	36,022	25,044
Accrued expenses	$ 182,765	$ 100,046

Accrued payroll-related expenses at December 31, 2016 included $15.0 million of severance and related employee costs as a result of the Raptor acquisition. The Company anticipates that a significant amount of the Raptor acquisition-related cash payments will be complete by the fourth quarter of 2017. Accrued payroll-related expenses at December 31, 2015 included $8.5 million of severance and related employee costs as a result of the Hyperion acquisition.

Accrued expenses as of December 31, 2016 included $32.5 million in relation to a litigation settlement with Express Scripts. See Note 15 for further details of this settlement.

“Accrued other” as of December 31, 2016 included $9.5 million related to a loss on inventory purchase commitments. During the year ended December 31, 2016, the Company committed to purchase additional units of ACTIMMUNE from Boehringer Ingelheim. These additional units of ACTIMMUNE were intended to cover anticipated demand if the results of the STEADFAST study of ACTIMMUNE for the treatment of FA had been successful. Following the discontinuation of the STEADFAST program, the Company recorded a loss of $14.3 million in “cost of goods sold” in the consolidated statement of comprehensive loss for firm, non-cancellable and unconditional purchase commitments for quantities in excess of the Company’s current forecasts for future demand. “Other long-term liabilities” as of December 31, 2016 includes an additional $4.8 million related to this loss on inventory purchase commitments. “Accrued other” as of December 31, 2016 also included $4.0 million related to costs to be incurred to discontinue the clinical trial.

NOTE 11 – ACCRUED ROYALTIES

Changes to the liability for royalties for medicines acquired through business combinations during the years ended December 31, 2016 and 2015 consisted of the following (in thousands):

Balance as of December 31, 2014	$74,212
Assumed RAVICTI and BUPHENYL contingent royalty liabilities	86,800
Assumed RAVICTI and BUPHENYL accrued royalties	579
Remeasurement of royalty liabilities	21,151
Royalty payments	(27,611)
Accretion expense	20,088
Balance as of December 31, 2015	175,219
Accrued royalties - current portion as of December 31, 2015	51,700
Accrued royalties, net of current as of December 31, 2015	123,519
Assumed KRYSTEXXA and MIGERGOT contingent royalty liabilities	51,300
Assumed KRYSTEXXA and MIGERGOT accrued royalties	1,401
Assumed PROCYSBI contingent royalty liabilities	102,000
Assumed PROCYSBI and QUINSAIR accrued royalties	2,705
Remeasurement of royalty liabilities	386
Royalty payments	(39,448)
Accretion expense	40,616
Other royalty expense	95
Balance as of December 31, 2016	334,274
Accrued royalties - current portion as of December 31, 2016	61,981
Accrued royalties, net of current as of December 31, 2016	$272,293

During the year ended December 31, 2016, based on higher sales of KRYSTEXXA and RAVICTI versus the Company's previous expectations and estimates for future sales of these medicines, the Company recorded a total charge of $24.6 million to cost of goods sold ($15.4 million related to KRYSTEXXA and $9.2 million related to RAVICTI). The Company also recorded a reduction of $24.2 million to cost of goods sold related to ACTIMMUNE and VIMOVO as a result of updated estimates of future sales of these medicines ($8.7 million related to ACTIMMUNE, including $2.5 million in connection with FA, and $15.5 million related to VIMOVO).

NOTE 12 – LONG-TERM INVESTMENTS

During the third quarter of 2015, the Company purchased 2,250,000 shares of common stock of Depomed, Inc. ("Depomed"), representing 3.75% of Depomed's then outstanding common stock. The shares were acquired at a cost of $71.8 million. During the fourth quarter of 2015, following the Company's decision to withdraw its offer to acquire Depomed, the Company sold all of its shares in Depomed, receiving sales proceeds of $42.8 million and the Company recognized a realized loss of $29.0 million in the consolidated statement of comprehensive income.

There were no gains or losses on long-term investments during the years ended December 31, 2016 or 2014.

NOTE 13 – SEGMENT AND OTHER INFORMATION

The Company has determined that it operates in one operating segment, which is the identification, development, acquisition and commercialization of differentiated and accessible medicines that address unmet medical needs. The Company's operating segment is reported in a manner consistent with the internal reporting provided to the chief operating decision maker ("CODM"). The Company's CODM has been identified as its chief executive officer.

The following table presents a summary of total net revenues by medicine (in thousands):

	Year Ended December 31,		
	2016	2015	2014
PENNSAID 2%	$304,433	$147,010	$—
DUEXIS	173,728	190,357	83,243
RAVICTI	151,532	86,875	—
VIMOVO	121,315	166,672	162,954
ACTIMMUNE	104,624	107,444	25,251
KRYSTEXXA	91,102	—	—
RAYOS	47,356	40,329	19,020
PROCYSBI	25,268	—	—
BUPHENYL	16,879	13,458	—
MIGERGOT	4,651	—	—
LODOTRA	4,193	4,899	6,487
QUINSAIR	1,039	—	—
Litigation settlement	(65,000)	—	—
Total net revenues	$981,120	$757,044	$296,955

The following table presents a summary of total net revenues by geography (in thousands):

	Year Ended December 31,		
	2016	2015	2014
United States	$964,041	$744,036	$290,396
Rest of world	17,079	13,008	6,559
Total net revenues	$981,120	$757,044	$296,955

The following table presents the amount and percentage of gross sales from customers that represented more than 10% of the Company’s gross sales included in its single operating segment (in thousands):

	Year ended December 31,								
	2016			2015			2014		
	Amount	% of Gross Sales		Amount	% of Gross Sales		Amount	% of Gross Sales	
Customer A	$1,413,774	44	%	$607,771	30	%	$256,237	43	%
Customer B	667,031	21	%	166,661	8	%	105,487	17	%
Customer C	355,920	11	%	207,009	10	%	113,751	19	%
Other Customers	797,463	24	%	1,075,853	52	%	125,356	21	%
Gross Sales	$3,234,188	100	%	$2,057,294	100	%	$600,831	100	%

The following table presents total tangible long-lived assets by location (in thousands):

	As of December 31,	
	2016	2015
United States	$19,542	$11,734
Ireland	3,550	1,985
Other	392	301
Total long-lived assets (1)	$23,484	$14,020

(1) Long-lived assets consist of property and equipment.

NOTE 14 – FAIR VALUE MEASUREMENTS

The following tables and paragraphs set forth the Company's financial instruments that are measured at fair value on a recurring basis within the fair value hierarchy. Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. The following describes three levels of inputs that may be used to measure fair value:

Level 1—Observable inputs such as quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company utilizes the market approach to measure fair value for its money market funds. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets or liabilities.

As of December 31, 2016, the Company's restricted cash included bank time deposits which were measured at fair value using Level 2 inputs and their carrying values were approximately equal to their fair values. Level 2 inputs, obtained from various third-party data providers, represent quoted prices for similar assets in active markets, or these inputs were derived from observable market data, or if not directly observable, were derived from or corroborated by other observable market data.

Other current assets recorded at fair value on a recurring basis are composed of investments held in a rabbi trust related to deferred compensation arrangements. Quoted prices for these investments, primarily in mutual funds, are available in active markets. Thus, the Company's investments related to deferred compensation arrangements are classified as Level 1 measurements in the fair value hierarchy.

There were no transfers between the different levels of the fair value hierarchy in 2016 or in 2015.

Assets and liabilities measured at fair value on a recurring basis

The following table sets forth the Company's financial assets and liabilities at fair value on a recurring basis as of December 31, 2016 and December 31, 2015 (in thousands):

	December 31, 2016			
	Level 1	Level 2	Level 3	Total
Assets:				
Bank time deposits	$—	$3,000	$ —	$3,000
Money market funds	170,000	—	—	170,000
Other current assets	3,038	—	—	3,038
Total assets at fair value	$173,038	$3,000	$ —	$176,038

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
Assets:				
Bank time deposits	$—	$1,000	$ —	$1,000
Money market funds	280,053	—	—	280,053
Other current assets	773	—	—	773
Total assets at fair value	$280,826	$1,000	$ —	$281,826

In accordance with the pronouncement guidance in ASC Topic 815 “Derivatives and Hedging”, the conversion option included within the Convertible Senior Notes was deemed to include an embedded derivative, which required the Company to bifurcate and separately account for the embedded derivative as a separate liability on its consolidated balance sheets. The estimated fair value was derived utilizing the binomial lattice approach for the valuation of convertible instruments. Assumptions used in the calculation included, among others, determining the appropriate credit spread using benchmarking analysis and solving for the implied credit spread, calculating the fair value of the stock component using a discounted risk free rate and borrowing cost and calculating the fair value of the note component using a discounted credit adjusted discount rate. Based on the assumptions used to determine the fair value of the derivative liability associated with the Convertible Senior Notes, the Company concluded that these inputs were Level 3 inputs.

The following table presents the assumptions used by the Company to determine the fair value of the conversion option embedded in the Convertible Senior Notes as of June 27, 2014, the date the HPI stockholders approved the issuance of in excess of 13,164,951 shares of HPI’s common stock upon conversion of the Convertible Senior Notes:

	June 27, 2014
Stock price	$15.96
Risk free rate	1.43 %
Borrowing cost	3.75 %
Weights	—
Credit spread (in basis points)	900
Volatility	40.00%
Initial conversion price	$5.36
Remaining time to maturity (in years)	4.4

On June 27, 2014, the Company conducted a fair value assessment to reflect the market value adjustments for the embedded derivative due to the increase in HPI’s common stock value and for changes in the fair value assumptions, and the Company recorded a $215.0 million loss in its results of operations for the three and six months ended June 30, 2014, respectively. The entire fair value of the derivative liability of $324.4 million was reclassified to additional paid-in capital on June 27, 2014.

NOTE 15 – COMMITMENTS AND CONTINGENCIES

Lease Obligations

The Company has the following office space lease agreements in place for real properties:

Location	Approximate Square Footage	Lease Expiry Date
Dublin, Ireland	18,900	November 3, 2029
Lake Forest, Illinois (1)	160,000	March 31, 2024

Novato, California	61,000	August 31, 2021
Deerfield, Illinois (2)	53,500	June 30, 2018
Brisbane, California	20,100	November 30, 2019
Mannheim, Germany	14,300	December 31, 2018
Chicago, Illinois	6,500	December 31, 2018
Utrecht, the Netherlands	5,400	October 31, 2019
Reinach, Switzerland	3,500	May 31, 2020

(1) In connection with the Lake Forest lease, the Company has provided a $2.0 million letter of credit to the landlord, through a commercial bank.

(2) The Company vacated the premises in Deerfield, Illinois, and began occupying the premises in Lake Forest, Illinois, in January 2016.

The Company recognizes rent expense on a monthly basis over the lease term based on a straight-line method. Rent expense was $5.1 million, $2.5 million and $0.6 million for the years ended December 31, 2016, 2015 and 2014, respectively.

As of December 31, 2016, minimum future cash payments due under lease obligations were as follows (in thousands):

	2017	2018	2019	2020	2021	2022 & Thereafter	Total
Operating lease obligations	$7,716	$7,611	$6,753	$5,968	$5,316	$ 15,856	$49,220

Annual Purchase Commitments

In August 2007, the Company entered into a manufacturing and supply agreement with Jagotec AG (“Jagotec”), which was amended in March 2011 and in January 2017. Under the agreement, Jagotec or its affiliates are required to manufacture and supply RAYOS/LODOTRA exclusively to the Company in bulk. The earliest the agreement can expire is December 31, 2023, and the minimum purchase commitment is in force until December 2023. At December 31, 2016, the minimum purchase commitment based on tablet pricing in effect under the agreement was $6.9 million through December 2023.

In May 2011, the Company entered into a manufacturing and supply agreement with Sanofi-Aventis U.S. LLC (“Sanofi-Aventis U.S.”), and amended the agreement effective as of September 25, 2013. Pursuant to the agreement, as amended, Sanofi-Aventis U.S. is obligated to manufacture and supply DUEXIS to the Company in final, packaged form, and the Company is obligated to purchase DUEXIS exclusively from Sanofi-Aventis U.S. for the commercial requirements of DUEXIS in North America, South America and certain countries and territories in Europe, including the European Union member states and Scandinavia. At December 31, 2016, the Company had a binding purchase commitment to Sanofi-Aventis U.S. for DUEXIS of $3.0 million, which is to be delivered through March 2017.

In July 2013, Vidara and Boehringer Ingelheim entered into an exclusive supply agreement, which the Company assumed as a result of the Vidara Merger and amended effective as of June 1, 2015. Under the agreement, Boehringer Ingelheim is required to manufacture and supply interferon gamma-1b (ACTIMMUNE) to the Company. The Company is required to purchase minimum quantities of finished medicine per annum through July 2020. During the year ended December 31, 2016, the Company committed to purchase additional amounts of ACTIMMUNE from Boehringer Ingelheim. These additional amounts were intended to cover anticipated demand if the results of the STEADFAST study of ACTIMMUNE for the treatment of FA had been successful. As of December 31, 2016, the minimum binding purchase commitment to Boehringer Ingelheim was $23.9 million (converted using a Dollar-to-Euro exchange rate of 1.052) through July 2020. Following the discontinuation of the STEADFAST program, the Company recorded a loss of $14.3 million in “cost of goods sold” in the consolidated statement of comprehensive loss for a portion of this commitment which represented firm, non-cancellable and unconditional purchase commitments for quantities in excess of the Company’s current forecasts for future demand. During the year ended December 31, 2016, the Company also committed to incur an additional $14.9 million for the harmonization of the drug substance manufacturing process with Boehringer Ingelheim. These additional costs will be incurred during the years 2017 through 2021 and have not been included in the Company’s consolidated statement of comprehensive loss or consolidated balance sheet at December 31, 2016.

In November 2013, the Company entered into a long-term master manufacturing services and product agreement with Patheon Pharmaceuticals Inc. (“Patheon”) pursuant to which Patheon is obligated to manufacture VIMOVO for the Company through December 31, 2019. The Company agreed to purchase a specified percentage of VIMOVO requirements for the United States from Patheon. The Company must pay an agreed price for final, packaged VIMOVO supplied by Patheon as set forth in the Patheon manufacturing agreement, subject to adjustments, including certain unilateral adjustments by Patheon, such as annual adjustments for inflation and adjustments to account for certain increases in the cost of components of VIMOVO other than active materials. The Company issues 12-month

forecasts of the volume of VIMOVO that the Company expects to order. The first six months of the forecast are considered binding firm orders. At December 31, 2016, the Company had a binding purchase commitment with Patheon for VIMOVO of $1.1 million through March 2017.

In October 2014, in connection with the acquisition of the U.S. rights to PENNSAID 2% from Nuvo, the Company and Nuvo entered into an exclusive supply agreement. Under the supply agreement, which was amended in February 2016, Nuvo is obligated to manufacture and supply PENNSAID 2% to the Company. The term of the supply agreement is through December 31, 2029, but the agreement may be terminated earlier by either party for any uncured material breach by the other party of its obligations under the supply agreement or upon the bankruptcy or similar proceeding of the other party. At least 90 days prior to the first day of each calendar month during the term of the supply agreement, the Company submits a binding written purchase order to Nuvo for PENNSAID 2% in minimum batch quantities. At December 31, 2016, the Company had a binding purchase commitment with Nuvo for PENNSAID 2% of $3.6 million through March 2017.

In November 2010, Raptor and Patheon entered into a manufacturing services agreement, which the Company assumed as a result of its acquisition of Raptor. Under the agreement, which was amended in April 2012 and June 2013, Patheon is obligated to manufacture PROCYSBI for the Company through December 31, 2019. The Company must provide Patheon with rolling, non-binding forecasts of PROCYSBI, with a portion of the forecast being a firm written order. In November 2010, Raptor and Cambrex Profarmaco Milano ("Cambrex") entered into an API supply agreement, which the Company assumed as a result of its acquisition of Raptor. Under the agreement, which was amended in April 2013 and August 2016, Cambrex is obligated to manufacture PROCYSBI API for the Company through November 30, 2020. The Company must provide Cambrex with rolling, non-binding forecasts, with a portion of the forecast being the minimum floor of the firm order that must be placed. At December 31, 2016, the Company had a binding purchase commitment with Patheon for PROCYSBI of $1.2 million through April 2017 and with Cambrex for PROCYSBI API of $1.6 million through March 2017.

Excluding the above, additional purchase orders relating to the manufacture of BUPHENYL, PROCYSBI, QUINSAIR and RAVICTI of $6.1 million were outstanding at December 31, 2016. In addition to these purchase orders, the Company's manufacturing agreement with Lyne Laboratories Inc. in relation to RAVICTI provides for a minimum purchase amount of $0.5 million for 2017.

In March 2007, Savient Pharmaceuticals, Inc. (as predecessor in interest to Crealta), entered into a commercial supply agreement with Bio-Technology General (Israel) Ltd ("BTG Israel") for the production of the bulk KRYSTEXXA medicine ("bulk product"). The Company assumed this agreement as part of the Crealta acquisition and amended the agreement in September 2016 (the "September 2016 Amendment"). Under this agreement, the Company has agreed to purchase certain minimum annual order quantities and is obligated to purchase at least 80 percent of its annual world-wide bulk product requirements from BTG Israel. The term of the agreement runs until December 31, 2030, and will automatically renew for successive three year periods unless earlier terminated by either party upon three years prior written notice. The agreement may be terminated earlier by either party in the event of a force majeure, liquidation, dissolution, bankruptcy or insolvency of the other party, uncured material breach by the other party or after January 1, 2024, upon three years prior written notice. Under the agreement if the manufacture of the bulk product is moved out of Israel, the Company may be required to obtain the approval of the Israeli Office of the Chief Scientist ("OCS") because certain KRYSTEXXA intellectual property was initially developed with a grant funded by the OCS and the Company may be required to pay the OCS additional amounts as a repayment for the OCS grant funding. In December 2015, Crealta received a notice of termination from BTG Israel and, as of the Crealta acquisition date, it had been considered probable that the manufacture of the KRYSTEXXA bulk product would be moved outside of Israel and the Company would have been required to pay additional amounts to OCS, estimated at approximately $6.9 million. This estimated obligation was recorded as an assumed contingent liability as of the Crealta acquisition date (see Note 4 for further details) and was included in "Other long-term liabilities" in the consolidated balance sheet. Following the execution of the September 2016 Amendment, the Company determined it would not move the manufacture of the KRYSTEXXA bulk product outside of Israel, and released the $6.9 million assumed contingent liability to "other income (expense)" in the consolidated statement of comprehensive loss during the year ended December 31, 2016. The Company issues 18-month forecasts of the volume of KRYSTEXXA that the Company expects to order. The first six months of the forecast are considered binding firm orders. At December 31, 2016, the Company has a binding purchase commitment with BTG Israel for KRYSTEXXA of $5.0 million per annum through December 31, 2030.

