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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, 2015

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: 001-33500

JAZZ PHARMACEUTICALS PUBLIC LIMITED COMPANY
(Exact name of registrant as specified in its charter)

Ireland	**98-1032470**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

Fourth Floor, Connaught House
One Burlington Road, Dublin 4, Ireland
011-353-1-634-7800
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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 Stock Market LLC**

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 Web site, 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 registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, as of June 30, 2015, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $7,451,638,590 based upon the last sale price reported for the registrant's ordinary shares on such date on The NASDAQ Global Select Market. The calculation of the aggregate market value of voting and non-voting common equity excludes 18,973,047 ordinary shares of the registrant held by executive officers, directors and shareholders that the registrant concluded were affiliates of the registrant on that date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of February 17, 2016, a total of 61,184,623 ordinary shares, nominal value $0.0001 per share, of the registrant were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III, Items 10-14 of this Form 10-K is incorporated by reference to the registrant's definitive Proxy Statement for the 2016 Annual General Meeting of Shareholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K, provided that if such Proxy Statement is not filed within such period, such information will be included in an amendment to this Form 10-K to be filed within such 120-day period.

JAZZ PHARMACEUTICALS PLC
2015 ANNUAL REPORT ON FORM 10-K

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We own or have rights to various copyrights, trademarks, and trade names used in our business in the United States and/or other countries, including the following: Jazz Pharmaceuticals®, Xyrem® (sodium oxybate) oral solution, Erwinaze® (asparaginase *Erwinia chrysanthemi*), Erwinase®, Defitelio® (defibrotide), Prialt® (ziconotide) intrathecal infusion, FazaClo® (clozapine, USP) and Leukotac™ (inolimomab). This report also includes trademarks, service marks, and trade names of other companies. Service marks, trademarks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "propose," "intend," "continue," "potential," "possible," "foreseeable," "likely," "unforeseen" and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading "Risk Factors." Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this filing. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify our forward-looking statements by our cautionary statements. Except as required by law, we assume no obligation to update our forward-looking statements publicly, or to update the reasons that actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

NOTE REGARDING COMPANY REFERENCE

In this report, unless otherwise indicated or the context otherwise requires, all references to "Jazz Pharmaceuticals," "the registrant," "we," "us," and "our" refer to Jazz Pharmaceuticals plc and its consolidated subsidiaries, except when the context makes clear that the time period being referenced is prior to January 18, 2012, in which case such terms are references to Jazz Pharmaceuticals, Inc. and its consolidated subsidiaries. On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company, or Azur Pharma, were combined in a merger transaction, or the Azur Merger, in connection with which Azur Pharma was re-named Jazz Pharmaceuticals plc and we became the parent company of and successor to Jazz Pharmaceuticals, Inc., with Jazz Pharmaceuticals, Inc. becoming our wholly owned subsidiary. Jazz Pharmaceuticals, Inc. was treated as the acquiring company in the Azur Merger for accounting purposes, and as a result, the historical consolidated financial statements of Jazz Pharmaceuticals, Inc. became our consolidated financial statements.

PART I

Item 1. Business

Overview

Jazz Pharmaceuticals plc is an international biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing meaningful products that address unmet medical needs.

We have a diverse portfolio of products and product candidates, with a focus in the areas of sleep and hematology/oncology.

Our lead marketed products are:

- **Xyrem® (sodium oxybate) oral solution**, the only product approved by the U.S. Food and Drug Administration, or FDA, for the treatment of both cataplexy and excessive daytime sleepiness, or EDS, in patients with narcolepsy;
- **Erwinaze® (asparaginase *Erwinia chrysanthemi*)**, a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia, or ALL, who have developed hypersensitivity to *E. coli*-derived asparaginase; and
- **Defitelio® (defibrotide)**, a product approved in Europe for the treatment of severe hepatic veno-occlusive disease, or VOD, in adults and children undergoing hematopoietic stem cell transplantation, or HSCT, therapy.

Our strategy is to create shareholder value by:

- Growing sales of the existing products in our portfolio, including by identifying and investing in growth opportunities such as new treatment indications;
- Acquiring clinically meaningful and differentiated products that are on the market or product candidates that are in late-stage development; and
- Pursuing targeted development of post-discovery differentiated product candidates.

We apply a disciplined approach to allocating our resources between investments in our current commercial and development portfolio and acquisitions or in-licensing of new assets.

Our research and development activities currently include clinical development of new product candidates, activities related to line extensions and new indications for existing products and the generation of additional clinical data for existing products. A summary of our ongoing development activities is provided below:

Project	Disease Area	Status
Sleep		
JZP-110	EDS in narcolepsy	Phase 3 clinical trial initiated in second quarter of 2015; preliminary data expected in fourth quarter of 2016
	EDS in obstructive sleep apnea, or OSA	Two Phase 3 clinical trials initiated in second quarter of 2015; preliminary data expected in fourth quarter of 2016
JZP-386	EDS in narcolepsy	Phase 1 clinical trials completed; further evaluation ongoing
Xyrem	Cataplexy with narcolepsy in children and adolescents	Phase 3 clinical trial ongoing; enrollment completion expected in second half of 2016
Hematology/Oncology		
Defibrotide	VOD with evidence of multi-organ dysfunction following HSCT	New drug application, or NDA, accepted for filing with priority review by the FDA in third quarter of 2015; Prescription Drug User Fee Act, or PDUFA, date of March 31, 2016
Defibrotide	Prevention of VOD in high-risk patients	Preparing to initiate clinical trial

Our Products

Xyrem

Xyrem is the only treatment approved by the FDA for both EDS and cataplexy in patients with narcolepsy. Sodium oxybate, the active pharmaceutical ingredient in Xyrem, is a formulation of the sodium salt of gamma-hydroxybutyrate, or GHB, an endogenous neurotransmitter and metabolite of gamma-aminobutyric acid. Xyrem was approved in the U.S. for the treatment of cataplexy in patients with narcolepsy in 2002 and was approved for EDS in patients with narcolepsy in 2005. The American Academy of Sleep Medicine recommended Xyrem as a standard of care for the treatment of both EDS and cataplexy associated with narcolepsy.