Royalty Agreements

RAYOS/LODOTRA

In connection with an August 2004 development and license agreement with Vectura Group plc (as successor in interest to SkyePharma AG) ("Vectura"), and Jagotec, a wholly owned subsidiary of Vectura, regarding certain proprietary technology and know-how owned by Vectura, Jagotec is entitled to receive a single digit percentage royalty on net sales of RAYOS/LODOTRA and on any sub-licensing income, which includes any payments not

calculated based on the net sales of RAYOS/LODOTRA, such as license fees, lump sum and milestone payments.

VIMOVO

The Company entered into a license agreement with Pozen Inc. who subsequently entered into a business combination with Tribute Pharmaceuticals Canada Inc. to become known as Aralez Pharmaceuticals Inc. ("Aralez"). Under this agreement, the Company is required to pay Aralez a flat 10% royalty on net sales of VIMOVO and other medicines sold by the Company, its affiliates or sublicensees during the royalty term that contain gastroprotective agents in a single fixed combination oral solid dosage form with nonsteroidal anti-inflammatory drugs, subject to minimum annual royalty obligations of $7.5 million. These minimum royalty obligations will continue for each year during which one of Aralez's patents covers such medicines in the United States and there are no competing medicines in the United States. The royalty rate may be reduced to a mid-single digit royalty rate as a result of loss of market share to competing medicines. The Company's obligation to pay royalties to Aralez will expire upon the later of (a) expiration of the last-to-expire of certain patents covering such medicines in the United States, and (b) ten years after the first commercial sale of such medicines in the United States.

In November 2013, the Company, AstraZeneca AB ("AstraZeneca") and Aralez entered into a letter agreement. Under the letter agreement, the Company and AstraZeneca agreed to pay Aralez milestone payments upon the achievement by the Company and AstraZeneca, collectively, of certain annual aggregate global net sales thresholds ranging from $550.0 million to $1.25 billion with respect to VIMOVO. The aggregate milestone payment amount that may be owed by AstraZeneca and the Company, collectively, under the letter agreement is $260.0 million, with the amount payable by each of the Company and AstraZeneca with respect to each milestone to be based upon the proportional sales achieved by each of the Company and AstraZeneca, respectively, in the applicable year.

ACTIMMUNE

Under a license agreement, as amended, with Genentech Inc. ("Genentech"), who was the original developer of ACTIMMUNE, the Company is or was obligated to pay royalties to Genentech on its net sales of ACTIMMUNE as follows:

- For the period from November 26, 2014 through May 5, 2018, a royalty in the 20% to 30% range for the first $3.7 million in net sales achieved in any calendar year and in the 1% to 9% range for all additional net sales in any year; and
- From May 6, 2018 and for so long as the Company continues to commercially sell ACTIMMUNE, an annual royalty in the low single digits as a percentage of annual net sales.

Under the terms of an assignment and option agreement with Connetics Corporation (which was the predecessor parent company to InterMune Pharmaceuticals Inc. and is now part of GlaxoSmithKline), ("Connetics"), the Company is obligated to pay royalties to Connetics on the Company's net sales of ACTIMMUNE as follows:

- Low-single digits as a percentage of net sales of ACTIMMUNE in the United States.

RAVICTI

Under the terms of an asset purchase agreement with Ucyclyd, the Company is obligated to pay to Ucyclyd tiered mid to high single-digit royalties on its global net sales of RAVICTI. Under the terms of a license agreement with Saul W. Brusilow, M.D. and Brusilow, the Company is obligated to pay low single-digit royalties to Brusilow on net sales of RAVICTI that are covered by a valid claim of a licensed patent.

BUPHENYL

Under the terms of an amended and restated collaboration agreement with Ucyclyd, the Company is obligated to pay to Ucyclyd tiered mid to high single-digit royalties on its net sales in the United States of BUPHENYL to urea cycle disorder patients outside of the U.S. Food and Drug Administration ("FDA")-approved labeled age range for RAVICTI.

KRYSTEXXA

Under the terms of a license agreement with Duke and MVP, the Company is obligated to pay Duke a mid-single digit royalty on its global net sales of KRYSTEXXA and a low-double digit royalty on any global sublicense revenue. The Company is also obligated to pay MVP a mid-single digit royalty on its net sales of KRYSTEXXA outside of the United States and a low-double digit royalty on any sublicense revenue outside of the United States.

PROCYSBI

Under the terms of a license agreement with UCSD, the Company is obligated to pay to UCSD tiered low to mid single-digit royalties on its net sales of PROCYSBI.

The royalty obligations for ACTIMMUNE, BUPHENYL, KRYSTEXXA, MIGERGOT, PROCYSBI, QUINSAIR, RAVICTI and VIMOVO are included in accrued royalties on the Company's consolidated balance sheets.

For all of the royalty agreements entered into by the Company, a total expense of $46.5 million, $45.5 million and $21.4 million was recorded in cost of goods sold for the years ended December 31, 2016, 2015 and 2014, respectively.

Other Agreements

On November 8, 2016, the Company entered into a collaboration and option agreement with a privately held life-science entity. Under the terms of the agreement, the privately held life-science entity will conduct certain research and pre-clinical and clinical development activities. Upon execution of the agreement, the Company paid $0.1 million for the option to acquire certain of the privately held life-science entity's assets for $25.0 million, which is exercisable on specified key dates. Under the collaboration and option agreement, the Company will be required to pay up to $9.8 million upon the attainment of various milestones, primarily to fund clinical development costs for the medicine.

Contingencies

The Company is subject to claims and assessments from time to time in the ordinary course of business. The Company's management does not believe that any such matters, individually or in the aggregate, will have a material adverse effect on the Company's business, financial condition, results of operations or cash flows. In addition, the Company from time to time has billing disputes with vendors in which amounts invoiced are not in accordance with the terms of their contracts.

In November 2015, Express Scripts filed suit against the Company in Delaware Superior Court, Newcastle County, asserting claims for breach of contract, breach of the implied covenant of good faith and fair dealing, unjust enrichment, and declaratory relief arising from the parties' 2012 Preferred Savings Grid Rebate Program Agreement. The Company filed a counter-claim against Express Scripts for breach of contract, breach of the implied covenant of good faith and fair dealing, and declaratory relief arising from Express Scripts' breach of the rebate agreement. In September 2016, the Company entered into a settlement agreement and mutual release with Express Scripts pursuant to which the Company and Express Scripts were released from any and all claims relating to the litigation without admitting any fault or wrongdoing and the Company agreed to pay Express Scripts $65.0 million. The settlement amount will be paid to Express Scripts in installments, with 50 percent of the installment paid in the fourth quarter of 2016, 25 percent due in the first quarter of 2017 and 25 percent due in the second quarter of 2017. The full amount of this settlement has been accounted for as a reduction of "net sales" in the consolidated statements of comprehensive loss for the year ended December 31, 2016.

In November 2015, the Company received a subpoena from the U.S. Attorney's Office for the Southern District of New York requesting documents and information related to its patient access programs and other aspects of its marketing and commercialization activities. The Company is unable to predict how long this investigation will continue or its outcome, but it has incurred and anticipates that it may continue to incur significant costs in connection with the investigation, regardless of the outcome. The Company may also become subject to similar investigations by other governmental agencies. The investigation by the U.S. Attorney's Office and any additional investigations of the Company's patient access programs and sales and marketing activities may result in damages, fines, penalties or other administrative sanctions against the Company.

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnifications. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future, but have not yet been made. In connection with the federal securities class action litigation (described in Note 16 below), the Company has received notice from the Underwriter Defendants (as defined below) of their intention to seek indemnification and has received, but not yet paid, several invoices from the Underwriter Defendants. The Company may record charges in the future as a result of these indemnification obligations.

In accordance with its memorandum and articles of association, the Company has indemnification obligations to its officers and directors for certain events or occurrences, subject to certain limits, while they are serving at the Company's request in such capacity. Additionally, the Company has entered into, and intends to continue to enter into, separate indemnification agreements with its directors and executive officers. These agreements, among other things, require the Company to indemnify its directors and executive officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of their services as one of the Company's directors or executive officers, or any of the Company's subsidiaries or any other company or enterprise to which the person provides services at the Company's request. In connection with the federal securities class action litigation (described in Note 16 below), the Company has paid legal fees and costs on behalf of itself and the current and former officers and directors of the Company who are named as defendants in that litigation. The Company also has a director and officer insurance policy that enables it to recover a portion of any amounts paid for future potential claims. Certain of the Company's officers and directors had also entered into separate indemnification agreements with HPI prior to the Vidara Merger.

NOTE 16 – LEGAL PROCEEDINGS

On July 15, 2013, the Company received a Paragraph IV Patent Certification from Watson Laboratories, Inc.—Florida, known as Actavis Laboratories FL, Inc. ("Actavis FL"), advising that Actavis FL had filed an Abbreviated New Drug Application ("ANDA") with the FDA for a generic version of RAYOS, containing up to 5 mg of prednisone. On August 26, 2013, the Company, together with Jagotec, filed suit in the United States District Court for the District of New Jersey against Actavis FL, Actavis Pharma, Inc., Andrx Corp., and Actavis, Inc. seeking an injunction to prevent the approval of the ANDA.

On October 1, 2015, the Company's subsidiary Horizon Pharma Switzerland GmbH, as well as Jagotec, entered into a license and settlement agreement (the "Actavis settlement agreement") with Actavis FL relating to the Company's and Jagotec's patent infringement litigation against Actavis FL. In accordance with legal requirements, the Company, Jagotec and Actavis FL agreed to submit the Actavis settlement agreement to the U.S. Federal Trade Commission ("FTC") and the U.S. Department of Justice ("DOJ") for review. The parties submitted the Actavis settlement agreement to the FTC and DOJ for review and no issues were raised by either. The parties agreed to file stipulations of dismissal with the court regarding the litigation and the court entered the stipulation and closed the case on December 4, 2015. The Actavis settlement agreement provides for a full settlement and release by each party of all claims that relate to the litigation or under the patents with respect to Actavis FL's generic version of RAYOS tablets.

Under the Actavis settlement agreement, the Company and Jagotec granted Actavis FL a non-exclusive license to manufacture and commercialize Actavis FL's generic version of RAYOS tablets in the United States after the generic entry date (as defined below) and to take steps necessary to develop inventory of, and prepare to commercialize, Actavis FL's generic version of RAYOS tablets during certain limited periods prior to the generic entry date. The

Company and Jagotec also agreed that during the 180 days after the generic entry date, the license granted to Actavis FL would be exclusive with respect to any third-party generic version of RAYOS tablets.

Under the Actavis settlement agreement, the generic entry date is December 23, 2022; however, Actavis FL may be able to enter the market earlier under certain circumstances. Such events relate to the resolution of any other third-party RAYOS patent litigation, the entry of other generic versions of RAYOS tablets or certain substantial reductions in RAYOS prescriptions over specified periods of time.

The Company and Jagotec also agreed not to sue or assert any claim against Actavis FL for infringement of any patent or patent application owned or controlled by the Company or Jagotec during the term of the Actavis settlement agreement based on Actavis FL's generic version of RAYOS tablets in the United States. In turn, Actavis FL agreed not to challenge the validity or enforceability of the licensed patents.

If the Company or Jagotec enter into any similar agreements with other parties with respect to generic versions of RAYOS tablets, the Company and Jagotec agreed to amend the Actavis settlement agreement to provide Actavis FL with terms that are no less favorable than those provided to such other parties with respect to the license terms, generic entry date, permitted pre-market activities and notice provisions.

On November 13, 2014, the Company received a Paragraph IV Patent Certification from Watson Laboratories, Inc. ("Watson Laboratories") advising that Watson Laboratories had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On December 23, 2014, the Company filed suit in the United States District Court for the District of New Jersey against Watson Laboratories, Actavis, Inc., and Actavis plc (collectively "Actavis") seeking an injunction to prevent the approval of the ANDA. Since then, Watson Laboratories, Inc. changed its name to Actavis Laboratories UT, Inc., and remains the current holder of the ANDA. The lawsuit alleged that Actavis has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market a generic version of PENNSAID 2% prior to the expiration of certain of the Company's patents listed in the FDA's Orange Book ("Orange Book"). The commencement of the patent infringement lawsuit stays, or bars, FDA approval of Actavis' ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid.

On June 30, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of U.S. Patent No. 9,066,913. On August 11, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of U.S. Patent No. 9,101,591. On September 17, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of U.S. Patent No. 9,132,110. All three patents, U.S. Patent Nos. 9,066,913, 9,101,591, and 9,132,110 are listed in the Orange Book and have claims that cover PENNSAID 2%. These three cases have since been consolidated with the case filed against Actavis on December 23, 2014.

On October 27, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of U.S. Patent Nos. 9,168,304 and 9,168,305. On February 5, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of U.S. Patent No. 9,220,784. All three patents, U.S. Patent Nos. 9,168,304, 9,168,305, and 9,220,784 are listed in the Orange Book and have claims that cover PENNSAID 2%. These two cases have since been consolidated with the cases filed against Actavis on December 23, 2014, June 30, 2015, August 11, 2015, and September 17, 2015. A trial date for these actions has been set for March 21, 2017.

On August 18, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of U.S. Patent Nos. 9,339,551, 9,339,552, 9,370,501, and 9,375,412. All four patents, U.S. Patent Nos. 9,339,551, 9,339,552, 9,370,501, and 9,375,412, are listed in the Orange Book and have claims that cover PENNSAID 2%. This case is still pending, but has been stayed pending resolution of the trial in the above consolidated actions.

The Company received from Actavis a Paragraph IV Patent Certification Notice Letter dated September 27, 2016, against Orange Book listed U.S. Patent Nos. 9,415,029, advising that Actavis had filed an ANDA with the FDA for a generic version of PENNSAID 2%.

On December 2, 2014, the Company received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,741,956 from Paddock Laboratories, LLC ("Paddock") advising that Paddock had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On

January 9, 2015, the Company received from Paddock another Paragraph IV Patent Certification against newly Orange Book listed U.S. Patent No. 8,871,809. On January 13, 2015 and January 14, 2015, the Company filed suits in the United States District Court for the District of New Jersey and the United States District Court for the District of Delaware, respectively, against Paddock seeking an injunction to prevent the approval of the ANDA. The lawsuits alleged that Paddock has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% prior to the expiration of certain of the Company's patents listed in the Orange Book.

On May 6, 2015, the Company entered into a settlement and license agreement (the "Perrigo settlement agreement") with Perrigo Company plc and its subsidiary Paddock (collectively, "Perrigo"), relating to the Company's patent infringement litigation against Perrigo. The Perrigo settlement agreement provides for a full settlement and release by both the Company and Perrigo of all claims that were or could have been asserted in the litigation and that arise out of the issues that were the subject of the litigation or Perrigo's generic version of PENNSAID 2%. The Perrigo settlement agreement also contemplated the filing of a joint stipulation of dismissal by the parties. This stipulation of dismissal was entered by the district court on May 13, 2015.

Under the Perrigo settlement agreement, the Company granted Perrigo a non-exclusive license to manufacture and commercialize Perrigo's generic version of PENNSAID 2% in the United States after the license effective date (as defined below) and to take steps necessary to develop inventory of, and prepare to commercialize, Perrigo's generic version of PENNSAID 2% during certain limited periods prior to the license effective date.

Under the Perrigo settlement agreement, the license effective date is January 10, 2029; however, Perrigo may be able to enter the market earlier under certain circumstances. Such events relate to the resolution of any other third-party PENNSAID 2% patent litigation, the entry of other third-party generic versions of PENNSAID 2% or certain substantial reductions in the Company's PENNSAID 2% shipments over specified periods of time.

Under the Perrigo settlement agreement, the Company also agreed not to sue or assert any claim against Perrigo for infringement of any patent or patent application owned or controlled by the Company during the term of the license granted in the Perrigo settlement agreement based on the manufacture, use, sale, offer for sale, or importation of Perrigo's generic version of PENNSAID 2% in the United States.

In certain circumstances following the entry of other third-party generic versions of PENNSAID 2%, the Company may be required to supply Perrigo PENNSAID 2% as its authorized distributor of generic PENNSAID 2%, with the Company receiving specified percentages of any net sales by Perrigo. The Company also agreed that if it enters into any similar agreements with other parties with respect to generic versions of PENNSAID 2%, the Company will amend the Perrigo settlement agreement to provide Perrigo with terms that are no less favorable than those provided to such other parties.

On February 2, 2015, the Company received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 from Taro Pharmaceuticals USA, Inc. and Taro Pharmaceutical Industries, Ltd. (collectively, "Taro") advising that Taro had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On March 13, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Taro seeking an injunction to prevent the approval of the ANDA.

On September 9, 2015, certain subsidiaries of the Company (the "Horizon Subsidiaries") entered into a settlement and license agreement with Taro (the "Taro settlement agreement") relating to the Horizon Subsidiaries' patent infringement litigation against Taro. In accordance with legal requirements, the Horizon Subsidiaries and Taro submitted the Taro settlement agreement to the FTC and DOJ for review, and no issues have been raised by the FTC and DOJ. The Horizon Subsidiaries and Taro have also filed stipulations of dismissal with the courts regarding the litigation, with these dismissals being entered by the district court on November 3, 2015. The Taro settlement agreement provides for a full settlement and release by both us and Taro of all claims that were or could have been asserted in the Litigation and that arise out of the issues that were subject of the litigation or Taro's generic version of PENNSAID 2%.

Under the Taro settlement agreement, the Horizon Subsidiaries granted Taro a non-exclusive license to manufacture and commercialize Taro's generic version of PENNSAID 2% in the United States after the license effective date (as defined below) and to take steps necessary to develop inventory of, and prepare to commercialize, Taro's generic version of PENNSAID 2% during certain limited periods prior to the license effective date.

Under the Taro settlement agreement, the license effective date is January 10, 2029; however, Taro may be able to enter the market earlier under certain circumstances. Such events relate to the resolution of any other third-party PENNSAID 2% patent litigation, the entry of other third-party generic versions of PENNSAID 2% or certain substantial reductions in the Company's PENNSAID 2% shipments over specified periods of time.

Under the Taro settlement agreement, the Horizon Subsidiaries also agreed not to sue or assert any claim against Taro for infringement of any patent or patent application owned or controlled by the Horizon Subsidiaries during the term of the license granted in the Taro settlement agreement based on the manufacture, use, sale, offer for sale, or importation of Taro's generic version of PENNSAID 2% in the United States.

The Horizon Subsidiaries also agreed that if they enter into any similar agreements with other parties with respect to generic versions of PENNSAID 2%, the Horizon Subsidiaries will amend the Taro settlement agreement to provide Taro with terms that are no less favorable than those provided to the other parties.

On March 18, 2015, the Company received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 from Lupin Limited advising that Lupin Limited had filed an ANDA with the FDA for generic version of PENNSAID 2%. On April 30, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Lupin Limited and Lupin Pharmaceuticals Inc. (collectively, "Lupin"), seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that Lupin has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% prior to the expiration of certain of the Company's patents listed in the Orange Book. The commencement of the patent infringement lawsuit stays, or bars, FDA approval of Lupin's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid.

On June 30, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Lupin for patent infringement of U.S. Patent No. 9,066,913. On August 11, 2015, the Company filed an amended complaint in the United States District Court for the District of New Jersey against Lupin that added U.S. Patent No. 9,101,591 to the litigation with respect to U.S. Patent No. 9,066,913. On September 17, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Lupin for patent infringement of U.S. Patent No. 9,132,110. All three patents, U.S. Patent Nos. 9,066,913, 9,101,591, and 9,132,110 are listed in the Orange Book and have claims that cover PENNSAID 2%.

On October 27, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Lupin for patent infringement of U.S. Patent Nos. 9,168,304 and 9,168,305. On February 5, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Lupin for patent infringement of U.S. Patent No. 9,220,784. On August 18, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Lupin for patent infringement of U.S. Patent Nos. 9,339,551, 9,339,552, 9,370,501, and 9,375,412. All seven patents, U.S. Patent Nos. 9,168,304, 9,168,305, 9,220,784, 9,339,551, 9,339,552, 9,370,501, and 9,375,412 are listed in the Orange Book and have claims that cover PENNSAID 2%. All of the infringement actions brought against Lupin remain pending. The court has not yet set a trial date for the Lupin actions.

The Company received from Teligent, Inc., formerly known as IGI Laboratories, Inc. ("Teligent"), a Paragraph IV Patent Certification dated March 24, 2015 against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 advising that Teligent had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On May 21, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Teligent seeking an injunction to prevent the approval of the ANDA. The lawsuit alleged that Teligent has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% prior to the expiration of certain of the Company's patents listed in the Orange Book. The commencement of the patent infringement lawsuit stays, or bars, FDA approval of Teligent's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid.

On June 30, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Teligent for patent infringement of U.S. Patent No. 9,066,913. On August 11, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Teligent for patent infringement of U.S. Patent No.

9,101,591. On September 17, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Teligent for patent infringement of U.S. Patent No. 9,132,110. All three patents, U.S. Patent Nos. 9,066,913, 9,101,591, and 9,132,110 are listed in the Orange Book and have claims that cover PENNSAID 2%.

On October 27, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Teligent for patent infringement of U.S. Patent Nos. 9,168,304 and 9,168,305. On February 5, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Teligent for patent infringement of U.S. Patent No. 9,220,784. All three patents, U.S. Patent Nos. 9,168,304, 9,168,305, and 9,220,784 are listed in the Orange Book and have claims that cover PENNSAID 2%.

The Company entered into a settlement and license agreement with Teligent (the "Teligent settlement agreement"), effective May 9, 2016, relating to the patent infringement litigation against Teligent. In accordance with legal requirements, the Company and Teligent submitted the Teligent settlement agreement to the FTC and DOJ for review, and no issues have been raised by the FTC and DOJ. The Company and Teligent have also filed stipulations of dismissal with the district court regarding the litigation, with these dismissals having been entered by the district court on May 2, 2016. The Teligent settlement agreement provides for a full settlement and release by both the Company and Teligent of all claims that were or could have been asserted in the litigation and that arise out of the issues that were subject of the litigation or Teligent's generic version of PENNSAID 2%.

Under the Teligent settlement agreement, the Company granted Teligent a non-exclusive license to manufacture and commercialize Teligent's generic version of PENNSAID 2% in the United States after the license effective date (as defined below) and to take steps necessary to develop inventory of, and prepare to commercialize, Teligent's generic version of PENNSAID 2% during certain limited periods prior to the license effective date.

Under the Teligent settlement agreement, the license effective date is January 10, 2029; however, Teligent may be able to enter the market earlier under certain circumstances. Such events relate to the resolution of any other third-party PENNSAID 2% patent litigation, the entry of other third-party generic versions of PENNSAID 2% or certain substantial reductions in the Company's PENNSAID 2% shipments over specified periods of time.

Under the Teligent settlement agreement, the Company also agreed not to sue or assert any claim against Teligent for infringement of any patent or patent application owned or controlled by the Company during the term of the license granted in the Teligent settlement agreement based on the manufacture, use, sale, offer for sale, or importation of Teligent's generic version of PENNSAID 2% in the United States.

In certain circumstances following the entry of other third-party generic versions of PENNSAID 2%, the Company may be required to supply Teligent PENNSAID 2% as an authorized distributor of generic PENNSAID 2%, with the Company receiving specified percentages of any net sales by Teligent. The Company also agreed that if it enters into any similar agreements with other parties with respect to generic versions of PENNSAID 2%, the Company will amend the Teligent settlement agreement to provide Teligent with terms that are no less favorable than those provided to the other parties.

The Company received from Amneal Pharmaceuticals LLC ("Amneal") a Paragraph IV Patent Certification dated April 2, 2015 against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 advising that Amneal had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On May 15, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Amneal seeking an injunction to prevent the approval of the ANDA. The lawsuit alleged that Amneal has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% prior to the expiration of certain of the Company's patents listed in the Orange Book. The commencement of the patent infringement lawsuit stays, or bars, FDA approval of Amneal's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid.

On June 30, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Amneal for patent infringement of U.S. Patent No. 9,066,913. On August 11, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Amneal for patent infringement of U.S. Patent No.

9,101,591. On September 17, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Amneal for patent infringement of U.S. Patent No. 9,132,110. All three patents, U.S. Patent Nos. 9,066,913, 9,101,591, and 9,132,110 are listed in the Orange Book and have claims that cover PENNSAID 2%.

On October 27, 2015, the Company filed suit in the United States District Court for the District of New Jersey against Amneal for patent infringement of U.S. Patent Nos. 9,168,304 and 9,168,305. On February 5, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Amneal for patent infringement of U.S. Patent No. 9,220,784. All three patents, U.S. Patent Nos. 9,168,304, 9,168,305, and 9,220,784 are listed in the Orange Book and have claims that cover PENNSAID 2%.

On April 18, 2016, the Company entered into a settlement and license agreement (the "Amneal settlement agreement") with Amneal relating to the Company's patent infringement litigation against Amneal. In accordance with legal requirements, the Company and Amneal submitted the Amneal settlement agreement to the FTC and DOJ for review, and no issues have been raised by the FTC and DOJ. The Company and Amneal have also filed a stipulation of dismissal with the court regarding the litigation. The Amneal settlement agreement provides for a full settlement and release by both the Company and Amneal of all claims that were or could have been asserted in the litigation and that arise out of the issues that were the subject of the litigation or Amneal's generic version of PENNSAID 2%.

Under the Amneal settlement agreement, the Company granted Amneal a non-exclusive license to manufacture and commercialize Amneal's generic version of PENNSAID 2% in the United States after the license effective date (as defined below) and to take steps necessary to develop inventory of, and prepare to commercialize, Amneal's generic version of PENNSAID 2% during certain limited periods prior to the license effective date.

Under the Amneal settlement agreement, the license effective date is January 10, 2029; however, Amneal may be able to enter the market earlier under certain circumstances. Such events relate to the resolution of any other third-party PENNSAID 2% patent litigation or the entry of other third-party generic versions of PENNSAID 2%.

Under the Amneal settlement agreement, the Company also agreed not to sue or assert any claim against Amneal for infringement of any patent or patent application owned or controlled by the Company during the term of the license granted in Amneal settlement agreement based on the manufacture, use, sale, offer for sale, or importation of Amneal's generic version of PENNSAID 2% in the United States.

In certain circumstances following the entry of other third-party generic versions of PENNSAID 2%, the Company may be required to supply Amneal PENNSAID 2% as a non-exclusive, authorized distributor of generic PENNSAID 2%, with the Company receiving specified percentages of any net sales by Amneal. The Company also agreed that if it enters into any similar agreements with other parties with respect to generic versions of PENNSAID 2%, the Company will amend the Amneal settlement agreement to provide Amneal with terms that are no less favorable than those provided to the other parties.

The Company received from Apotex Inc. ("Apotex") a Paragraph IV Patent Certification Notice Letter dated April 1, 2016, against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, 8,871,809, 9,066,913, 9,101,591, 9,132,110, 9,168,304, 9,168,305 and 9,220,784 advising that Apotex had filed an ANDA with the FDA for a generic version of PENNSAID 2%. The Company also received from Apotex a second Paragraph IV Patent Certification Notice Letter dated June 30, 2016, against Orange Book listed U.S. Patent Nos. 9,339,551 and 9,339,552, advising that Apotex had filed an ANDA with the FDA for a generic version of PENNSAID 2%. The Company also received from Apotex a third Paragraph IV Patent Certification Notice Letter dated September 21, 2016, against Orange Book listed U.S. Patent No. 9,415,029, advising that Apotex had filed an ANDA with the FDA for a generic version of PENNSAID 2%.

Currently, patent litigation is pending in the United States District Court for the District of New Jersey against three generic companies intending to market VIMOVO prior to the expiration of certain of the Company's patents listed in the Orange Book. These cases are in the United States District Court for the District of New Jersey. They are collectively known as the VIMOVO cases, and involve the following sets of defendants: (i) Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd. (collectively, "Dr. Reddy's"); (ii) Lupin Ltd. and Lupin Pharmaceuticals Inc. (collectively, "Lupin"); and (iii) Mylan Pharmaceuticals Inc., Mylan Laboratories Limited, and Mylan Inc. (collectively, "Mylan").Patent litigation in the United States District Court for the District of New Jersey against a fourth generic company, Actavis Laboratories FL., Inc. and Actavis Pharma, Inc. (collectively, "Actavis Pharma"), was dismissed on January 10, 2017 after the court granted Actavis' motion to compel enforcement of a settlement agreement. On February 3, 2017, the Company appealed this dismissal decision to the Court of Appeals for the Federal Circuit. Patent litigation in the United States District Court for the District of New Jersey against a fifth generic company, Anchen Pharmaceuticals Inc. ("Anchen"), was dismissed on June 9, 2014 after Anchen recertified under Paragraph III. The Company understands that Dr. Reddy's has entered into a settlement with AstraZeneca with respect to patent rights directed to Nexium for the commercialization of VIMOVO, and that according to the settlement agreement, Dr. Reddy's is now able to commercialize VIMOVO under AstraZeneca's Nexium patent rights. The settlement agreement, however, has no effect on the Aralez VIMOVO patents, which are still the subject of patent litigations. As part of the Company's acquisition of the U.S. rights to VIMOVO, the Company has taken over and is responsible for the patent litigations that include the Aralez patents licensed to the Company under the amended and restated collaboration and license agreement for the United States with Aralez.

The VIMOVO cases were filed on April 21, 2011, July 25, 2011, October 28, 2011, January 4, 2013, May 10, 2013, June 28, 2013, October 23, 2013, May 13, 2015 and November 24, 2015 and collectively include allegations of infringement of U.S. Patent Nos. 6,926,907, 8,557,285, 8,852,636, and 8,858,996 (the "'996 patent"). On June 18, 2015, the Company amended the complaints to add a charge of infringement of U.S. Patent No. 8,865,190 (the "'190 patent"). On January 7, 2016, Actavis Pharma asserted a counterclaim for declaratory judgment of invalidity and non-infringement of U.S. Patent No. 8,945,621 (the "'621 patent"). On January 25, 2016, the Company filed a new case against Actavis Pharma including allegations of infringement of U.S. Patent Nos. 9,161,920 and 9,198,888. This case was subsequently consolidated with the Actavis Pharma case involving the '996 patent, the '190 patent and U.S. Patent No. 8,852,636. On February 10, 2016, the Company amended the complaints against Dr. Reddy's, Lupin, and Mylan to add charges of infringement of U.S. Patent Nos. 9,161,920 and 9,198,888. On February 19, 2016, Mylan asserted a counterclaim for declaratory judgment of invalidity and non-infringement of U.S. Patent No. 9,220,698. On August 11, 2016, the Company filed new complaints asserting the '621 patent and U.S. Patent Nos. 9,220,698, and 9,345,695 against the defendants. On December 6, 2016, the Company asserted U.S. Patent No. 9,393,208 (the "'208 patent") against Lupin, Mylan, and Actavis in amended complaints, and against Dr. Reddy's in a new complaint.

"Case I" consists of the cases asserting U.S. Patent Nos. 8,557,285 and 6,926,907. "Case II" consists of the cases asserting the '996 patent, the '190 patent and U.S. Patent Nos. 8,852,636, 9,161,920, and 9,198,888. "Case III" consists of the cases asserting U.S. Patent Nos. 8,945,621, 9,220,698, 9,345,695, and the '208 patent against Lupin and Mylan, and the case asserting U.S. Patent Nos. 8,945,621, 9,220,698, and 9,345,695 against Dr. Reddy's. "Case IV" consists of the case asserting the '208 patent against Dr. Reddy's.

The Case I cases have been consolidated for discovery. The court has issued a claim construction order for Case I and set a trial date for January 12, 2017. On May 12, 2016, the court granted Dr. Reddy's motion for summary judgment of non-infringement of U.S. Patent No. 6,926,907 with respect to one of Dr. Reddy's two ANDAs.

The Case II cases have been consolidated for discovery. The court has not issued a claim construction order in Case II. On August 23, 2016, the court entered an order denying Mylan's motion to consolidate Case I with Case II.

On October 14, 2016, defendant Dr. Reddy's filed a motion to dismiss all counts in Case III and a motion for summary judgment relevant to Cases I, II, and III. No briefing schedule for defendant Dr. Reddy's motion to dismiss has been set. Briefing for defendant Dr. Reddy's motion for summary judgment was included in the parties' trial briefing.

On December 19, 2016, defendant Actavis filed a motion to compel enforcement of settlement agreement related to Cases I, II, and III. On December 22, 2016, a hearing before Magistrate Judge Arpert was held on defendant Actavis' motion. On December 22, 2016, Magistrate Judge Arpert entered a report and recommendation that Actavis' motion to compel the enforcement of settlement be granted. On December 30, 2016, the Honorable Judge Mary Cooper order the adoption of the report and recommendation. On January 10, 2017, an order of dismissal was entered for all claims in Cases I, II and III. The Company filed a Notice of Appeal with the district court on February 9, 2017.

On December 20, 2016, an initial case management conference was held for Case III (the cases asserting U.S. Patent Nos. 8,557,285, 945,621, 9,220,698, 9,345,695 and 9,393,208 against Lupin and Mylan, and the case asserting the U.S. Patent Nos. 8,945,621, 9,220,698 and 9,345,695 against Dr. Reddy's).

On January 12, 2017, a six-day bench trial commenced against defendants Dr. Reddy's and Mylan before Honorable Judge Mary Cooper in the District of New Jersey for Case I. The patents at issue in this trial included two Orange Book listed patents: U.S. Patent Nos. 6,926,907 and 8,557,285. Defendant Lupin formerly entered into a stay pending the entry of judgment in Case I. Currently, closing arguments and post-trial filings are not scheduled.

On January 19, 2017, the court entered a scheduling order for Case II and Case III. This scheduling order requires, inter alia, disclosure of asserted claims by January 31, 2017. A trial date for Cases II and III has not yet been set.

The Company understands the cases arise from Paragraph IV Patent Certification notice letters providing notice of the filing of ANDAs with the FDA seeking regulatory approval to market generic versions of VIMOVO before the expiration of the patents-in-suit. The Company understands the Dr. Reddy's notice letters were dated March 11, 2011, November 20, 2012 and April 20, 2015; the Lupin notice letters were dated June 10, 2011, March 12, 2014 and July 26, 2016; the Mylan notice letters were dated May 16, 2013, February 9, 2015, January 26, 2016, February 26, 2016, July 19, 2016 and September 22, 2016; the Actavis Pharma notice letters were dated March 29, 2013, November 5, 2013, May 29, 2015, October 9, 2015, December 10, 2015, March 1, 2016, April 6, 2016, July 22, 2016 and September 8, 2016; and the Anchen notice letter was dated September 16, 2011.