Narcolepsy is a chronic neurological disorder caused by a loss of neurons that produce the neurotransmitter hypocretin (also known as orexin), which is hypothesized to stabilize sleep-wake states. The primary symptoms of narcolepsy include EDS, cataplexy, sleep paralysis, hypnogogic hallucinations and disrupted nighttime sleep. EDS is an essential symptom of narcolepsy, is present in all narcolepsy patients and is characterized by chronic, pervasive sleepiness as well as sudden irresistible and overwhelming urges to sleep (inadvertent naps and sleep attacks). Cataplexy, the sudden loss of muscle tone, can be one of the most debilitating symptoms of narcolepsy. Cataplexy is present in approximately 70% of patients with narcolepsy. Cataplexy can range from slight weakness or a drooping of facial muscles to the complete loss of muscle tone resulting in postural collapse. It may also impair a patient's vision or speech. Cataplexy is often triggered by strong emotions such as laughter, anger or surprise. Cataplexy can severely impair a patient's quality of life and ability to function.

Narcolepsy may affect many areas of life, including limiting a patient's education and employment opportunities and leading to driving or machinery accidents or difficulties at work resulting in disability or job dismissal. Patients with narcolepsy may also suffer from significant medical comorbidities, including depression, suicide risk, anxiety, diseases of the digestive system, respiratory diseases and cardiac disorders.

It is estimated that narcolepsy affected approximately 1 in 2,000 people in the U.S., or approximately 160,000 people, in 2015. Less than half of those people have been definitively diagnosed with narcolepsy. In the fourth quarter of 2015, the average number of active Xyrem patients in the U.S. was approximately 12,550 patients, and we believe that there are significantly more narcoleptic patients with cataplexy and/or EDS who might benefit from treatment with Xyrem. In an effort to reach more patients, we continue to implement initiatives such as outreach to prescribers who treat narcolepsy, physician/healthcare provider education, enhanced patient and physician support services and unbranded disease awareness programs for the public.

In 2015, net product sales of Xyrem were $955.2 million, which represented 72.5% of our total net product sales.

We promote Xyrem in the U.S. through a specialty sales force of approximately 100 sales professionals dedicated to Xyrem. Our marketing, sales and distribution of Xyrem are subject to a risk evaluation and mitigation strategy, or REMS, which is required by the FDA to ensure the safe distribution of Xyrem and minimize the risk of misuse, abuse and diversion of

sodium oxybate. Under the Xyrem REMS, all of the Xyrem sold in the U.S. must be dispensed and shipped directly to patients through a central pharmacy. Xyrem may not be stocked in retail pharmacies. Physicians and patients must complete an enrollment process prior to fulfillment of Xyrem prescriptions, and each physician and patient receives materials concerning the risks and benefits of Xyrem before the physician can prescribe, or a patient can receive, the product. Whenever a prescription is received by the central pharmacy, the central pharmacy verifies the prescription and must speak with the patient before each prescription of Xyrem is filled and sent to the patient. The central pharmacy ships the product directly to the patient by a courier service, and the patient or his/her designee signs for the package. The initial shipment may include only up to a one-month supply, and refill orders may include only up to a three-month supply.

We have an agreement with Express Scripts Specialty Distribution Services, Inc. and its affiliate CuraScript, Inc., which we refer to together as Express Scripts, to exclusively distribute Xyrem in the U.S. and provide customer support services related to the sales and marketing of Xyrem. Pursuant to the agreement, Express Scripts provides reimbursement support to patients by coordinating insurance coverage for Xyrem and, as applicable, referring qualified patients to various patient savings or assistance programs. Our agreement with Express Scripts, which has been in effect since July 2002, expires on June 30, 2017, subject to automatic two-year extensions unless either party provides notice to the other of its intent to terminate the agreement not less than 120 days before the end of the then-current term. Under the agreement, we own all standard operating procedures, business rules and the related intellectual property. The agreement provides for Express Scripts to assist in the orderly transfer of the services that Express Scripts provides to us and the related intellectual property, including intellectual property related to the patient database, to any new pharmacy that we may we engage.

Seven companies have sent us notices that they have filed abbreviated new drug applications, or ANDAs, with the FDA seeking approval to market a generic version of Xyrem. We have filed lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and the litigation proceedings are ongoing. We cannot predict the timing or outcome of these proceedings. Although no trial date has been set in any of the ANDA suits, we anticipate that trial on some of the patents in the case against the first ANDA filer, Roxane Laboratories, Inc., or Roxane, could occur as early as the second quarter of 2016. Some of the ANDA filers have also filed petitions for *inter partes* review, or IPR, by the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO, with respect to the validity of certain distribution, method of use and formulation patents covering Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to petitions related to certain patents covering the Xyrem distribution system, and we expect the PTAB to issue final decisions on the validity of those patents in July 2016. For a description of these matters, see “Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K. We have also been engaged in discussions with the ANDA filers with respect to potential development of a single shared REMS for Xyrem and generic sodium oxybate, and the outcome of these discussions is uncertain. For further discussion regarding these and other challenges we face with respect to Xyrem, see “Business—Government Regulation—*The Hatch-Waxman Act*” in this Part I, Item 1 and the risk factors under the headings “Risks Related to Xyrem and the Significant Impact of Xyrem Sales” and “Risks Related to Our Intellectual Property” in Part I, Item 1A of this Annual Report on Form 10-K.