On February 24, 2015, Dr. Reddy's filed a Petition for inter partes review ("IPR") of U.S. Patent No. 8,557,285, one of the patents in litigation in the above referenced VIMOVO cases. On October 9, 2015, the United States Patent and Trademark Office (the "U.S. PTO") denied such Petition for IPR.

On May 21, 2015, the Coalition for Affordable Drugs VII LLC ("Coalition for Affordable Drugs") filed a Petition for IPR of U.S. Patent No. 6,926,907, one of the patents in litigation in the above referenced VIMOVO cases. On December 8, 2015, the U.S. PTO denied such Petition for IPR.

On June 5, 2015, the Coalition for Affordable Drugs filed another Petition for IPR of the '996 patent, one of the patents in litigation in the above referenced VIMOVO cases. On December 17, 2015, the U.S. PTO denied such Petition for IPR.

On August 7, 2015, the Coalition for Affordable Drugs filed another Petition for IPR of U.S. Patent No. 8,852,636, one of the patents in litigation in the above referenced VIMOVO cases. On February 11, 2016, the U.S. PTO denied such Petition for IPR.

On August 12, 2015, the Coalition for Affordable Drugs filed another Petition for IPR of the '621 patent, one of the patents in litigation in the above referenced VIMOVO cases. On February 22, 2016, the Patent Trial and Appeal Board (the "PTAB") issued a decision to institute the IPR. The PTAB hearing for the '621 patent was held on November 16, 2016. The PTAB issued a final written decision finding the '621 patent valid on February 21, 2017.

On August 19, 2015, Lupin filed Petitions for IPR of the '996 patent, the '190 patent and U.S. Patent No. 8,852,636, all patents in litigation in the above referenced VIMOVO cases. On March 1, 2016, the PTAB issued decisions to institute the IPRs for the '996 patent" and the '190 patent. On March 1, 2016, the PTAB denied the Petition for IPR for U.S. Patent No. 8,852,636. The PTAB hearings for the '996 patent and '190 patent were both held on November 29, 2016. The PTAB must issue a final written decision on the IPRs of the '996 patent and the '190 patent no later than March 1, 2017.

On March 17, 2014, Hyperion received notice from Par Pharmaceutical, Inc. ("Par Pharmaceutical") that it had filed an ANDA with the FDA seeking approval for a generic version of the Company's medicine RAVICTI. The ANDA contained a Paragraph IV Patent Certification alleging that two of the patents covering RAVICTI, U.S. Patent No. 8,404,215, titled "Methods of therapeutic monitoring of nitrogen scavenging drugs," which expires in March 2032 (the "'215 patent"), and U.S. Patent No. 8,642,012, titled "Methods of treatment using ammonia scavenging drugs," which expires in September 2030 (the "'012 patent"), are invalid and/or will not be infringed by Par Pharmaceutical's manufacture, use or sale of the medicine for which the ANDA was submitted. Par Pharmaceutical did not challenge the validity, enforceability, or infringement of the Company's primary composition of matter patent for RAVICTI, U.S. Patent No. 5,968,979 titled "Triglycerides and ethyl esters of phenylalkanoic acid and phenylalkanoic acid useful in treatment of various disorders," which would have expired on February 7, 2015, but as to which Hyperion was granted an interim term of extension until February 7, 2016 and to which the U.S. PTO has granted a final term extension of 1,267 days, which extends the expiration date to July 28, 2018. Hyperion filed suit in the United States District Court for the Eastern District of Texas, Marshall Division, against Par Pharmaceutical on April 23, 2014 seeking an injunction to prevent the approval of Par Pharmaceutical's ANDA and/or to prevent Par Pharmaceutical from selling a generic version of RAVICTI, and the Company has taken over and is responsible for this patent litigation. On September 15, 2015, the Company received notice from Par Pharmaceutical that it had filed a Paragraph IV Patent Certification alleging that U.S. Patent No. 9,095,559 (the "'559 patent") is invalid and/or will not be infringed by Par Pharmaceutical's manufacture, use or sale of the medicine for which the ANDA was submitted. On March 14, 2016, the Company received notice from Par Pharmaceutical that it had filed a Paragraph IV Patent Certification alleging that U.S. Patent No. 9,254,278 (the "'278 patent") is invalid and/or will not be infringed by Par Pharmaceutical's manufacture, use or sale of the medicine for which the ANDA was submitted. On June 3, 2016, the Company received notice from Par Pharmaceutical that it had filed a Paragraph IV Patent Certification alleging that U.S. Patent No. 9,326,966 (the "'966 patent") is invalid and/or will not be infringed by Par Pharmaceutical's manufacture, use or sale of the medicine for which the ANDA was submitted. The Company filed suit in the United States District Court for the District of New Jersey against Par Pharmaceutical on June 30, 2016 ("the Par New Jersey action"), seeking an injunction to prevent the approval of Par Pharmaceutical's ANDA and/or to prevent Par Pharmaceutical from selling a generic version of RAVICTI. The lawsuit alleges that Par Pharmaceutical has infringed the '559 patent, the '278 patent and the '966 patent by filing an ANDA seeking approval from the FDA to market generic versions of RAVICTI prior to the expiration of the patents. The subject patents are listed in the Orange Book. The Par New Jersey action has been stayed pending the resolution of the PTAB's IPR of the '559 patent.

On April 29, 2015, Par Pharmaceutical filed Petitions for IPR of the '215 patent and the '012 patent. The PTAB issued decisions instituting such IPRs on November 4, 2015. On December 14, 2015, the District Court Judge Roy Payne issued a stay pending a final written decision from the PTAB with respect to the IPRs of the '215 patent and the '012 patent. On September 29, 2016, the PTAB issued a final written decision holding all the claims of the '215 patent unpatentable. The Company has not appealed the PTAB's decision concerning the '215 patent to the Federal Circuit. On November 3, 2016, the PTAB issued a final written decision holding all of the claims of the '012 patent patentable. On December 29, 2016, Par filed a notice of appeal with the Federal Circuit to appeal the final written decision of the PTAB concerning the patentability of the '012 patent.

On September 4, 2015, the Company received notice from Lupin of Lupin's Paragraph IV Patent Certification against the '215 patent and the '012 patent, advising that Lupin had filed an ANDA with the FDA for a generic version of RAVICTI. On November 6, 2015, the Company also received Notice of Lupin's Paragraph IV Patent Certification against the '559 patent. Lupin has not advised the Company as to the timing or status of the FDA's review of its filing. On October 19, 2015 the Company filed suit in the United States District Court for the District of New Jersey against Lupin seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that Lupin has infringed the '215 patent, the '012 patent and the '559 patent by filing an ANDA seeking approval from the FDA to market generic versions of RAVICTI prior to the expiration of the patents. The subject patents are listed in the Orange Book. On April 6, 2016, the Company filed an amended complaint in the United States District Court for the District of New Jersey against Lupin alleging that Lupin has infringed the '559 patent by filing an ANDA seeking approval from the FDA to market generic versions of RAVICTI prior to expiration of the '559 patent. The commencement of the patent infringement lawsuit stays, or bars, FDA approval of Lupin's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. On April 18, 2016, the Company received notice from Lupin of Lupin's Paragraph IV Patent Certification against the '278 patent. On July 6, 2016, the Company received notice from Lupin of Lupin's Paragraph IV Patent Certification against the '966 patent. The Company filed suit in the United States District Court for the District of New Jersey against Lupin on July 21, 2016, seeking an injunction to prevent the approval of Lupin's ANDA and/or to prevent Lupin from selling a generic version of RAVICTI. The lawsuit alleges that Lupin has infringed the '278 patent and the '966 patent by filing an ANDA seeking approval from the FDA to market generic versions of RAVICTI prior to the expiration of the patents. The subject patents are listed in the Orange Book. The Lupin New Jersey actions have been stayed pending the resolution of the PTAB's IPR of the '559 patent.

On April 1, 2016, Lupin filed a Petition to request an IPR of the '559 patent. On September 30, 2016, the PTAB issued a decision to institute the IPR for the '559 patent. The PTAB must issue a final written decision on the IPR of the '559 patent no later than September 30, 2017.

In November 2015, Express Scripts filed suit against the Company in Delaware Superior Court, Newcastle County, asserting claims for breach of contract, breach of the implied covenant of good faith and fair dealing, unjust enrichment, and declaratory relief arising from the parties' 2012 Preferred Savings Grid Rebate Program Agreement. The Company filed a counter-claim against Express Scripts for breach of contract, breach of the implied covenant of good faith and fair dealing, and declaratory relief arising from Express Scripts' breach of the rebate agreement. In September 2016, the Company entered into a settlement agreement and mutual release with Express Scripts pursuant to which the Company and Express Scripts were released from any and all claims relating to the litigation without admitting any fault or wrongdoing and the Company agreed to pay Express Scripts $65.0 million.

Beginning on March 8, 2016, two federal securities class action lawsuits (captioned Schaffer v. Horizon Pharma plc, et al., Case No. 16-cv-01763-JMF and Banie v. Horizon Pharma plc, et al., Case No. 16-cv-01789-JMF) were filed in the United States District Court for the Southern District of New York against the Company and certain of the Company's current and former officers (the "Officer Defendants"). On March 24, 2016, the court consolidated the two actions under Schaffer v. Horizon Pharma plc, et al. On June 3, 2016, the court appointed Locals 302 and 612 of the International Union of Operating Engineers-Employers Construction Industry Retirement Trust and the Carpenters Pension Trust Fund for Northern California as lead plaintiffs and Labaton Sucharow LLP as lead counsel. On July 25, 2016, lead plaintiffs and additional named plaintiff Automotive Industries Pension Trust Fund filed their consolidated complaint, which they subsequently amended on October 7, 2016, including additional current and former officers, the Company's Board of Directors (the "Director Defendants"), and underwriters involved with the Company's April 2015 public offering (the "Underwriter Defendants") as defendants. The plaintiffs allege that certain of the Company and the Officer Defendants violated sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, by making false and/or misleading statements about, among other things: (a) the Company's financial performance, (b) the Company's business prospects and drug-pricing practices, (c) the Company's sales and promotional practices, and (d) the Company's design, implementation, performance, and risks associated with the Company's Prescriptions-Made-Easy program. The plaintiffs allege that certain of the Company, the Director Defendants and the

Underwriter Defendants violated sections 11, 12(a)(2) and 15 of the Securities Act of 1933, as amended, (the "Securities Act") in connection with the Company's April 2015 public offering. The plaintiffs seek, among other things, an award of damages allegedly sustained by plaintiffs and the putative class, including a reasonable allowance for costs and attorneys' fees. On November 14, 2016, all defendants moved to dismiss the plaintiffs' amended complaint. Plaintiffs' filed their opposition to the motion to dismiss on December 21, 2016. Briefing on the Motion to Dismiss was completed on January 27, 2017 and the parties await the Court's ruling.

Between October 5 and October 7, 2016, two complaints (captioned Lavrenov v. Raptor Pharmaceutical Corp., et al., Case No. 16-cv-00901, and Jordan v. Raptor Pharmaceutical Corp., et al., Case No. 16-cv-00913) were filed in the United States District Court for the District of Delaware. Both actions were filed against Raptor and each member of Raptor's board of directors. The Company and Misneach Corporation, a wholly owned subsidiary of the Company, were named as defendants in the Lavrenov action, but not the Jordan action. The actions were brought by purported stockholders of Raptor, on their own behalf and as a putative class of Raptor stockholders, and assert causes of action under Sections 14 and 20 of the Securities Exchange Act of 1934, as amended. The Lavrenov action also asserts breach of fiduciary duty and aiding and abetting claims under Delaware law. The complaints allege, among other things, that the process leading up to the Raptor acquisition was inadequate and that the Schedule 14D-9 filed by Raptor with the Securities and Exchange Commission (the "SEC") omits certain material information, which allegedly renders the information disclosed materially misleading. The complaints seek, among other things, to enjoin the Raptor acquisition, or in the event the Raptor acquisition is consummated, to recover money damages. On October 17, 2016, Raptor filed an amended Schedule 14D-9 with the SEC. Plaintiffs did not file a motion to preliminarily enjoin the Raptor acquisition, which was completed on October 25, 2016. On December 2, 2016, named plaintiffs dismissed both suits with prejudice as to named plaintiffs, and without prejudice to any other potential party. The Court has retained jurisdiction solely for the purpose of ruling upon plaintiffs' motion for attorney fees, in the event such a motion is filed.

NOTE 17 – DEBT AGREEMENTS

The Company's outstanding debt balances as of December 31, 2016 and 2015 consisted of the following (in thousands):

	As of December 31	
	2016	2015
2015 Term Loan Facility	$394,000	$398,000
2016 Incremental Loan Facility	375,000	—
2023 Senior Notes	475,000	475,000
2024 Senior Notes	300,000	—
Exchangeable Senior Notes	400,000	400,000
Total face value	1,944,000	1,273,000
Debt discount	(126,352)	(127,885)
Deferred financing fees	(10,155)	(8,359)
Total long-term debt	1,807,493	1,136,756
Less: current maturities	7,750	4,000
Long-term debt, net of current maturities	$1,799,743	$1,132,756

Scheduled maturities with respect to the Company's long-term debt are as follows (in thousands):

2017	$7,750
2018	7,750
2019	7,750

2020	7,750
2021	738,000
Thereafter	1,175,000
Total	$1,944,000

The Company adopted ASU No. 2015-03, Interest-Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs on January 1, 2016. The amendments in this ASU require that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. See Note 2 for further details of the impact this adoption has had on the financial statements.

2015 Senior Secured Credit Facility

On May 7, 2015, HPI, the Company and certain of its subsidiaries entered into a credit agreement with Citibank, N.A., as administrative and collateral agent, and the lenders from time to time party thereto (as amended by the 2016 Amendment described below, the "credit agreement") providing for (i) the six-year $400.0 million term loan facility (the "2015 Term Loan Facility"); (ii) an uncommitted accordion facility subject to the satisfaction of certain financial and other conditions; and (iii) one or more uncommitted refinancing loan facilities with respect to loans thereunder (collectively the "2015 Senior Secured Credit Facility"). The initial borrower under the 2015 Term Loan Facility is HPI. The credit agreement allows for the Company and certain other subsidiaries of the Company to become borrowers under the accordion or refinancing facilities. Loans under the 2015 Term Loan Facility bear interest, at each borrower's option, at a rate equal to either the London Inter-Bank Offer Rate ("LIBOR"), plus an applicable margin of 3.5% per year (subject to a 1.0% LIBOR floor), or the adjusted base rate plus 2.5%. The adjusted base rate is defined as the greater of (a) LIBOR (using one-month interest period) plus 1%, (b) prime rate, (c) fed funds plus ½ of 1%, and (d) 2%. The Company borrowed the full $400.0 million available under the 2015 Term Loan Facility on May 7, 2015 as a LIBOR-based borrowing. In connection with the financing for the acquisition of Raptor, the credit agreement was amended to add a $375.0 million incremental loan facility and change the interest rate margins applicable to the 2015 Term Loan Facility, as further described below.

The obligations under the credit agreement and any swap obligations and cash management obligations owing to a lender (or an affiliate of a lender) thereunder are and will be guaranteed by the Company and each of the Company's existing and subsequently acquired or organized direct and indirect subsidiaries (other than certain immaterial subsidiaries, subsidiaries whose guarantee would result in material adverse tax consequences and subsidiaries whose guarantee is prohibited by applicable law). The obligations under the credit agreement and any such swap and cash management obligations are secured, subject to customary permitted liens and other agreed upon exceptions, by a perfected security interest in (i) all tangible and intangible assets of the borrowers and the guarantors, except for certain customary excluded assets, and (ii) all of the capital stock owned by the borrowers and guarantors thereunder (limited, in the case of the stock of certain non-U.S. subsidiaries of the borrowers, to 65% of the capital stock of such subsidiaries).

The borrowers are permitted to make voluntary prepayments at any time without payment of a premium. HPI is required to make mandatory prepayments of loans under the 2015 Term Loan Facility (without payment of a premium) with (a) net cash proceeds from certain non-ordinary course asset sales (subject to reinvestment rights and other exceptions), (b) casualty proceeds and condemnation awards (subject to reinvestment rights and other exceptions), (c) net cash proceeds from issuances of debt (other than certain permitted debt), and (d) beginning with the fiscal year ending December 31, 2016, 50% of the Company's excess cash flow (subject to decrease to 25% or 0% if the Company's first lien leverage ratio is less than 2.25:1 and 1.75:1, respectively). The loans under the 2015 Term Loan Facility will amortize in equal quarterly installments in an aggregate annual amount equal to 1% of the original principal amount thereof, with any remaining balance payable on the final maturity date of the loans under the 2015 Term Loan Facility.

The credit agreement contains customary representations and warranties and customary affirmative and negative covenants, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness and dividends and other distributions, and customary events of default.

The Company was, as of December 31, 2016, and is currently in compliance with this credit agreement.

As of December 31, 2016, the fair value of the 2015 Term Loan Facility was approximately $394.0 million, categorized as a Level 2 instrument, as defined in Note 14.

2016 Amendment to Credit Agreement

On October 25, 2016, HPI and Horizon Pharma USA, Inc., a wholly owned subsidiary of the Company ("HPUSA") (together, in such capacity, the "Incremental Borrowers") entered into an amendment to the credit agreement (the "2016 Amendment") with Citibank, N.A., as administrative and collateral agent, and Bank of America, N.A., as the incremental B-1 lender thereunder, pursuant to which the Incremental Borrowers borrowed $375.0 million aggregate principal amount of loans (the "2016 Incremental Loan Facility"). The 2016 Incremental Loan Facility was incurred as a separate class of term loans under the credit agreement with the same terms as the loans under the 2015 Term Loan Facility, except as described below.

Loans under the 2016 Incremental Loan Facility bear interest, at each Incremental Borrowers' option, at a rate equal to either LIBOR plus an applicable margin of 4.50% per year (subject to a LIBOR floor of 1.0%), or the adjusted base rate plus 3.50%. The terms of the loans under the 2015 Term Loan Facility (the "2015 Loans") provided for an amendment such that the effective yield of the 2015 Loans would not be less than the effective yield of the loans under the 2016 Incremental Loan Facility (the "2016 Incremental Loans") minus 0.50%. Consequently, the issuance of the 2016 Incremental Loans resulted in an increase of the interest rate applicable to the 2015 Loans, as of October 25, 2016, to LIBOR plus 4.00%, subject to a LIBOR floor of 1.0% (an initial interest rate of 5.00%). Borrowers under the credit agreement are permitted to make voluntary prepayments of the loans under the credit agreement at any time without payment of a premium, except that with respect to the 2016 Incremental Loans, a 1% premium will apply to a repayment of the 2016 Incremental Loans in connection with a repricing of, or any amendment to the credit agreement in a repricing of, such loans effected on or prior to the date that is twelve months following October 25, 2016.

The Company was, as of December 31, 2016, and is currently in compliance with this credit agreement.

As of December 31, 2016, the fair value of the 2016 Incremental Loan Facility was approximately $378.8 million, categorized as a Level 2 instrument, as defined in Note 14.

2023 Senior Notes

On April 29, 2015, Horizon Pharma Financing Inc. ("Horizon Financing") a wholly owned subsidiary of the Company, completed a private placement of $475.0 million aggregate principal amount of 6.625% Senior Notes due 2023 (the "2023 Senior Notes") to certain investment banks acting as initial purchasers who subsequently resold the 2023 Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act, and in offshore transactions to non-U.S. persons in reliance on Regulation S under the Securities Act.

In connection with the closing of the Hyperion acquisition on May 7, 2015, Horizon Financing merged with and into HPI and, as a result, the 2023 Senior Notes became HPI's general unsecured senior obligations and the Company and all of the Company's direct and indirect subsidiaries that are guarantors under the 2015 Senior Secured Credit Facility fully and unconditionally guaranteed on a senior unsecured basis HPI's obligations under the 2023 Senior Notes.

The 2023 Senior Notes accrue interest at an annual rate of 6.625% payable semiannually in arrears on May 1 and November 1 of each year, beginning on November 1, 2015. The 2023 Senior Notes will mature on May 1, 2023, unless earlier exchanged, repurchased or redeemed.

Except as described below, the 2023 Senior Notes may not be redeemed before May 1, 2018. Thereafter, some or all of the 2023 Senior Notes may be redeemed at any time at specified redemption prices, plus accrued and unpaid interest to the redemption date. At any time prior to May 1, 2018, some or all of the 2023 Senior Notes may be redeemed at a price equal to 100% of the aggregate principal amount thereof, plus a make-whole premium and accrued and unpaid interest to the redemption date. Also prior to May 1, 2018, up to 35% of the aggregate principal amount of the 2023 Senior Notes may be redeemed at a redemption price of 106.625% of the aggregate principal amount thereof, plus accrued and unpaid interest, with the net proceeds of certain equity offerings. In addition, the 2023 Senior Notes may be redeemed in whole but not in part at a redemption price equal to 100% of the principal amount plus accrued and unpaid interest and additional amounts, if any, to, but excluding, the redemption date, if on the next date on which any amount would be payable in respect of the 2023 Senior Notes, HPI or any guarantor is or would be required to pay additional amounts as a result of certain tax-related events.

If the Company undergoes a change of control, HPI will be required to make an offer to purchase all of the 2023 Senior Notes at a price in cash equal to 101% of the aggregate principal amount thereof plus accrued and unpaid interest to, but not including, the repurchase date. If the Company or certain of its subsidiaries engages in certain asset sales, HPI will be required under certain circumstances to make an offer to purchase the 2023 Senior Notes at 100% of the principal amount thereof, plus accrued and unpaid interest to the repurchase date.

The indenture governing the 2023 Senior Notes contains covenants that limit the ability of the Company and its restricted subsidiaries to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales, merge, consolidate with or merge or sell all or substantially all of their assets, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries, and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to the Company. Certain of the covenants will be suspended during any period in which the notes receive investment grade ratings. The indenture also includes customary events of default.

The Company was, as of December 31, 2016, and is currently in compliance with the indenture governing the 2023 Senior Notes.

As of December 31, 2016, the fair value of the 2023 Senior Notes was approximately $449.5 million, categorized as a Level 2 instrument, as defined in Note 14.

2024 Senior Notes

On October 25, 2016, HPI and HPUSA (together, the "2024 Issuers"), completed a private placement of $300.0 million aggregate principal amount of 2024 Senior Notes to certain investment banks acting as initial purchasers who subsequently resold the 2024 Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act.

The 2024 Senior Notes are the 2024 Issuers' general unsecured senior obligations and the Company and all of the Company's direct and indirect subsidiaries that are guarantors under the 2015 Senior Secured Credit Facility and the 2016 Incremental Loan Facility fully and unconditionally guaranteed on a senior unsecured basis the 2024 Issuers' obligations under the 2024 Senior Notes.

The 2024 Senior Notes accrue interest at an annual rate of 8.75% payable semiannually in arrears on May 1 and November 1 of each year, beginning on May 1, 2017. The 2024 Senior Notes will mature on November 1, 2024, unless earlier exchanged, repurchased or redeemed.

Except as described below, the 2024 Senior Notes may not be redeemed before November 1, 2019. Thereafter, some or all of the 2024 Senior Notes may be redeemed at any time at specified redemption prices, plus accrued and unpaid interest to the redemption date. At any time prior to November 1, 2019, some or all of the 2024 Senior Notes may be redeemed at a price equal to 100% of the aggregate principal amount thereof, plus a make-whole premium and accrued and unpaid interest to the redemption date. Also prior to November 1, 2019, up to 35% of the aggregate principal amount of the 2024 Senior Notes may be redeemed at a redemption price of 108.75% of the aggregate principal amount thereof, plus accrued and unpaid interest, with the net proceeds of certain equity offerings. In addition, the 2024 Senior Notes may be redeemed in whole but not in part at a redemption price equal to 100% of the principal amount plus accrued and unpaid interest and additional amounts, if any, to, but excluding, the redemption date, if on the next date on which any amount would be payable in respect of the 2024 Senior Notes, the 2024 Issuers or any guarantor is or would be required to pay additional amounts as a result of certain tax-related events.

If the Company undergoes a change of control, the 2024 Issuers will be required to make an offer to purchase all of the 2024 Senior Notes at a price in cash equal to 101% of the aggregate principal amount thereof plus accrued and unpaid interest to, but not including, the repurchase date. If the Company or certain of its subsidiaries engages in certain asset sales, the 2024 Issuers will be required under certain circumstances to make an offer to purchase the 2024 Senior Notes at 100% of the principal amount thereof, plus accrued and unpaid interest to the repurchase date.

The indenture governing the 2024 Senior Notes contains covenants that limit the ability of the Company and its restricted subsidiaries to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales, merge, consolidate with or merge or sell all or substantially all of their assets, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries, and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to the Company. Certain of the covenants will be suspended during any period in which the notes receive investment grade ratings. The indenture also includes customary events of default.

The Company was, as of December 31, 2016, and is currently in compliance with the indenture governing the 2024 Senior Notes.

As of December 31, 2016, the fair value of the 2024 Senior Notes was approximately $301.5 million, categorized as a Level 2 instrument, as defined in Note 14.

Exchangeable Senior Notes

On March 13, 2015, Horizon Investment completed a private placement of $400.0 million aggregate principal amount of Exchangeable Senior Notes to several investment banks acting as initial purchasers who subsequently resold the Exchangeable Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act. The net proceeds from the offering of the Exchangeable Senior Notes were approximately $387.2 million, after deducting the initial purchasers' discount and offering expenses payable by Horizon Investment.

The Exchangeable Senior Notes are fully and unconditionally guaranteed, on a senior unsecured basis, by the Company (the "Guarantee"). The Exchangeable Senior Notes and the Guarantee are Horizon Investment's and the Company's senior unsecured obligations. The Exchangeable Senior Notes accrue interest at an annual rate of 2.50% payable semiannually in arrears on March 15 and September 15 of each year, beginning on September 15, 2015. The Exchangeable Senior Notes will mature on March 15, 2022, unless earlier exchanged, repurchased or redeemed. The initial exchange rate is 34.8979 ordinary shares of the Company per $1,000 principal amount of the Exchangeable Senior Notes (equivalent to an initial exchange price of approximately $28.66 per ordinary share). The exchange rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date or upon a tax redemption, Horizon Investment will increase the exchange rate for a holder who elects to exchange its Exchangeable Senior Notes in connection with such a corporate event or a tax redemption in certain circumstances.

Other than as described below, the Exchangeable Senior Notes may not be redeemed by the Company.

Issuer Redemptions:

Optional Redemption for Changes in the Tax Laws of a Relevant Taxing Jurisdiction: Horizon Investment may redeem the Exchangeable Senior Notes at its option, prior to March 15, 2022, in whole but not in part, in connection with certain tax-related events.

Provisional Redemption on or After March 20, 2019: On or after March 20, 2019, Horizon Investment may redeem for cash all or a portion of the Exchangeable Senior Notes if the last reported sale price of ordinary shares of the Company has been at least 130% of the exchange price then in effect for at least 20 trading days whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which Horizon Investment provide written notice of redemption. The redemption price will be equal to 100% of the principal amount of the Exchangeable Senior Notes to be redeemed, plus accrued and unpaid interest to, but not including, the redemption date; provided that if the redemption date occurs after a regular record date and on or prior to the corresponding interest payment date, Horizon Investment will pay the full amount of accrued and unpaid interest due on such interest payment date to the record holder of the Exchangeable Senior Notes on the regular record date corresponding to such interest payment date, and the redemption price payable to the holder who presents an Exchangeable Senior Note for redemption will be equal to 100% of the principal amount of such Exchangeable Senior Note.

Holder Exchange Rights:

Holders may exchange all or any portion of their Exchangeable Senior Notes at their option at any time prior to the close of business on the business day immediately preceding December 15, 2021 only upon satisfaction of one or more of the following conditions:

1. Exchange upon Satisfaction of Sale Price Condition – During any calendar quarter commencing after the calendar quarter ending on June 30, 2015 (and only during such calendar quarter), if the last reported sale price of ordinary shares of the Company for at least 20 trading days (whether or not consecutive) during the period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to

130% of the applicable exchange price on each applicable trading day.

2. Exchange upon Satisfaction of Trading Price Condition – During the five business day period after any ten consecutive trading day period in which the trading price per $1,000 principal amount of Exchangeable Senior Notes for each trading day of such period was less than 98% of the product of the last reported sale price of ordinary shares of the Company and the applicable exchange rate on such trading day.
3. Exchange upon Notice of Redemption – Prior to the close of business on the business day immediately preceding December 15, 2021, if Horizon Investment provides a notice of redemption, at any time prior to the close of business on the second scheduled trading day immediately preceding the redemption date.

As of December 31, 2016, none of the above conditions had been satisfied and no exchange of Exchangeable Senior Notes had been triggered.

On or after December 15, 2021, a holder may exchange all or any portion of its Exchangeable Senior Notes at any time prior to the close of business on the second scheduled trading day immediately preceding the maturity date regardless of the foregoing conditions.

Upon exchange, Horizon Investment will settle exchanges of the Exchangeable Senior Notes by paying or causing to be delivered, as the case may be, cash, ordinary shares or a combination of cash and ordinary shares, at its election.

The Company recorded the Exchangeable Senior Notes under the guidance in Topic ASC 470-20, Debt with Conversion and Other Options, and separated them into a liability component and equity component. The carrying amount of the liability component of $268.9 million was determined by measuring the fair value of a similar liability that does not have an associated equity component. The carrying amount of the equity component of $119.1 million represented by the embedded conversion option was determined by deducting the fair value of the liability component of $268.9 million from the initial proceeds of $387.2 million ascribed to the convertible debt instrument as a whole. The initial debt discount of $131.1 million is being charged to interest expense over the life of the Exchangeable Senior Notes using the effective interest rate method.

As of December 31, 2016, the fair value of the Exchangeable Senior Notes was approximately $380.5 million, categorized as a Level 2 instrument, as defined in Note 14.

2014 Senior Secured Credit Facility

On June 17, 2014, the Company entered into a credit agreement with a group of lenders and Citibank, N.A., as administrative and collateral agent to provide the Company with $300.0 million in financing through a five-year senior secured credit facility (the “2014 Senior Secured Credit Facility”). Loans under the five-year $300.0 million term loan facility (“2014 Term Loan Facility”) bore interest, at each borrower’s option, at a rate equal to either the LIBOR, plus an applicable margin of 8.0% per year (subject to a 1.0% LIBOR floor), or the prime lending rate, plus an applicable margin equal to 7.0% per year. The Company borrowed the full $300.0 million available on the 2014 Term Loan Facility on September 19, 2014 as a LIBOR-based borrowing.

On May 7, 2015, the Company repaid the entire $300.0 million outstanding amount under the 2014 Senior Secured Credit Facility in connection with the closing of the Hyperion acquisition and recognized a $56.8 million loss on debt extinguishment as a result of the early repayment.

Convertible Senior Notes

On November 22, 2013, the Company issued $150.0 million aggregate principal amount of Convertible Senior Notes and received net proceeds of $143.6 million, after deducting fees and expenses of $6.4 million.

During 2015, the Company entered into separate, privately-negotiated conversion agreements with certain holders of the Convertible Senior Notes (“2015 Conversions”) which were on substantially the same terms as prior conversion agreements entered into by the Company. Under the 2015 Conversions, the applicable holders agreed to convert an aggregate principal amount of $61.0 million of Convertible Senior Notes held by them and the Company agreed to settle such conversions by issuing an aggregate of 11,368,921 ordinary shares. In addition, pursuant to such conversion agreements, the Company made an aggregate cash payment of $10.0 million to the applicable holders for additional exchange consideration and $0.9 million for accrued and unpaid interest, and recognized a non-cash charge of $10.1 million related to the extinguishment of debt as a result of the note conversions. The number of shares issued

equaled the number of shares based on the underlying conversion option. The aggregate cash payments to the holders for additional exchange consideration were recorded as part of the extinguishment loss. Following the closings under the 2015 Conversions, there were no Convertible Senior Notes remaining outstanding.

NOTE 18 – SHAREHOLDERS' EQUITY

During the year ended December 31, 2016, the Company issued an aggregate of:

- 666,984 ordinary shares in net settlement of vested restricted stock units;

- 581,840 ordinary shares in connection with the exercise of stock options and received $3.9 million in proceeds;
- 513,659 ordinary shares pursuant to employee stock purchase plans and received $6.5 million in proceeds; and
- 13,584 ordinary shares in net settlement of vested performance stock units;

During the year ended December 31, 2016, the Company issued an aggregate of 1,750 ordinary shares upon the cash exercise of warrants and the Company received proceeds of $8,000 representing the aggregate exercise price for such warrants. In addition, warrants to purchase an aggregate of 207,110 ordinary shares of the Company were exercised in cashless exercises, resulting in the issuance of 161,259 ordinary shares. As of December 31, 2016, there were outstanding warrants to purchase 1,372,660 ordinary shares of the Company.

During the year ended December 31, 2016, the Company made payments of $5.5 million for employee withholding taxes relating to share-based awards.

In May 2016, the Company's board of directors authorized a share repurchase program pursuant to which the Company may repurchase up to 5,000,000 of its ordinary shares. The timing and amount of repurchases, including whether the Company decides to repurchase any shares pursuant to the authorization, will depend on a variety of factors, including the price of the Company's ordinary shares, alternative investment opportunities, the Company's cash resources, restrictions under the Company's credit agreement, and market conditions. As of December 31, 2016, the Company had not purchased any of its ordinary shares under this repurchase program.

NOTE 19 – EQUITY INCENTIVE PLANS

Employee Stock Purchase Plan

2014 Employee Stock Purchase Plan. On May 17, 2014, HPI's board of directors adopted the 2014 Employee Stock Purchase Plan (the "2014 ESPP"). On September 18, 2014, at a special meeting of the stockholders of HPI (the "Special Meeting"), HPI's stockholders approved the 2014 ESPP. Upon consummation of the Vidara Merger, the Company assumed the 2014 ESPP, which serves as the successor to the Company's 2011 Employee Stock Purchase Plan. As described below, effective as of May 3, 2016, the number of ordinary shares authorized for issuance under the 2014 ESPP was reduced by 5,000,000 shares.

As of December 31, 2016, an aggregate of 3,824,400 ordinary shares were authorized and available for future issuance under the 2014 ESPP.

Share-Based Compensation Plans

2005 Stock Plan. In October 2005, HPI adopted the 2005 Stock Plan (the "2005 Plan"). Upon the signing of the underwriting agreement related to HPI's initial public offering, on July 28, 2011, no further option grants were made under the 2005 Plan. All stock awards granted under the 2005 Plan prior to July 28, 2011 continue to be governed by the terms of the 2005 Plan. Upon consummation of the Vidara Merger, the Company assumed the 2005 Plan.

2011 Equity Incentive Plan. In July 2010, HPI's board of directors adopted the 2011 Equity Incentive Plan (the "2011 EIP"). In June 2011, HPI's stockholders approved the 2011 EIP, and it became effective upon the signing of the underwriting agreement related to HPI's initial public offering on July 28, 2011. Upon consummation of the Vidara Merger, the Company assumed the 2011 EIP, and upon the effectiveness of the Horizon Pharma Public Limited Company 2014 Equity Incentive Plan (the "2014 EIP"), no additional stock awards were or will be made under the 2011 Plan, although all outstanding stock awards granted under the 2011 Plan continue to be governed by the terms of the 2011 Plan.