Xyrem is a controlled substance in the U.S., subject to regulation by the U.S. Drug Enforcement Administration, or DEA, under the Controlled Substances Act, or CSA. Therefore, its manufacturing and distribution are highly restricted. The finished product and active pharmaceutical ingredient for Xyrem are each manufactured for us by a single source supplier. For more information regarding Xyrem supply, see “Business—Manufacturing” in this Part I, Item 1 and the risk factor under the heading “*The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy, and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem*” in Part I, Item 1A of this Annual Report on Form 10-K.

Outside of the U.S., UCB Pharma Limited, or UCB, has an exclusive license to market Xyrem for the treatment of narcolepsy in 54 countries and currently sells the product in 18 countries. We have licensed to Valeant Canada Limited, or Valeant, the Canadian marketing rights to Xyrem for the treatment of narcolepsy. We supply Xyrem to UCB and Valeant.

We have 20 U.S. patents covering Xyrem, which expire at various times from December 2019 to March 2033. Our issued patents relate to Xyrem’s stable and microbially resistant formulation, its manufacturing process, its method of use, including its restricted distribution system, and its method of administration.

Erwinaze

Erwinaze (called Erwinase in markets outside the U.S., and which we refer to in this report as Erwinaze unless otherwise indicated or the context otherwise requires) is a biologic product used in conjunction with chemotherapy to treat patients with ALL who have developed hypersensitivity to *E. coli*-derived asparaginase. Erwinaze is an asparaginase, a type of enzyme that can deprive leukemic cells of an amino acid essential for their growth. It is derived from a rare bacterium (*Erwinia chrysanthemi*) and is immunologically distinct from *E. coli*-derived asparaginase and suitable for patients with hypersensitivity to *E. coli*-derived treatments. For ALL patients with hypersensitivity to *E. coli*-derived asparaginase, Erwinaze can be a crucial

component of their therapeutic regimen. Erwinaze was originally developed by Public Health England, a U.K. national executive agency. First approved by the FDA under a biologics license application, or BLA, for administration via intramuscular injection in conjunction with chemotherapy, Erwinaze was launched in the U.S. in November 2011. In December 2014, the FDA approved a supplemental BLA for administration of Erwinaze via intravenous infusion in conjunction with chemotherapy. In Europe and elsewhere around the world, Erwinase is sold pursuant to marketing authorizations, named patient programs, temporary use authorizations or similar authorizations.

ALL is the most common childhood cancer. Based on data from the U.S. National Cancer Institute, the U.S. Census Bureau and the American Cancer Society, we estimate that approximately 5,000 to 6,000 new cases of ALL were diagnosed in the U.S. in 2014. Approximately 50% of ALL patients were diagnosed under age 15 and approximately 20% were diagnosed between 15 and 39 years of age, which suggests that approximately 3,500 to 4,200 ALL patients were pediatric, adolescent or young adults. A study published by Dana Farber Cancer Institute, with median follow-up of 57 months, concluded that the intensive use of high-dose asparaginase has an important role in the treatment of children with ALL. Data reported in two separate papers published in *Pediatric Blood & Cancer* and *Journal of Clinical Oncology*, respectively, suggest that up to 20% of ALL patients may develop hypersensitivity to *E. coli*-derived asparaginase. Current treatment guidelines and protocols recommend switching a patient receiving *E. coli*-derived asparaginase to treatment with Erwinaze if the patient's hypersensitivity reaction to the *E. coli*-derived asparaginase is Grade 2-4, indicating that the hypersensitivity reaction has resulted in an intervention or interruption in infusion occurring in the patient's treatment regimen. While pediatric treatment protocols commonly include asparaginase, adult protocols do not. A retrospective comparison to determine whether the outcome for ALL patients between 15 and 39 years of age differed depending on their enrollment in pediatric compared with adult cooperative group trials showed that the seven-year overall survival rate among the adolescent and young adult ALL patients treated on pediatric protocols was 67% compared to 46% for those patients treated on adult protocols. As more treatment protocols in adult centers incorporate the use of asparaginase-based regimens, we expect to see increased use of Erwinaze. In addition, we believe that Erwinaze has the potential for use in patients with silent hypersensitivity, a situation in which *E. coli*-derived asparaginase may induce antibodies that can neutralize the enzyme or increase its clearance, thereby depriving patients of its therapeutic benefits without manifesting the clinical symptoms of hypersensitivity. A third party has introduced an assay to determine the enzyme activity of asparaginase in patients who have been treated with any *E. coli*-derived asparaginase or Erwinaze. With this assay, physicians may be able to monitor asparaginase levels to identify patients with silent hypersensitivity and maintain asparaginase activity by switching asparaginase preparations. We expect adoption of this assay to be limited until its use is included in existing pediatric and adult treatment protocols.

In 2015, net product sales of Erwinaze were $203.3 million, which represented 15.4% of our total net product sales.

We promote Erwinaze in the U.S. through a specialty sales force of approximately 35 sales professionals who will also promote defibrotide in the U.S. if it is approved by the FDA. We provide reimbursement support through our JumpStart™ Access & Reimbursement Solutions program, a dedicated Erwinaze call center. Our field-based and office-based reimbursement team provides additional reimbursement support, dealing specifically with the more complex needs of physicians and payors.

Our hematology and oncology sales force outside of the U.S. has approximately 33 hematology field specialists responsible for promoting Erwinase and Defitelio in approved markets where we commercialize these products. In those markets where Erwinase is not currently approved, approximately 17 medical science liaisons and eight medical directors are responsible for responding to medical information requests and for providing information consistent with local treatment protocols.

Erwinaze is exclusively licensed to us for worldwide marketing, sales and distribution by Porton Biopharma Limited, or PBL, a company that is wholly owned by the U.K. Secretary of State for Health. PBL also manufactures the product for us and is our sole supplier for Erwinaze. We are obligated to make tiered royalty payments to PBL based on worldwide net sales of Erwinaze. For more information regarding Erwinaze supply, see "Business—Manufacturing" in this Part I, Item 1 and the risk factor under the heading *"We depend on single source suppliers for each of our products, product candidates and their active pharmaceutical ingredients. The loss of any of these suppliers, or delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, could materially and adversely affect our business, financial condition, results of operations and growth prospects"* in Part I, Item 1A of this Annual Report on Form 10-K.

Erwinaze has no patent protection. It was awarded orphan drug exclusivity for the treatment of ALL in the U.S. until November 2018, and we believe that it is protected by exclusivity that prevents approval of a biosimilar in the U.S. through late 2023 under the U.S. Biologics Price Competition and Innovation Act, or BPCIA.

Defitelio/defibrotide

Defibrotide, the active pharmaceutical ingredient in Defitelio, is the sodium salt of a complex mixture of single-stranded oligodeoxyribonucleotides derived from porcine DNA. In *in vitro* studies, defibrotide has shown a number of pharmacological

effects that suggest it has a role in both protection of the endothelial cells that form the inner lining of blood vessels and restoration of the balance between clot formation and breakdown in the blood.

Defibrotide has been developed for the treatment and prevention of VOD, a potentially life-threatening complication of HSCT. Stem cell transplantation is a frequently used treatment modality for hematologic cancers and other conditions in both adults and children. Certain conditioning regimens used as part of HSCT can damage the cells that line the hepatic vessels, which is thought to lead to the development of VOD, a blockage of the small vessels in the liver, that leads to liver failure and can result in significant dysfunction in other organs such as the kidneys and lungs. The condition is also referred to as "sinusoidal obstruction syndrome." Severe VOD is the most extreme form of VOD and is associated with multi-organ failure and high rates of morbidity and mortality. An analysis of retrospective data, prospective cohort studies and clinical trials published between 1979 and 2007 found that the 100-day mortality rate in severe VOD cases is greater than 80%. Based on data from published surveys and our market research, we calculated that, in Europe, of the estimated approximately 35,000 patients undergoing HSCT in 2014, approximately 6,300 were considered at high risk for the development of VOD, and the incidence of VOD was approximately 3,600 patients; in the U.S., of the estimated approximately 20,000 patients undergoing HSCT in 2014, approximately 3,000 were considered at high risk for the development of VOD, and the incidence of VOD was approximately 1,000 to 2,000 patients. Our review of relevant literature and market research also suggests that about one-third to two-thirds of VOD patients may be eligible for treatment using defibrotide.

In October 2013, the European Commission, or EC, granted marketing authorization under exceptional circumstances for Defitelio for the treatment of severe VOD in adults and children undergoing HSCT. Defitelio is the first approved treatment in the European Union, or EU, for this potentially life-threatening condition. Defitelio has generally been well-tolerated; the most frequent adverse reactions observed during pre-marketing use of the product are hemorrhage, hypotension and coagulopathy.

We launched Defitelio in certain European countries in 2014 and continued to launch in additional European countries on a rolling basis through 2015. We are in the process of making pricing and reimbursement submissions with respect to Defitelio in those European countries where Defitelio is not yet launched, including in countries where pricing and reimbursement approvals are required for launch. We promote Defitelio along with Erwinase to many hematology and oncology specialists who operate in the same hospitals, and we believe that we benefit from operational synergies from this overlap. In addition, in those European markets where Defitelio is approved but not yet launched, our medical science liaisons and medical directors respond to medical information requests regarding defibrotide and provide information consistent with local treatment protocols. We intend eventually to commercialize Defitelio in all European markets where it has marketing authorization. We also continue to provide patients access to defibrotide where it is not commercially available outside the U.S. on a named patient basis.

Defitelio/defibrotide product sales were $70.7 million in 2015, which represented 5.4% of our total net product sales.

In August 2014, we acquired from Sigma-Tau Pharmaceuticals, Inc., or Sigma-Tau, the rights to defibrotide for the treatment and prevention of VOD in North America, Central America and South America. In exchange for the rights to defibrotide in the Americas, we made an upfront payment of $75.0 million to Sigma-Tau and also agreed to make milestone payments of up to $175.0 million comprised of (i) $25.0 million upon the acceptance for filing by the FDA of the first NDA for defibrotide for VOD, which we paid to Sigma-Tau in the fourth quarter of 2015; and (ii) up to an additional $150.0 million based on the timing of potential FDA approval of defibrotide for VOD.