2014 Equity Incentive Plan and 2014 Non-Employee Equity Plan. On May 17, 2014, HPI's board of directors adopted the 2014 EIP and the Horizon Pharma Public Limited Company 2014 Non-Employee Equity Plan (the "2014 Non-Employee Equity Plan"). At the Special Meeting, HPI's stockholders approved the 2014 EIP and 2014 Non-Employee Equity Plan. Upon consummation of the Vidara Merger, the Company assumed the 2014 EIP and 2014 Non-Employee Equity Plan, which serve as successors to the 2011 EIP.

The 2014 EIP provides for the grant of incentive and nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards and other stock awards that may be settled in cash, shares or other property to the employees of the Company (or a subsidiary company). The number of ordinary shares of the Company that were initially authorized for issuance under the 2014 EIP was no more than 22,052,130, which number consisted of (i) 15,500,000 ordinary shares of the Company; plus (ii) the number of shares available for issuance pursuant to the grant of future awards under the 2011 EIP; plus (iii) any shares subject to outstanding stock awards granted under the 2011 EIP and the 2005 Plan that expire or terminate for any reason prior to exercise or settlement or are forfeited, redeemed or repurchased because of the failure to meet a contingency or condition required to vest such shares; less (iv) 10,000,000 shares, which is the additional number of shares which were previously approved as an increase to the share reserve of the 2011 EIP. On March 23, 2015, the compensation committee of the Company's board of directors approved amending the 2014 EIP subject to shareholder approval to, among other things, increase the aggregate number of shares authorized for issuance under the 2014 EIP by 14,000,000 shares. On May 6, 2015, the shareholders of the Company approved the amendment to the 2014 EIP. On February 25, 2016, the compensation committee of the Company's board of directors approved, subject to shareholder approval, amending the 2014 EIP to, among other things, increase the aggregate number of shares authorized for issuance under the 2014 EIP beyond those remaining available for future grant under the 2014 EIP by 6,000,000 shares and also approved a reduction in the number of shares authorized under the Company's 2014 Non-Employee Equity Plan and 2014 ESPP by 1,000,000 shares and 5,000,000 shares, respectively, contingent on shareholder approval of the amendment to the 2014 EIP. On May 3, 2016, the shareholders of the Company approved the amendment to the 2014 EIP. The Company's board of directors has authority to suspend or terminate the 2014 EIP at any time.

The 2014 Non-Employee Equity Plan provides for the grant of nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards and other forms of stock awards that may be settled in cash, shares or other property to the non-employee directors and consultants of the Company (or a subsidiary company). The total number of ordinary shares of the Company that were initially authorized for issuance under the 2014 Non-Employee Equity Plan is 2,500,000. As described above, effective as of May 3, 2016, the number of ordinary shares authorized for issuance under the 2014 Non-Employee Equity Plan was reduced by 1,000,000 shares. The Company's board of directors has authority to suspend or terminate the 2014 Non-Employee Equity Plan at any time.

As of December 31, 2016, an aggregate of 6,952,414 and 963,567 ordinary shares were authorized and available for future grants under the 2014 EIP and 2014 Non-Employee Equity Plan, respectively.

Stock Options

The following table summarizes stock option activity during the year ended December 31, 2016:

	Options	Weighted Average Exercise Price	Weighted Average Contractual Term Remaining (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2015	13,385,791	$ 17.73		
Granted	2,057,247	17.90		
Exercised	(581,840)	6.73		
Forfeited	(1,139,933)	18.49		
Expired	(93,746)	15.99		
Outstanding as of December 31, 2016	13,627,519	$ 18.17	7.60	$ 35,157
Exercisable and fully vested as of December 31, 2016	7,021,797	$ 15.65	6.79	30,017

Stock options typically have a contractual term of ten years from grant date.

The following table summarizes the Company's outstanding stock options at December 31, 2016:

	Options Outstanding			Options Exercisable and Fully Vested		
Exercise Price Ranges	Number of options outstanding	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Number Exercisable	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)
$2.01 - $4.00	880,261	$ 2.65	6.10	832,503	$ 2.64	6.07
$4.01 - $8.00	1,278,964	6.29	5.56	1,128,647	6.13	5.37
$8.01 - $12.00	866,586	9.14	6.50	610,226	9.20	6.10
$12.01 - $17.00	2,271,218	14.28	7.42	1,350,199	13.87	6.62
$17.01 - $22.00	2,148,781	18.77	8.81	352,362	19.25	8.03
$22.01 - $28.00	3,580,450	22.31	8.23	1,552,310	22.30	8.23
$28.01 - $36.00	2,601,259	29.48	7.74	1,195,550	29.30	6.96
	13,627,519	$ 18.17	7.60	7,021,797	$ 15.65	6.79

During the years ended December 31, 2016, 2015 and 2014, the Company granted stock options to purchase an aggregate of 2,057,247, 8,010,638 and 3,902,836 ordinary shares (or prior to the Vidara Merger, shares of HPI common stock), respectively, with a weighted average grant date fair value of $17.90, $23.92 and $10.71, respectively.

The total intrinsic value of the options exercised during the years ended December 31, 2016, 2015 and 2014 was $6.9 million, $15.6 million, and $3.9 million, respectively. The total fair value of stock options vested during the years ended December 31, 2016, 2015 and 2014 was $55.6 million, $11.4 million, and $8.2 million, respectively.

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option pricing model. The determination of the fair value of each stock option is affected by the Company's share price on the date of grant, as well as assumptions regarding a number of highly complex and subjective variables. These variables include, but are not limited to, the Company's expected share price volatility over the expected life of the awards and actual and projected stock option exercise behavior. The weighted average fair value per share of stock option awards granted during the years ended December 31, 2016, 2015 and 2014, and assumptions used to value stock options, are as follows:

	For the Years Ended December 31,		
	2016	2015	2014
Dividend yield	—	—	—
Risk-free interest rate	1.3%-2.2%	1.3% - 2.2%	1.6% - 2.1%
Weighted average volatility	73.2 %	77.1 %	83.1 %
Expected life (in years)	6.02	6.07	6.11
Weighted average grant date fair value per share of options granted	$11.58	$ 16.07	$ 8.88

Dividend yields

The Company has never paid dividends and does not anticipate paying any dividends in the near future. Additionally, the 2015 Senior Secured Credit Facility, as amended by the 2016 Amendment, as well as the 2023 Senior Notes and the 2024 Senior Notes (each described in Note 17 above), contain covenants that restrict the Company from issuing dividends.

Risk-Free Interest Rate

The Company determined the risk-free interest rate by using a weighted average assumption equivalent to the expected term based on the U.S. Treasury constant maturity rate as of the date of grant.

Volatility

The Company used an average historical share price volatility of comparable companies to be representative of future share price volatility, as the Company did not have sufficient trading history for its ordinary shares.

Expected Term

Given the Company's limited historical exercise behavior, the expected term of options granted was determined using the "simplified" method since the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. Under this approach, the expected term is presumed to be the average of the vesting term and the contractual life of the option.

Forfeitures

As share-based compensation expense recognized in the consolidated statements of comprehensive (loss) income is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures based on actual forfeiture experience, analysis of employee turnover and other factors. ASC Topic 718, Compensation-Stock Compensation ("ASC 718") requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Restricted Stock Units

The following table summarizes restricted stock unit activity for the year ended December 31, 2016:

	Number of Units	Weighted Average Grant-Date Fair Value Per Units
Outstanding as of December 31, 2015	3,361,746	$ 18.71
Granted	1,384,104	17.07
Vested	(970,197)	17.38
Forfeited	(407,782)	18.42
Outstanding as of December 31, 2016	3,367,871	$ 18.45

The grant-date fair value of restricted stock units is the closing price of the Company's shares on the date of grant.

During the years ended December 31, 2016, 2015 and 2014, the Company granted 1,384,104, 2,361,948 and 1,312,722 restricted stock units to acquire shares of the Company's ordinary shares (or prior to the Vidara Merger, shares of HPI common stock) to its employees and non-executive directors, respectively, with a weighted average grant date fair value of $17.07, $23.36 and $10.55, respectively. The restricted stock units vest over a four-year period on each anniversary of the vesting commencement date. The Company accounts for the restricted stock units as equity-settled awards in accordance with ASC 718. The total fair value of restricted stock units vested during the years ended December 31, 2016, 2015 and 2014 was $16.2 million, $9.0 million and $3.4 million, respectively.

Performance Stock Unit Awards

The following table summarizes performance stock unit awards ("PSUs") activity for the year ended December 31, 2016:

	Weighted	Recorded

	Number of Units	Average Grant-Date Fair Value Per Unit	Average Illiquidity Discount	Weighted Average Fair Value Per Unit
Outstanding as of December 31, 2015	13,049,000			
Granted	260,000	$ 7.99	8.2 %	$ 7.34
Vested	(20,000)	18.97	0.0 %	18.97
Forfeited	(1,243,344)	14.68	10.9 %	13.08
Outstanding as of December 31, 2016	12,045,656			

In January 2016, the compensation committee of the Company's board of directors (the "Committee") approved the grant of 260,000 PSUs to certain members of the Company's senior leadership team.

In March 2015, the Committee approved the grant of 10,604,000 PSUs to certain members of the Company's executive committee, senior leadership team and other key employees. 7,998,000 of these PSUs were granted subject to shareholder approval of certain amendments of the 2014 EIP, which occurred on May 6, 2015. In May 2015, the Committee granted 1,264,000 PSUs to new and promoted key employees. In the third and fourth quarters of 2015, the Committee granted 1,120,000 PSUs to a new member of the Company's executive committee and key employees and 388,000 PSUs to non-executive committee members, respectively.

In 2014, the Company granted 25,000 PSUs. All other outstanding PSUs were granted in 2015 and 2016 and may vest if the Company's total compounded annual shareholder rate of return ("TSR") over three performance measurement periods summarized below equals or exceeds a minimum of 15%.

Vesting Tranche	Percent of Total PSU Award	Beginning of Performance Measurement Period	End of Performance Measurement Period	Length of Performance Measurement Period (Years)
Tranche One	33.3 %	March 23, 2015	December 22, 2017	2.75
Tranche Two	33.3 %	March 23, 2015	March 22, 2018	3.00
Tranche Three	33.3 %	March 23, 2015	June 22, 2018	3.25

These outstanding PSUs granted in 2015 and 2016 may vest in amounts ranging from 25% to 100% based on the achievement of the following TSR over the three performance periods:

TSR Achieved	Vesting Amount
15%	25 %
30%	50 %
45%	75 %
60%	100 %

The TSR will be based on the volume weighted average trading price ("VWAP") of the Company's ordinary shares over the 20 trading days ending on the last day of each of the three performance measurement periods versus the VWAP of the Company's ordinary shares over the twenty trading days ended March 23, 2015 of $21.50. The PSUs are subject to a post vesting holding period of one year for 50% of the PSUs and two years for 50% of the PSUs for those who were members of the executive committee at the date of grant, and one year for 50% of the PSUs for all who were not executive committee members at the date of grant.

The Company accounts for the PSUs as equity-settled awards in accordance with ASC 718. Because the value of the PSUs is dependent upon the attainment of a level of TSR, it requires the impact of the market condition to be considered when estimating the fair value of the PSUs. As a result, the Monte Carlo model is applied and the most significant valuation assumptions used include:

	For the Years Ended December 31,		
	2016	2015	2014

Valuation date stock price	$ 17.72 - 21.07	$ 16.81 - 35.06	$ —
Expected volatility	76.8% - 77.6%	64.6% - 72.3%	—%
Risk-free rate	1.0% - 1.2%	1.0% - 1.1%	—%

The average estimated fair value of each outstanding PSU granted under the 2014 EIP is as follows (allocated between groupings based on grant-date classification):

	Number of Units	Weighted Average Fair Value Per Unit	Average Illiquidity Discount	Recorded Weighted Average Fair Value Per Unit
Executive committee members	8,889,656	$ 15.15	18.9 %	$ 12.29
Non-executive committee members	3,131,000	13.55	7.3 %	12.56
	12,020,656	$ 14.74	16.1 %	$ 12.36

For the year ended December 31, 2016, the Company recorded $48.6 million of expense related to PSUs.

Cash Long-Term Incentive Program

On November 5, 2014, the Committee approved a performance cash long-term incentive program for the members of the Company's executive committee and executive leadership team, including its executive officers (the "Cash Bonus Program"). Participants in the Cash Bonus Program will be eligible for a specified cash bonus. The Cash Bonus Program pool funding of approximately $16.0 million was determined based on the Company's actual TSR over the period from November 5, 2014 to May 6, 2015, and the bonus will be earned and payable only if the TSR for the period from November 5, 2014 to November 4, 2017 is greater than 15%. The portion of the total bonus pool payable to individual participants is based on allocations established by the Company's compensation committee. Participants must remain employed by the Company through November 4, 2017 unless a participant's earlier departure from employment is due to death, disability, termination without cause or a change in control transaction. Bonus payments under the Cash Bonus Program, if any, will be made after November 4, 2017.

The Company accounts for the Cash Bonus Program under the liability method in accordance with ASC 718. Because vesting of the bonus pool is dependent upon the attainment of a VWAP of $18.37 or higher over the 20 trading days ending November 4, 2017, the Cash Bonus Program will be considered to be subject to a "market condition" for the purposes of ASC 718. ASC 718 requires the impact of the market condition to be considered when estimating the fair value of the bonus pool. As a result, the Monte Carlo simulation model is applied and the fair value is revalued at each reporting period. As of December 31, 2016 and December 31, 2015, the estimated fair value was $4.8 million and $6.0 million, respectively. For the years ended December 31, 2016 and 2015, the Company recorded $1.1 million and $2.2 million, respectively, of expense related to the Cash Bonus Program. The most significant valuation assumptions used include:

	For the Years Ended December 31,		
	2016	2015	2014
Valuation date stock price	$16.18	$21.67	$12.89
Expected volatility	74.7 %	74.8 %	71.8 %
Risk-free rate	0.78 %	1.00 %	1.03 %

Share-Based Compensation Expense

The following table summarizes share-based compensation expense included in the Company's consolidated statements of comprehensive (loss) income for the years ended December 31, 2016, 2015 and 2014 (in thousands):

	For the Years Ended December 31,		
	2016	2015	2014
Share-based compensation expense:			
Cost of goods sold	$26	$—	$—
Research and development	9,413	6,590	1,515
Sales and marketing	26,215	23,062	4,174
General and administrative	78,490	56,134	7,509
Total share-based compensation expense	$114,144	$85,786	$13,198

For the year ended December 31, 2016, no income tax benefit was recognized relating to share-based compensation expense. As of December 31, 2016, the Company estimates that pre-tax unrecognized compensation expense of $199.6 million for all unvested share-based awards, including both stock options and restricted stock units, will be recognized through the fourth quarter of 2020. The Company expects to satisfy the exercise of stock options and future distribution of shares for restricted stock units and PSUs by issuing new ordinary shares which have been reserved under the 2014 EIP.

NOTE 20 – INCOME TAXES

The Company's (loss) income before benefit for income taxes by jurisdiction for the years ended December 31, 2016, 2015 and 2014 is as follows (in thousands):

	For the Years Ended December 31,		
	2016	2015	2014
Ireland	$(27,955)	$(10,746)	$22,164
United States	(165,476)	(198,442)	(275,080)
Other foreign	(34,654)	76,476	(16,771)
Loss before benefit for income taxes	$(228,085)	$(132,712)	$(269,687)

The components of the benefit for income taxes were as follows for the years ended December 31, 2016, 2015 and 2014 (in thousands):

	For the Years Ended December 31,		
	2016	2015	2014
Current provision			
Ireland	$1,187	$1,924	$—
U.S. - Federal and State	10,491	6,355	815
Other foreign	679	328	55
Total current provision	12,357	8,607	870
Deferred benefit			
Ireland	$(2,054)	$(5,623)	$—
U.S. - Federal and State	(69,073)	(175,228)	(3,860)
Other foreign	(2,481)	—	(3,094)
Total deferred benefit	(73,608)	(180,851)	(6,954)
Total benefit for income taxes	$(61,251)	$(172,244)	$(6,084)

Total benefit for income taxes was $61.3 million, $172.2 million and $6.1 million for the years ended December 31, 2016, 2015 and 2014, respectively. The current tax provision of $12.4 million for the year ended December 31, 2016 was primarily attributable to U.S. state income tax liabilities and the U.S. Federal alternative minimum tax liabilities. The deferred tax benefit of $73.6 million for the year ended December 31, 2016 resulted primarily from the benefit recognized from the mix of income and losses incurred in various tax jurisdictions and the benefit recognized from the change in the U.S. state effective tax rate.

A reconciliation between the Irish income tax statutory rate to the Company's effective tax rate for 2016, 2015 and 2014 is as follows (in thousands):

	For the Years Ended December 31,		
	2016	2015	2014
Irish income tax at statutory rate (12.5%)	$(28,510)	$(16,586)	$(33,711)
Bargain purchase gain	—	—	(5,542)
Transaction costs	3,447	3,109	5,402
Excise tax	—	—	3,911
Share-based compensation	7,125	3,776	1,460
Foreign tax rate differential	(1,893)	(30,348)	(64,675)
Change in valuation allowance	(6,117)	(106,834)	7,360
Derivative liability	—	—	75,248
Notional interest deduction	(35,075)	(22,848)	(2,149)
Interest expense on convertible debt inducements	—	(1,218)	(4,789)
Book loss on debt extinguishment	—	6,396	10,286
Uncertain tax positions	2,837	3,012	(491)
Change in U.S. state effective tax rate	(17,246)	(9,061)	—
Disallowed interest	2,620	2,139	—
Disqualified compensation expense	2,555	3,949	30
Tax charges on intragroup profit	2,154	(9,955)	—
U.S. state income taxes	8,579	1,002	272
U.S. federal and state tax credits	(3,613)	—	—
Other, net	1,886	1,223	1,304
Benefit for income taxes	$(61,251)	$(172,244)	$(6,084)
Effective income tax rate	26.9%	129.8%	2.3%

The overall effective tax rate benefit for 2016 of 26.9% was a higher benefit rate than the Irish statutory rate of 12.5% primarily due to the notional interest deduction, the benefit realized in the change in U.S. state effective tax rate, and the change in valuation allowance. The net benefit to income taxes is partially offset by the increase in stock based compensation not deductible for tax purposes and the increase in U.S. state income taxes.