There are currently no approved treatments for VOD in the U.S. We provide patients in the U.S. access to defibrotide through an expanded access treatment protocol that is open under an investigational new drug application, or IND. In September 2015, the FDA accepted for filing with priority review our NDA for defibrotide for the treatment of VOD with evidence of multi-organ dysfunction following HSCT. Based on timelines established by the PDUFA, we expect FDA review of the NDA to be completed by March 31, 2016. However, the FDA does not always meet the timelines established by PDUFA, and it is possible that the FDA's review of our NDA will not be completed by the PDUFA date, in which case our plans for commercialization of defibrotide in the U.S. may be delayed. In any event, we cannot predict whether our NDA will be approved in a timely manner, if at all. For more information, see "Business—Government Regulation—Approval of Pharmaceutical Products" in this Part I, Item 1 and the risk factor under the heading *"We may not be able to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval of defibrotide in other countries, including the U.S., which could have a material adverse effect on our business, financial condition, results of operations and growth prospects"* in Part I, Item 1A of this Annual Report on Form 10-K. If defibrotide is approved by the FDA, we plan to promote defibrotide in the U.S. through our specialty sales force of approximately 35 sales professionals who currently promote Erwinaze in the U.S.

We are preparing to commence a clinical trial to evaluate the safety and efficacy of defibrotide for the prevention of VOD in high-risk patients. We expect to finalize the protocol and complete site activation in the first half of 2016 and to initiate patient enrollment in the third quarter of 2016. We are also assessing the potential for approval of defibrotide in other countries and for development of defibrotide in additional indications. Defibrotide has received orphan drug designation to treat and

prevent VOD from the European Medicines Agency, or EMA, and the Korean Ministry of Food and Drug Safety. The Commonwealth of Australia-Department of Health has granted defibrotide orphan drug designation for the treatment of VOD. In addition, the EMA also granted orphan drug designation to defibrotide for the prevention of graft vs. host disease, or GvHD, another potentially fatal complication of HSCT that afflicts up to 50% of all donor transplant patients.

The drug substance defibrotide was developed and is manufactured in a facility in Italy that we acquired in connection with our acquisition of Gentium S.r.l., or Gentium, in January 2014, which we refer to as the Gentium Acquisition. The finished product is manufactured for us by a single source supplier. For more information regarding Defitelio/defibrotide supply, see "Business—Manufacturing" in this Part I, Item 1 and the risk factor under the heading "*We depend on single source suppliers for each of our products, product candidates and their active pharmaceutical ingredients. The loss of any of these suppliers, or delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in Part I, Item 1A of this Annual Report on Form 10-K.

The unique process of deriving defibrotide from porcine DNA is extensive and uses both chemical and biological processes which rely on complex characterization methods. We have a portfolio of U.S. and non-U.S. patents and patent applications relating to various compositions, methods of use and methods of characterization, which will expire at various times between April 2017 and June 2035.

Prialt and other products

We also commercialize a portfolio of other products, including Prialt. Prialt is an intrathecally administered infusion of ziconotide, approved by the FDA in December 2004 for the management of severe chronic pain in patients for whom intrathecal therapy is warranted, and who are intolerant of or refractory to other treatment, such as systemic analgesics, adjunctive therapies or intrathecal morphine. Intrathecal therapy is the delivery of the drug into the intrathecal space in the spine through an infusion system comprised of a programmable infusion pump and catheter. For most patients who achieve good pain relief and tolerability with Prialt, pain relief can be maintained over time without cumulative toxicity. Prialt is the only FDA-approved non-opioid intrathecal analgesic. We have worldwide rights to Prialt, excluding certain countries outside of the U.S. licensed by Eisai Co. Limited, or Eisai, from Elan Pharmaceuticals, Inc. (subsequently acquired by Perrigo Company plc) in May 2010. We do not currently sell the product outside of the U.S. We supply Prialt to Eisai.

We also sell psychiatry and other products in the U.S.

Research and Development

Our development projects currently include clinical development of new product candidates, activities related to line extensions for existing products and the generation of additional clinical data for existing products. These projects are concentrated in our sleep and hematology/oncology therapeutic areas.

In the sleep area, we have ongoing and planned development programs for Xyrem and certain product candidates.

- *JZP-110.*

  Phase 3 Clinical Trials. JZP-110 is a late-stage investigational compound being developed for potential treatment of EDS in patients with narcolepsy and EDS in patients with OSA. We acquired worldwide development, manufacturing and commercial rights to JZP-110 from Aerial BioPharma LLC, or Aerial, in January 2014, other than in certain jurisdictions in Asia where SK Biopharmaceuticals Co., Ltd, or SK, retains rights. We initiated patient enrollment in our Phase 3 clinical program in the second quarter of 2015. We are conducting one Phase 3 clinical trial in patients with EDS associated with narcolepsy and two Phase 3 clinical trials in patients with EDS associated with OSA. Approximately 880 patients are expected to be enrolled in these three trials in the aggregate. In addition, we expect to enroll up to 450 patients from two of our Phase 3 clinical trials in an open label extension trial evaluating the long-term safety of JZP-110. We expect to receive preliminary data results from these trials in the fourth quarter of 2016.

  Other Activities. We are also exploring additional potential indications for JZP-110.

- *Xyrem.*

  Phase 3 Clinical Trial of Xyrem in Children and Adolescents. While in many patients narcolepsy can begin during childhood and adolescence, there is limited information on the treatment of pediatric narcolepsy patients with Xyrem. We have worked with the FDA and several leading specialists to design a clinical trial to generate additional data on the treatment of pediatric narcolepsy patients with Xyrem. In the fourth quarter of 2014, we initiated a Phase 3 clinical trial to assess the safety and efficacy of Xyrem in children and adolescents aged seven to 17 who have narcolepsy with cataplexy. We expect to complete enrollment in this trial in the second half of 2016.

Other Activities. We are also pursuing other activities related to the potential development of options for narcolepsy patients that would provide clinically meaningful improvements compared to Xyrem, including once-nightly dosing. Although results from our Phase 1 trial of JZP-386, a deuterium-modified analog of sodium oxybate, which we licensed from Concert Pharmaceuticals, Inc., or Concert, in February 2013, did not support advancing JZP-386 into a later-stage clinical trial, the clinical data demonstrated that JZP-386 provided favorable deuterium-related effects, including higher serum concentrations and correspondingly increased pharmacodynamics effects at clinically relevant time points compared to Xyrem, and a safety profile similar to that observed with Xyrem. We are exploring formulation options designed to leverage the positive effects observed in the studies.

In the hematology and oncology area, we also have ongoing and planned development activities.

- *Defibrotide.*

  Planned Phase 3 Clinical Trial. We are preparing to commence a clinical trial to evaluate the safety and efficacy of defibrotide for the prevention of VOD in high-risk patients. We expect to initiate patient enrollment in the third quarter of 2016.

  Other Activities. We are also exploring additional potential indications for defibrotide and assessing the potential to pursue regulatory approval of defibrotide in additional countries.

- *Erwinaze.* We are pursuing activities related to the potential development of an effective and well-tolerated long-acting recombinant crisantaspase that would offer benefits compared to Erwinaze. We are also assessing the potential to pursue regulatory approval of Erwinaze in additional countries.

We recorded research and development expenses of $135.3 million, $85.2 million and $41.6 million in 2015, 2014 and 2013, respectively. We also recorded charges of $202.6 million and $5.0 million to in-process research and development in 2014 and 2013, respectively.

Sales and Marketing

We have commercial operations primarily in the U.S. and Europe. In the U.S., our products are marketed through our commercial teams, including more than 150 trained, experienced sales professionals who promote Xyrem, Erwinaze and Prialt directly to physicians in specialties appropriate for each product. Outside of the U.S., our hematology and oncology sales force has approximately 33 hematology field specialists responsible for promoting Erwinase and Defitelio in approved markets where we commercialize these products.

Our commercial activities include marketing-related services, distribution services and commercial support services. We employ third party vendors, such as advertising agencies, market research firms and suppliers of marketing and other sales support-related services, to assist with our commercial activities.

We currently have a relatively small number of sales representatives compared with the number of sales representatives of most other pharmaceutical companies with marketed products. Each of our sales representatives is responsible for a geographic territory of significant size. We believe that the size of our sales force is appropriate to effectively reach our target audience for our marketed products in the specialty markets in which we currently operate. We recently expanded our sales force by approximately 10 sales professionals in anticipation of the potential launch of defibrotide in the U.S. Continued growth of our current marketed products and the launch of any future products may require further expansion of our sales force and sales support organization in the U.S. and internationally, and we may need to commit significant additional funds, management and other resources to the growth of our sales organization.

Competition

The pharmaceutical industry is highly competitive and dominated by a number of large, established pharmaceutical companies, as well as specialty pharmaceutical companies that market products and develop product candidates in sleep, hematology/oncology, pain and other therapeutic areas. Many of these companies, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources than we do. They can spend more on, and have more expertise in, research and development, regulatory, manufacturing, distribution and sales activities. As a result, our competitors may obtain regulatory approvals for their product candidates more rapidly than we may and may market their products more effectively than we do. Smaller or earlier stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our ability to continue to grow requires that we compete successfully with other specialty pharmaceutical companies for product and product candidate acquisition and in-licensing opportunities. These competitors include established companies that may have a competitive advantage over us due to their size and financial resources.

We also face competition from manufacturers of generic drugs. Generic competition often results in decreases in the prices at which branded products can be sold, particularly when there is more than one generic available in the marketplace. In

addition, legislation enacted in the U.S. allows for, and in a few instances in the absence of specific instructions from the prescribing physician mandates, the dispensing of generic products rather than branded products where a generic version is available. Other companies could also develop products that are similar, but not identical, to our marketed products, such as an alternative formulation of our product or an alternative formulation combined with a different delivery technology, and seek approval in the U.S. by referencing our products and relying, to some degree, on the FDA's finding that our products are safe and effective in their approved indications.

Our products and product candidates may also compete in the future with new products currently under development by others. Any products that we develop are likely to be in a highly competitive market, and many of our competitors may succeed in developing products that may render our products obsolete or noncompetitive.

Our lead marketed products face competition as described below:

- *Xyrem*. Xyrem is the only product approved by the FDA for the treatment of both cataplexy and EDS in patients with narcolepsy. No product other than Xyrem is approved by the FDA for the treatment of cataplexy. The only other products approved by the FDA for the treatment of EDS in patients with narcolepsy are Provigil® (modafinil) and Nuvigil® (armodafinil), which are marketed by Teva Pharmaceutical Industries Limited, or Teva, and generic versions of Provigil. Provigil, its generic equivalents and Nuvigil are also approved for improving wakefulness in patients with EDS associated with treated OSA or shift work disorder. Xyrem is often used in conjunction with stimulants and wake-promoting drugs, which are administered during the day.