The overall effective tax rate benefit for 2015 of 129.8% was a higher benefit rate than the Irish statutory rate of 12.5% primarily due to the release of valuation allowances in the United States following the acquisition of Hyperion in that year, the benefit realized on the foreign rate differential and the benefit realized on the notional interest deduction.

The decrease in the effective tax rate in 2016 compared to 2015 was primarily due to the one-time benefit recognized in 2015 for the release in valuation allowance.

During the year ended December 31, 2014, the Company released a portion of its valuation allowances as a result of the Vidara Merger. In connection with the Vidara Merger, the Company recorded additional deferred tax liabilities related to certain acquired assets. Accordingly, the Company recorded a net benefit for income taxes of $3.0 million for the release of its valuation allowances during the third quarter of 2014. In addition, the Company eliminated its deferred tax liability of $3.0 million at its Swiss subsidiary related to the intercompany sale of intellectual property in the fourth quarter of 2014.

The increase in the effective tax rate benefit in 2015 compared to 2014 was largely attributable to the 2015 release of valuation allowances in the United States and the benefit realized on losses tax effected at a higher statutory rate than the Irish statutory rate of 12.5%.

The Company accounts for income taxes based upon an asset and liability approach. Deferred tax assets and liabilities represent the future tax consequences of the differences between the financial statement carrying amounts of assets and liabilities versus the tax basis of assets and liabilities. Under this method, deferred tax assets are recognized for future deductible temporary differences and operating loss and tax credit carryforwards. Deferred tax liabilities are recognized for future taxable temporary differences. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The impact of tax rate changes on deferred tax assets and liabilities is recognized in the period in which the change is enacted.

The tax effects of the temporary differences and net operating losses that give rise to significant portions of deferred tax assets and liabilities, before jurisdictional netting, are as follows (in thousands):

	As of December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$99,004	$95,401
Capital loss carryforwards	4,631	14,843
Alternative minimum tax credit	5,922	3,157
U.S. federal and state credits	48,758	25,739
Accrued compensation	65,733	39,951
Accruals and reserves	20,179	5,829
Contingent royalties	68,628	41,544
Intercompany interest	54,703	51,919
Other	—	3,813
Total deferred tax assets	367,558	282,196
Valuation allowance	(32,532)	(31,310)
Deferred tax assets, net of valuation allowance	335,026	250,886
Deferred tax liabilities:		
Inventories	$13,077	$—
Debt discount	23,050	26,424
Intangible assets	593,057	335,584
Other	1,499	—
Total deferred tax liabilities	630,683	362,008
Net deferred income tax liability	$295,657	$111,122

As of December 31, 2016, the Company had net operating loss carryforwards of approximately $179.5 million for U.S. federal, $293.0 million for various states and $176.2 million for non-U.S. losses. These net operating losses include the net operating losses acquired in the acquisition of Raptor and are available to reduce future taxable income, if any, in the jurisdiction in which the net operating losses have been generated. Net operating loss carryforwards for U.S. federal income tax purposes have a twenty-year carryforward life and the earliest layers will begin to expire in 2019. U.S. state net operating losses started to expire in 2016 for the earliest net operating loss layers. Swiss net operating loss carryovers have a seven-year carryforward life and a portion of the earliest layer will begin to expire in 2017 for lack of sufficient taxable income to fully absorb the available carryover loss. Irish net operating losses are carried forward indefinitely and therefore have no expiration. Utilization of the U.S. net operating loss carryforwards may be subject to annual limitations as prescribed by federal and state statutory provisions. The imposition of the annual limitations may result in the expiration of net operating loss carryforwards in acceleration of the carryforward period allowed under statute.

Utilization of certain net operating loss carryforwards in the United States is subject to an annual limitation due to ownership change limitations provided by Sections 382 and 383 of the Internal Revenue Code. The Company is limited under the annual limitation of $14.7 million for 2017 and $7.7 million from the year 2018 until 2028 on certain net operating losses generated before an August 2, 2012 ownership change date. We continue to carryforward the annual limitation related to Hyperion of $50.0 million resulting from the last ownership change in 2014. Further, as a result of the acquisition of Raptor, its acquired net operating losses are subject to certain annual limitations for federal and state purposes. The U.S. federal net operating loss carryforward limitation is cumulative such that any use of the carryforwards below the limitation in a particular tax year will result in a corresponding increase in the limitation for the subsequent tax year.

At December 31, 2016, the Company had $61.8 million and $3.7 million of U.S. federal and state income tax credits, respectively, to reduce future tax liabilities. These tax credits include the tax credits acquired resulting from the acquisition of Raptor. The federal income tax credits consisted primarily of orphan drug credits, research and development credits and alternative minimum tax credits. The U.S. state income tax credits consisted primarily of California research and development credits and the Illinois Economic Development for a Growing Economy (“EDGE”) tax credit. Both the U.S. federal orphan drug credits and research and development credits have a twenty-year carryforward life. The U.S. federal orphan drug credits will begin to expire in 2027 and the U.S. federal research and development credits will begin to expire in 2025. The U.S. federal alternative minimum tax credit and California research and development credits have indefinite lives and therefore are not subject to expiration. The Illinois EDGE credit has a five-year carryforward life following the year of generation and will begin to expire in 2019.

For the year ended December 31, 2016, the Company had $1.6 million of excess tax benefits from share-based compensation. Under the with-and-without approach, there is no benefit recognized as a result of share-based compensation deductions and the tax benefit of the $0.5 million of excess tax benefit is not recognized in the balance sheet.

A reconciliation of the beginning and ending amounts of valuation allowances for the years ended December 31, 2016, 2015 and 2014 is as follows (in thousands):

Valuation allowances at December 31, 2013	$(128,422)
Decrease for 2014 activity	17,166
Release of valuation allowances	6,478
Additions to valuation allowances due to acquisitions	(6,777)
Valuation allowances at December 31, 2014	$(111,555)
Increase for 2015 activity	(37,569)
Release of valuation allowances	117,814
Valuation allowances at December 31, 2015	$(31,310)
Increase for 2016 activity	(14,636)
Release of valuation allowances	15,056
Additions to valuation allowances due to acquisitions	(1,642)
Valuation allowances at December 31, 2016	$(32,532)

Deferred tax valuation allowances increased by $1.2 million during the year ended December 31, 2016, and decreased by $80.2 million and $16.9 million during the years ended December 31, 2015 and 2014, respectively. For the year ended December 31, 2016, the increase in valuation allowances resulted primarily from the valuation allowances acquired from the acquisition of Raptor as well as activity resulting from certain deferred tax assets for which the Company determined that the deferred tax benefits may not be realized in the foreseeable future. The net increase in valuation allowance is partially offset by the release of valuation allowances resulting from the utilization of U.S. Federal capital loss carryforwards which were established in the year ended December 31, 2015. For the year ended December 31, 2015, the increase in valuation allowances resulted from capital loss carryforwards generated by the restructure of the Company’s Swiss subsidiary, and a capital loss recognized on the sale of long-term investments. As capital losses can only be offset by capital gains, and capital losses can only be carried forward for five years, the Company believes that the benefit of the capital losses may not be realized in the foreseeable future.

No provision has been made for income taxes on undistributed earnings of subsidiaries because it is the Company’s intention to indefinitely reinvest undistributed earnings of its subsidiaries. In the event of the distribution of those earnings in the form of dividends, a sale of the subsidiaries, or certain other transactions, the Company may be liable for income taxes. The unremitted earnings of the Company as of December 31, 2016 were $280.9 million, and the Company estimates tax on unremitted earnings to be $16.7 million.

The Company is required to recognize the financial statement effects of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained upon examination. The Company accounts for the uncertainty in income taxes by utilizing a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of any uncertain tax positions that have been taken, or are expected to be taken, on an income tax return. The changes in the Company's uncertain income tax positions for the years ended December 31, 2016, 2015 and 2014, excluding interest and penalties, consisted of the following (in thousands):

	For the Years Ended December 31,	
	2016	2015
Beginning balance – uncertain tax positions	$9,812	$775
Tax positions in the year:		
Additions	471	2,604
Acquired uncertain tax positions	5,362	6,433
Tax positions related to prior years:		
Additions	2,102	—
Ending balance – uncertain tax positions	$17,747	$9,812

For the year ended December 31, 2016, the increase in uncertain tax positions primarily resulted from the acquired uncertain tax positions related to the acquisition of Raptor. In the Company's consolidated balance sheet, uncertain tax positions of $7.7 million were included in other long-term liabilities and an additional $10.7 million was offset against deferred tax assets.

Penalties of $0.1 million and interest of $0.6 million are included in the balance of the uncertain tax positions at December 31, 2016, and there were penalties of $0.1 million and interest of $0.3 million included in the balance of uncertain tax positions at December 31, 2015. The Company classifies interest and penalties with respect to income tax liabilities as a component of income tax expense. The Company assessed that its liability for uncertain tax positions will not significantly change within the next twelve months. If these uncertain tax positions are released, the impact on the Company's tax provision would be a benefit of $18.4 million, including interest and penalties.

The Company files income tax returns in Ireland, in the United States for federal and various states, as well as in certain other non-U.S. jurisdictions. At December 31, 2016, all open tax years in U.S. federal and certain state jurisdictions date back to 2005 due to the taxing authorities' ability to adjust operating loss carryforwards. In Ireland the statute of limitations expires five years from the end of the tax year or four years from the time a tax return is filed, whichever is later. Therefore the earliest year open to examination is 2012 with the lapse of statute occurring in 2017. No changes in settled tax years have occurred to date. The Company is not currently under any income tax examinations.

NOTE 21 – EMPLOYEE BENEFIT PLANS

The Company sponsors a defined contribution 401(k) retirement savings plan covering all of its U.S. employees, whereby an eligible employee may elect to contribute a portion of his or her salary on a pre-tax basis, subject to applicable federal limitations. The Company is not required to make any discretionary matching of employee contributions. Beginning in 2014, the Company made a matching contribution generally equal to 50% of each employee's elective contribution to the plan of up to six percent of the employee's eligible pay with a 20% graded vesting over five years. Beginning in 2017, the Company will make a matching contribution equal to 100% of each employee's elective contribution to the plan of up to 3% of the employee's eligible pay, and 50% for the next 2% of the employee's eligible pay. The full amount of this employer contribution will be immediately vested in the plan. For the years ended December 31, 2016, 2015 and 2014, the Company recorded defined contribution expense of $2.7 million, $2.1 million and $0.8 million, respectively.

The Company's wholly owned subsidiary, Horizon Pharma Switzerland GmbH, sponsors a defined benefit savings plan covering all of its employees in Switzerland. The Company's wholly owned subsidiaries sponsor defined contribution plans for its employees in Germany, the Netherlands, Belgium, Denmark, Sweden, Norway and the United Kingdom. For the years ended December 31, 2016, 2015 and 2014, the Company recognized immaterial expenses under these plans.

The Company's wholly owned subsidiary, Horizon Pharma Services Limited, sponsors a defined contribution plan covering all of its employees in Ireland. For the years ended December 31, 2016 and 2015, the Company recognized expenses of $0.4 million and $0.2 million, respectively, under this plan. No expense was recorded in 2014, as the entity became part of the consolidated group as a result of the Vidara Merger in September 2014.

The Company has a non-qualified deferred compensation plan for executives, which was established in April 2015. The deferred compensation plan obligations are payable in cash upon retirement, termination of employment and/or certain other times in a lump-sum distribution or in installments, as elected by the participant in accordance with the plan. As of December 31, 2016 and 2015, the deferred compensation plan liabilities totaled $3.1 million and $0.8 million, respectively, and are included in “other long-term liabilities” in the consolidated balance sheet. The Company held funds of approximately $3.1 million and $0.8 million in an irrevocable grantor's rabbi trust as of December 31, 2016 and 2015, respectively, related to this plan. Rabbi trust assets are classified as available-for-sale marketable securities and are included in “other current assets” in the consolidated balance sheets. Unrealized gains and losses on these marketable securities are included in “other income” in the consolidated statements of comprehensive (loss) income.

NOTE 22 – SELECTED QUARTERLY FINANCIAL INFORMATION (UNAUDITED)

The following table provides a summary of selected financial results of operations by quarter for the years ended December 31, 2016 and 2015 (in thousands, except per share data):

2016	First	Second	Third	Fourth
Net sales	$204,690	$257,378	$208,702	$310,350
Gross profit	127,457	176,252	123,541	160,598
Operating (loss) income	(27,204)	31,467	(21,322)	(130,108)
Net (loss) income	(45,406)	14,984	(5,870)	(130,542)
Net (loss) income per ordinary share - basic	$(0.28)	$0.09	$(0.04)	$(0.81)
Net (loss) income per ordinary share - diluted	(0.28)	0.09	(0.04)	(0.81)

2015	First	Second	Third	Fourth
Net sales	$113,141	$172,821	$226,544	$244,538
Gross profit	84,288	110,995	165,294	176,965
Operating income (loss)	4,764	(33,173)	45,732	38,049
Net (loss) income	(19,553)	31,814	3,277	23,994
Net (loss) income per ordinary share - basic	$(0.16)	$0.21	$0.02	$0.15
Net (loss) income per ordinary share - diluted	(0.16)	0.20	0.02	0.15

HORIZON PHARMA PLC

SCHEDULE II – VALUATION AND QUALIFYING ACCOUNTS

For Each of the Three Fiscal Years Ended December 31, 2016, 2015 and 2014:

Valuation and Qualifying Accounts (in thousands)	Balance at beginning of period	Acquisitions	Additions Charged to costs and expenses	Deductions from reserves	Balance at end of period
Year ended December 31, 2016:					
Allowance for discounts and returns	$ 14,964	$ 1,234	$ 81,089	$ (75,371)	$ 21,916
Allowance for slow moving and obsolete inventory	1,001	—	1,092	(782)	1,311
Deferred tax asset valuation allowances	31,310	1,642	14,636	(15,056)	32,532
Year ended December 31, 2015:					
Allowance for discounts and returns	4,483	236	55,702	(45,457)	14,964
Allowance for slow moving and obsolete inventory	842	—	1,189	(1,030)	1,001
Deferred tax asset valuation allowances	111,555	—	37,569	(117,814)	31,310
Year ended December 31, 2014:					
Allowance for discounts and returns	431	—	18,254	(14,202)	4,483
Allowance for slow moving and obsolete inventory	365	—	1,195	(718)	842
Deferred tax asset valuation allowances	128,422	6,777	—	(23,644)	111,555

INDEX TO EXHIBITS

Exhibit Number	Description of Document
2.1[15]	Transaction Agreement and Plan of Merger, dated March 18, 2014, by and among Horizon Pharma, Inc., Vidara Therapeutics Holdings LLC, Vidara Therapeutics International Ltd. (now known as Horizon Pharma Public Limited Company), Hamilton Holdings (USA), Inc. and Hamilton Merger Sub, Inc.†
2.2[17]	First Amendment to Transaction Agreement and Plan of Merger, dated June 12, 2014, by and between Horizon Pharma, Inc. and Vidara Therapeutics Holdings LLC.
2.3[25]	Agreement and Plan of Merger, dated March 29, 2015, by and among Horizon Pharma, Inc., Ghrian Acquisition Inc. and Hyperion Therapeutics, Inc.†
2.4**[26]	Agreement and Plan of Merger, dated December 10, 2015, by and among Horizon Pharma USA, Inc., HZNP Limited, Criostail LLC, Crealta Holdings LLC and the other parties thereto.††
2.5[4]	Agreement and Plan of Merger, dated September 12, 2016, by and among Horizon Pharma Public Limited Company, Misneach Corporation and Raptor Pharmaceutical Corp.†
3.1[21]	Memorandum and Articles of Association of Horizon Pharma Public Limited Company, as amended.
4.1[3]***	Form of Warrant issued by Horizon Pharma, Inc. pursuant to the Securities Purchase Agreement, dated February 28, 2012, by and among Horizon Pharma, Inc. and the Purchasers and Warrant Holders listed therein.
4.2[6]***	Form of Warrant issued by Horizon Pharma, Inc. in Public Offering of Units.
4.3[24]	Indenture, dated March 13, 2015, by and among Horizon Pharma Public Limited Company, Horizon Pharma Investment Limited and U.S. Bank National Association.
4.4[24]	Form of 2.50% Exchangeable Senior Note due 2022 (included in Exhibit 4.3).
4.5[19]	Indenture, dated April 29, 2015, by and between Horizon Pharma Financing Inc. and U.S. Bank National Association.
4.6[19]	Form of 6.625% Senior Note due 2023 (included in Exhibit 4.5).
4.7[18]	First Supplemental Indenture, dated May 7, 2015, by and among Horizon Pharma Public Limited Company, certain subsidiaries of Horizon Pharma Public Limited Company and U.S. Bank National Association.
4.8[27]	Indenture, dated October 25, 2016, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and U.S. Bank National Association, as trustee.

4.9[27]	Form of 8.75% Senior Note due 2024 (included in Exhibit 4.8).
10.1[20]	Form of Indemnification Agreement entered into by and between Horizon Pharma Public Limited Company and certain of its directors, officers and employees.
10.2[20]	Form of Indemnification Agreement entered into by and between Horizon Pharma, Inc. and certain directors, officers and employees of Horizon Pharma Public Limited Company.
10.3+[26]	Horizon Pharma Public Limited Company Non-Employee Director Compensation Policy, as amended.
10.4+[1]***	Horizon Pharma, Inc. 2005 Stock Plan and Form of Stock Option Agreement thereunder.
10.5+[11]***	Horizon Pharma, Inc. 2011 Equity Incentive Plan, as amended, and Form of Option Agreement and Form of Stock Option Grant Notice thereunder.
10.6+[1]***	Horizon Pharma, Inc. 2011 Employee Stock Purchase Plan and Form of Offering Document thereunder.
10.7+[7]	Horizon Pharma Public Limited Company 2014 Equity Incentive Plan, as amended, and Form of Option Agreement, Form of Stock Option Grant Notice, Form of Restricted Stock Unit Agreement and Form of Restricted Stock Unit Grant Notice thereunder.