  As alternatives to Xyrem, cataplexy is often treated with tricyclic antidepressants and selective serotonin reuptake inhibitors, or SSRIs, or selective norepinephrine reuptake inhibitors, or SNRIs, although these products are not approved by the FDA for the treatment of cataplexy. Tricyclic antidepressants are a class of antidepressant drugs first used in the 1950s. The use of these drugs can often result in somnolence, which exacerbates the EDS already experienced by all patients with narcolepsy. SSRIs and SNRIs are compounds typically used for the treatment of clinical depression. Somnolence and insomnia are commonly reported side effects with SSRIs, while loss of sleep is a commonly reported side effect with SNRIs. These side effects may be problematic for patients with narcolepsy.

  Seven companies have sent us notices that they have filed ANDAs with the FDA seeking approval to market a generic version of Xyrem. We have filed lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and the litigation proceedings are ongoing. Some of the ANDA filers have also filed petitions for IPR with respect to the validity of certain distribution, method of use and formulation patents covering Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to petitions related to certain patents covering the Xyrem distribution system, and we expect the PTAB to issue final decisions on the validity of those patents in July 2016. For a description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

  Other companies could also develop products that are similar, but not identical, to Xyrem, such as an alternative formulation or an alternative formulation combined with a different delivery technology, and seek approval in the U.S. by referencing Xyrem and relying, to some degree, on the FDA's approval of Xyrem and related determinations of safety and efficacy. For example, a company that is using its proprietary technology for delivery of a sodium oxybate formulation to eliminate second nighttime dosing for narcolepsy patients has stated that it anticipates commencing a Phase 3 pivotal trial in 2016 that is expected to run through early 2017. If this company is successful in developing a sodium oxybate formulation that could be effectively used with its delivery technology and is able to obtain FDA or other regulatory approval for its product to treat narcolepsy patients, we expect sales of Xyrem would be adversely affected.

- *Erwinaze*. Erwinaze is a biologic product used in conjunction with chemotherapy and is indicated for patients with ALL who have developed hypersensitivity to *E. coli*-derived asparaginase. While there is currently no direct competition to Erwinaze to treat ALL patients with hypersensitivity to *E. coli*-derived asparaginase, other companies have developed or are developing new treatments for ALL, including new asparaginase treatments that could reduce the rate of hypersensitivity in patients with ALL, and new treatment protocols are being developed for ALL that may not include asparaginase-containing regimens. For example, a number of companies are developing new immunotherapy treatments for relapsed or refractory ALL patients, including one treatment that was recently approved, and a company recently announced positive efficacy and safety results from its completed Phase 2/3 pivotal trial in Europe for an alternative asparaginase treatment consisting of L-asparaginase encapsulated inside donor-derived red blood cells. Any potential new treatment could reduce the market for Erwinaze. As a biologic product, Erwinaze also faces potential competition from biosimilar products.

- *Defitelio/defibrotide*. Defitelio is the first approved treatment in the EU for the treatment of severe VOD in adults and children undergoing HSCT, and in September 2015, the FDA accepted for filing with priority review our NDA for defibrotide for the treatment of VOD with evidence of multi-organ dysfunction following HSCT. Various anti-clotting strategies have been tried by researchers in patients with VOD with mixed results, including Activase (alteplase), a recombinant tissue plasminogen activator marketed by Genentech, Inc., generic heparin sodium

injection and Thrombate III (antithrombin III (human)), marketed by Grifols Therapeutics, Inc. While there is currently no direct competition to Defitelio to treat severe VOD, changes in the types of conditioning regimens used as part of HSCT may affect the incidence rate of VOD and demand for Defitelio.

With respect to all of our products and product candidates, we believe that our ability to successfully compete will depend on, among other things:

- the existence of competing or alternative products in the marketplace, including generic competition, and the relative price of those products;
- the efficacy, safety and reliability of our products and product candidates compared to competing or alternative products;
- product acceptance by physicians, other health care providers and patients;
- our ability to comply with applicable laws, regulations and regulatory requirements with respect to the commercialization of our products, including any changes or increases to regulatory restrictions;
- protection of our proprietary rights;
- obtaining reimbursement for our products in approved indications;
- our ability to complete clinical development and obtain regulatory approvals for our product candidates, and the timing and scope of regulatory approvals;
- our ability to provide a reliable supply of commercial quantities of a product to the market; and
- our ability to recruit, retain and develop skilled employees, including sales and marketing and clinical development employees.

Customers and Information About Geographic Areas

In the U.S., our lead marketed product, Xyrem, is sold to one specialty pharmacy, Express Scripts, which ships Xyrem directly to patients. Erwinaze is sold to hospitals through a specialty distributor, McKesson Corporation. Prialt is sold in the U.S. through an exclusive pharmacy to other pharmacies and medical facilities, and our other products are sold in the U.S. primarily to distributors who distribute the product to pharmacies and hospitals. We have standard distribution services agreements made in the ordinary course of business with these distributors, which include prompt payment discounts and various standard service fees or rebate arrangements. Purchases are made on a purchase order basis.

Outside of the U.S., we distribute Erwinase through Durbin PLC, a U.K.-based wholesaler and distributor, to hospitals and local wholesalers in Europe where we market Erwinase directly and, in markets where we do not market Erwinase directly, to local distributors and wholesalers in Europe and elsewhere in the world. We distribute Defitelio to the European countries where the product has been launched commercially primarily through IDIS Limited, or IDIS, a U.K.-based distributor. We also work with IDIS and a number of local distributors in Europe and elsewhere in the world to distribute defibrotide on a named patient basis. Xyrem is currently sold in 18 countries by UCB (which has rights to market Xyrem in 54 countries) and in Canada by Valeant. Eisai has rights to market Prialt in numerous countries outside of the U.S. While we retain the rights to Prialt in the remaining non-U.S. territories, we are not currently selling the product outside of the U.S.