Exhibit Number	Description of Document
10.8+(7)	Horizon Pharma Public Limited Company 2014 Non-Employee Equity Plan, as amended, and Form of Option Agreement, Form of Stock Option Grant Notice, Form of Restricted Stock Unit Agreement and Form of Restricted Stock Unit Grant Notice thereunder.
10.9+(7)	Horizon Pharma Public Limited Company 2014 Employee Share Purchase Plan, as amended.
10.10*(1)	Development and License Agreement, dated August 20, 2004, by and among Horizon Pharma Switzerland GmbH (formerly known as Horizon Pharma AG), Jagotec AG and Vectura Group plc (as successor in interest to SkyePharma AG).
10.11*(1)	Amendment to Development and License Agreement, dated August 3, 2007, by and among Horizon Pharma Switzerland GmbH (formerly known as Horizon Pharma AG), Jagotec AG and Vectura Group plc (as successor in interest to SkyePharma AG).
10.12*(1)	Manufacturing and Supply Agreement, dated August 3, 2007, by and between Horizon Pharma Ireland Limited (as successor in interest to Horizon Pharma Switzerland GmbH (formerly known as Horizon Pharma AG)) and Jagotec AG.
10.13+(1)	Form of Employee Proprietary Information and Inventions Agreement.
10.14+(1)	Amended and Restated Executive Employment Agreement, dated July 27, 2010, by and between Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Timothy P. Walbert.
10.15+(1)	Amended and Restated Executive Employment Agreement, dated July 27, 2010, by and between Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Jeffrey W. Sherman, M.D. FACP.
10.16*(1)	Amendment to Manufacturing and Supply Agreement, dated March 4, 2011, by and between Horizon Pharma Switzerland GmbH (formerly known as Horizon Pharma AG) and Jagotec AG.
10.17*(1)	Manufacturing and Supply Agreement, dated May 25, 2011, by and between Horizon Pharma USA, Inc. and Sanofi-Aventis U.S. LLC.
10.18*(1)	Sales Contract, dated July 1, 2010, by and between Horizon Pharma USA, Inc. and BASF Corporation.
10.19*(10)	Amendment to Manufacturing and Supply Agreement, effective as of September 25, 2013, by and between Horizon Pharma USA, Inc. and Sanofi-Aventis U.S. LLC.
10.20+(5)	Amended and Restated Severance Benefit Plan Dated March 1, 2012.
10.21*(10)	License Agreement, dated August 21, 2013, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc., Par Pharmaceutical Companies, Inc. and Par Pharmaceutical, Inc.
10.22*(16)	License Agreement, dated November 22, 2013, by and between Horizon Pharma USA, Inc. and AstraZeneca AB.
10.23*(16)	Amended and Restated Collaboration and License Agreement for the United States, dated November 18, 2013, by and between Horizon Pharma USA, Inc. and Aralez Pharmaceuticals Inc. (as successor in

	interest to Pozen Inc.).
10.24*(14)	Amendment No. 1 to Amended and Restated Collaboration and License Agreement for the United States, dated November 18, 2013, by and between Horizon Pharma USA, Inc. and Aralez Pharmaceuticals Inc. (as successor in interest to Pozen Inc.).
10.25*(14)	Letter Agreement, dated November 18, 2013, by and among Horizon Pharma USA, Inc., AstraZeneca AB and Aralez Pharmaceuticals Inc. (as successor in interest to Pozen Inc.).
10.26*(16)	Master Manufacturing Services Agreement, dated October 31, 2013, by and between Horizon Pharma, Inc. and Patheon Pharmaceuticals, Inc.
10.27+(13)	First Amendment to Amended and Restated Executive Employment Agreement, dated January 16, 2014, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Timothy P. Walbert.
10.28+(13)	First Amendment to Amended and Restated Executive Employment Agreement, dated January 16, 2014, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Jeffrey W. Sherman, M.D., FACP.

Exhibit Number	Description of Document
10.29+(14)	Executive Employment Agreement, effective March 5, 2014, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Robert F. Carey.
10.30+(17)	Executive Employment Agreement, effective June 23, 2014, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Paul W. Hoelscher.
10.31*(23)	Supply Agreement, dated October 17, 2014, by and between Horizon Pharma Ireland Limited and Nuvo Research Inc.
10.32(22)	Lease, dated November 4, 2014, by and among Horizon Pharma Public Limited Company, Horizon Pharma Services Limited and John Ronan and Castle Cove Property Developments Limited.
10.33**(22)	Consolidated Supply Agreement, dated July 31, 2013, by and between Vidara Therapeutics Research Limited and Boehringer Ingelheim RCV GmbH & Co KG.
10.34**(22)	License Agreement for Interferon Gamma, dated May 5, 1998, by and between Genentech, Inc. and Connetics Corporation.
10.35(22)	Amendment No. 1 to License Agreement for Interferon Gamma, dated December 28, 1998, by and between Genentech, Inc. and Connetics Corporation.
10.36**(22)	Amendment No. 2 to License Agreement for Interferon Gamma, dated January 15, 1999, by and between Genentech, Inc. and Connetics Corporation.
10.37**(22)	Amendment No. 3 to License Agreement for Interferon Gamma, dated April 27, 1999, by and between Genentech, Inc. and Connetics Corporation.
10.38(22)	Consent to Assignment Agreement, dated June 23, 2000 (Amendment No. 4), by and among Genentech, Inc., Connetics Corporation and InterMune Pharmaceuticals, Inc.
10.39(22)	Amendment No. 5 to License Agreement for Interferon Gamma, dated January 25, 2001, by and between Genentech, Inc. and InterMune Pharmaceuticals, Inc.
10.40**(22)	Amendment No. 6 to License Agreement for Interferon Gamma, dated February 27, 2006, by and between Genentech, Inc. and InterMune, Inc.
10.41**(22)	Amendment No. 7 to License Agreement for Interferon Gamma, dated December 17, 2013, by and between Genentech, Inc. and Vidara Therapeutics International Public Limited Company.
10.42+(22)	Consulting Agreement, dated March 18, 2014 between Horizon Pharma USA, Inc. and Virinder Nohria.
10.43+(22)	Executive Employment Agreement, effective September 18, 2014, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and Barry Moze.
10.44+(22)	Horizon Pharma Public Limited Company Cash Long Term Incentive Program.
10.45+(2)	Horizon Pharma, Inc. Deferred Compensation Plan.

10.46+(2)	Horizon Pharma Public Limited Company Equity Long Term Incentive Program.
10.47+(2)	Executive Employment Agreement, dated May 7, 2015, by and among Horizon Pharma Inc., Horizon Pharma USA, Inc. and Brian Beeler.
10.48(18)	Credit Agreement, dated May 7, 2015, by and among Horizon Pharma, Inc., as borrower, Horizon Pharma Public Limited Company, as Irish Holdco and a guarantor, the subsidiary guarantors party thereto, as subsidiary guarantors, the lenders party thereto and Citibank, N.A., as administrative agent and collateral agent.
10.49*(9)	Confidential Settlement and License Agreement, dated May 6, 2015, by and among Horizon Pharma Ireland Limited, HZNP Limited, Horizon Pharma USA, Inc., Perrigo Company and Paddock Laboratories, LLC.
10.50**(12)	Amended and Restated Collaboration Agreement, dated March 22, 2012, by and among Hyperion Therapeutics, Inc. and Ucyclyd Pharma, Inc.
10.51**(12)	License Agreement, dated April 16, 1999, by and among Saul Brusilow, M.D., Brusilow Enterprises, Inc. and Medicis Pharmaceutical Corporation.

Exhibit Number	Description of Document
10.52**(12)	Settlement Agreement and First Amendment to License Agreement, dated August 21, 2007, by and among Saul Brusilow, M.D., Brusilow Enterprises, Inc., Medicis Pharmaceutical Corporation and Ucyclyd Pharma, Inc.
10.53+(28)	Horizon Pharma Public Limited Company Share Clog Program Trust Deed, as amended, and Form of Clog Letter.
10.54+(8)	Executive Employment Agreement, dated August 6, 2015, by and among Horizon Pharma Inc., Horizon Pharma USA, Inc. and George P. Hampton.
10.55**(8)	Confidential Settlement and License Agreement, dated September 9, 2015, by and among Horizon Pharma Ireland Limited, HZNP Limited, Horizon Pharma USA, Inc., Taro Pharmaceuticals USA, Inc. and Taro Pharmaceuticals Industries, Ltd.
10.56**(26)	License and Settlement Agreement, dated October 1, 2015, by and among Horizon Pharma Switzerland GmbH (formerly known as Horizon Pharma AG), Jagotec AG and Actavis Laboratories FL, Inc. (formerly known as Watson Laboratories, Inc.).
10.57**(26)	License Agreement, dated August 12, 1998, by and among Mountain View Pharmaceuticals, Inc., Duke University and Crealta Pharmaceuticals LLC (as successor in interest to Bio-Technology General Corporation), as amended November 12, 2001, August 30, 2010, March 12, 2014 and July 16, 2015.
10.58**(26)	Commercial Supply Agreement, dated March 20, 2007, by and between Crealta Pharmaceuticals LLC (as successor in interest to Savient Pharmaceuticals, Inc.) and Bio-Technology General (Israel) Ltd., as amended September 24, 2007, January 24, 2009, July 1, 2010 and March 21, 2012.
10.59**(26)	Supply Agreement, dated August 3, 2015, by and between NOF Corporation and Crealta Pharmaceuticals LLC.
10.60(26)	Sublease, dated August 21, 2015, by and between Solo Cup Operating Corporation and Horizon Pharma USA, Inc. and Sublease Consent and Recognition Agreement, dated October 2, 2015, by and among Lake Forest Landmark II, LLC, Solo Cup Operating Corporation and Horizon Pharma USA, Inc.
10.61**(12)	Asset Purchase Agreement, dated March 22, 2012, by and between Hyperion Therapeutics, Inc. and Ucyclyd Pharma, Inc.
10.62**(26)	Amendment No. 1 to Supply Agreement, dated February 4, 2016, by and between Horizon Pharma Ireland Limited and Nuvo Research Inc.
10.63**(26)	Commercial Supply Agreement, dated October 16, 2008, by and between Exelead, Inc. (formerly known as Sigma Tau PharmaSource, Inc. (as successor in interest to Enzon Pharmaceuticals, Inc.)) and Crealta Pharmaceuticals LLC (as successor in interest to Savient Pharmaceuticals, Inc.), as amended October 5, 2009, October 22, 2009 and July 29, 2014.
10.64	Amendment to Manufacturing and Supply Agreement, dated January 1, 2017, by and between Horizon Pharma Ireland Limited and Jagotec AG.

10.65*(28)	Amendment No. 2 to the Consolidated Supply Agreement, effective as of June 1, 2015, by and between Horizon Pharma Ireland Limited (as successor in interest to Vidara Therapeutics Research Limited) and Boehringer Ingelheim Biopharmaceuticals GmbH (as successor in interest to Boehringer Ingelheim RCV GmbH & Co KG).
10.66**(29)	Fifth Amendment to Commercial Supply Agreement, effective as of August 31, 2016, by and between Horizon Pharma Ireland Limited and Bio-Technology General (Israel) Ltd.
10.67(27)	Amendment No. 1, dated October 25, 2016, to Credit Agreement, dated May 7, 2015, by and among Horizon Pharma, Inc., as borrower, Horizon Pharma Public Limited Company, as Irish Holdco and a guarantor, the subsidiary guarantors party thereto, as subsidiary guarantors, the lenders party thereto and Citibank, N.A., as administrative agent and collateral agent.
10.68**(29)	Amended and Restated License Agreement, effective October 30, 2012, by and between The Regents of the University of California and Horizon Orphan LLC (as successor in interest to Raptor Therapeutics Inc.), as amended March 1, 2013 and December 16, 2013.

Exhibit Number	Description of Document
10.69**(29)	API Supply Agreement, dated November 3, 2010, by and among Cambrex Profarmaco Milano, Horizon Orphan LLC (as successor in interest to Raptor Therapeutics Inc.) and Horizon Pharma Europe B.V. (as successor in interest to Raptor Pharmaceuticals Europe B.V.), as amended April 9, 2013.
10.70**(29)	Manufacturing Services Agreement, dated November 15, 2010, by and among Patheon Pharmaceuticals Inc., Horizon Orphan LLC (as successor in interest to Raptor Therapeutics Inc.) and Horizon Pharma Europe B.V. (as successor in interest to Raptor Pharmaceuticals Europe B.V.), as amended April 5, 2012 and June 21, 2013.
10.71**(29)	Confidential Settlement Agreement and Mutual Release, dated September 26, 2016, by and between Horizon Pharma USA, Inc. and Express Scripts, Inc.
10.72+	Executive Employment Agreement, effective as of October 25, 2016, by and among Horizon Pharma, Inc., Horizon Pharma USA, Inc. and David A. Happel.
10.73+**	Transition Agreement, dated October 13, 2016, by and between Horizon Pharmaceutical LLC (as successor in interest to Raptor Pharmaceutical Corp.) and David A. Happel.
10.74**	Amendment No. 1 to Sales Contract, effective as of January 1, 2016, by and between Horizon Pharma USA, Inc. and BASF Corporation.
21.1	Subsidiaries of Horizon Pharma Public Limited Company.
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.
32.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350.
32.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document

101.PRE XBRL Taxonomy Extension Presentation Linkbase Document

+ Indicates management contract or compensatory plan.

† Schedules have been omitted pursuant to Item 601(b)(2) of Regulation S-K. Horizon Pharma Public Limited Company undertakes to furnish supplemental copies of any of the omitted schedules upon request by the Securities and Exchange Commission.

‡ Schedules have been omitted pursuant to Item 601(b)(2) of Regulation S-K. Horizon Pharma Public Limited Company undertakes to furnish supplemental copies of any of the omitted schedules upon request by the Securities and Exchange Commission; provided, however, that Horizon Pharma Public Limited Company may request confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended, for any schedule so furnished.

* Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

** Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

*** Indicates an instrument, agreement or compensatory arrangement or plan assumed by Horizon Pharma Public Limited Company in the merger and no longer binding on Horizon Pharma, Inc.

(1) Incorporated by reference to Horizon Pharma, Inc.'s Registration Statement on Form S-1 (No. 333-168504), as amended.
(2) Incorporated by reference to Horizon Pharma Public Limited Company's Quarterly Report on Form 10-Q, filed on May 8, 2015.
(3) Incorporated by reference to Horizon Pharma, Inc.'s Current Report on Form 8-K, filed on March 1, 2012.
(4) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on September 12, 2016.
(5) Incorporated by reference to Horizon Pharma, Inc.'s Annual Report on Form 10-K, filed on March 23, 2012.
(6) Incorporated by reference to Horizon Pharma, Inc.'s Current Report on Form 8-K, filed on September 20, 2012.
(7) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on May 4, 2016.
(8) Incorporated by reference to Horizon Pharma Public Limited Company's Quarterly Report on Form 10-Q, filed on November 6, 2015.
(9) Incorporated by reference to Horizon Pharma Public Limited Company's Quarterly Report on Form 10-Q, filed on August 7, 2015.
(10) Incorporated by reference to Horizon Pharma, Inc.'s Quarterly Report on Form 10-Q, filed on November 8, 2013.
(11) Incorporated by reference to Horizon Pharma, Inc.'s Current Report on Form 8-K, filed on July 2, 2014.
(12) Incorporated by reference to Hyperion Therapeutics, Inc.'s Amendment No. 1 to the Registration Statement on Form S-1, filed on May 24, 2012.
(13) Incorporated by reference to Horizon Pharma, Inc.'s Current Report on Form 8-K, filed on January 16, 2014.
(14) Incorporated by reference to Horizon Pharma, Inc.'s Annual Report on Form 10-K, filed on March 13, 2014.
(15) Incorporated by reference to Horizon Pharma, Inc.'s Current Report on Form 8-K, filed on March 20, 2014.
(16) Incorporated by reference to Horizon Pharma, Inc.'s Amendment No.1 to Annual Report on Form 10-K, filed on May 23, 2014.
(17) Incorporated by reference to Horizon Pharma, Inc.'s Current Report on Form 8-K, filed on June 18, 2014.
(18) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on May 11, 2015.
(19) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on April 29, 2015.
(20) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on September 19, 2014.
(21) Incorporated by reference to Horizon Pharma Public Limited Company's Registration Statement on Form S-8, filed on May 4, 2016.
(22) Incorporated by reference to Horizon Pharma Public Limited Company's Annual Report on Form 10-K, filed on February 27, 2015.
(23) Incorporated by reference to Horizon Pharma Public Limited Company's Amendment No. 2 to Annual Report on Form 10-K, filed on April 10, 2015.
(24) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on March 13, 2015.
(25) Incorporated by reference to Horizon Pharma Public Limited Company's Amendment No. 1 to Current Report on Form 8-K, filed on April 9, 2015.
(26) Incorporated by reference to Horizon Pharma Public Limited Company's Annual Report on Form 10-K, filed on February 29, 2016.
(27) Incorporated by reference to Horizon Pharma Public Limited Company's Current Report on Form 8-K, filed on October 25, 2016.

(28) Incorporated by reference to Horizon Pharma Public Limited Company's Quarterly Report on Form 10-Q, filed on August 8, 2016.

(29) Incorporated by reference to Horizon Pharma Public Limited Company's Quarterly Report on Form 10-Q, filed on November 7, 2016.