Information on our total revenues attributed to U.S. and non-U.S. sources and customers who represented at least 10% of our total revenues in each of 2015, 2014 and 2013, as well as the location of our long-lived assets, is included in Note 14 to our consolidated financial statements in this Annual Report on Form 10-K.

We are headquartered in Dublin, Ireland. We also have offices in Palo Alto, California; Philadelphia, Pennsylvania; Oxford, United Kingdom; Lyon, France; Villa Guardia (Como), Italy; Athlone, Ireland; and elsewhere in Europe. For a discussion of risks related to our non-U.S. operations, see “Risk Factors —Risks Related to Our Business,” “—Risks Related to Our Industry” and “—Risks Related to Our Financial Condition” in Part I, Item 1A of this Annual Report on Form 10-K and “Quantitative and Qualitative Disclosure About Market Risk” in Part II, Item 7A of this Annual Report on Form 10-K.

Manufacturing

We have completed construction of a manufacturing and development facility in Ireland and expect to begin commercial operations at the facility in 2016. Currently, however, other than the manufacturing plant in Italy where we produce some active pharmaceutical ingredients, including the defibrotide drug substance, we do not have our own commercial manufacturing capability for our products or product candidates, or their active pharmaceutical ingredients, or the capability to package our products. We have a single source of supply for each of our marketed products and our product candidates and for the active pharmaceutical ingredients used in these products and product candidates. Our ability to develop and deliver products in a timely and competitive manner depends on our third party suppliers being able to continue to meet our ongoing

commercial and clinical trial needs (except with respect to the defibrotide drug substance, which we manufacture ourselves). Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production yields, process controls, quality control and quality assurance, including testing of stability, impurities and impurity levels and other product specifications by validated test methods, and compliance with strictly enforced U.S., state and non-U.S. regulations. These difficulties can be heightened when a supplier is required to scale up to produce increased quantities to meet growing demand. In addition, our suppliers are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and other rules and regulations prescribed by non-U.S. regulatory authorities. We depend on our third party suppliers to comply with these requirements, and they may not be able to continue to do so.

Xyrem. In 2010, we entered into an agreement with Siegfried (USA) Inc., subsequently renamed Siegfried USA, LLC, or Siegfried, for the supply of sodium oxybate, the active pharmaceutical ingredient of Xyrem. Siegfried was approved by the FDA as our supplier in November 2011. Although Siegfried has been our only supplier of sodium oxybate since 2012, we have the right to purchase a portion of our worldwide requirements of sodium oxybate from other suppliers. Under our agreement, we provide periodic rolling forecasts to Siegfried, and a portion of each rolling forecast constitutes a firm purchase order. The agreement with Siegfried expires in April 2018, subject to automatic three-year extensions until either party provides notice to the other of its intent to terminate the agreement at least 18 months before the end of the then-current term. Either party has the right to terminate the agreement in the event of the other party's uncured material breach or insolvency. During the term of the agreement and, under certain circumstances for 18 months after the agreement terminates, Siegfried is not permitted to manufacture sodium oxybate for any other company.

Effective October 1, 2015, we entered into a Master Manufacturing Services Agreement, or the Master Agreement, with Patheon Pharmaceuticals Inc., which we refer to together with its affiliates as Patheon. The Master Agreement supersedes a prior agreement with Patheon for the manufacturing, supply and packaging of Xyrem and establishes the general terms and conditions pursuant to which Patheon will provide manufacturing services for drug products, including Xyrem, as specified by us in product agreements entered into from time to time. Although Patheon is currently our sole supplier of Xyrem, we are not required to purchase Xyrem exclusively from Patheon. The Master Agreement expires on December 31, 2020 and may be extended for additional two-year terms if Patheon is then providing manufacturing services for any product, unless either party provides 18 months prior notice of termination. In addition, we may terminate the Master Agreement for any reason upon 12 months prior written notice, and either party has the right to terminate the agreement in the event of the other party's uncured material breach.

Quotas from the DEA are required in order to manufacture and package sodium oxybate and Xyrem in the U.S. DEA quotas are required for Siegfried to supply us with sodium oxybate and for Patheon to obtain sodium oxybate from Siegfried in order to supply us with Xyrem. Because the DEA typically grants quotas on an annual basis and requires a detailed submission and justification for a quota request, obtaining sufficient DEA quotas can be a difficult and time-consuming process. The need for quotas has prevented us in the past, and may prevent us in the future, from building significant inventories. For information related to DEA quota requirements, see "Business—Government Regulation—Other Regulatory Requirements—Controlled Substance Regulations" in Part I, Item 1 of this Annual Report on Form 10-K.

Erwinaze. Erwinaze is exclusively licensed to us, and manufactured for us, by PBL, which is our sole supplier for Erwinaze. Our agreement with PBL expires in December 2020, subject to automatic five-year extensions unless terminated by either party in writing prior to a fixed date before the end of the then-current term. Either party has the right to terminate the agreement in the event of the other party's uncured material breach or insolvency. We provide periodic rolling forecasts to PBL, and a portion of each rolling forecast constitutes a firm purchase order. We are obligated to make tiered royalty payments to PBL based on worldwide net sales of Erwinaze and Erwinase. The BLA approving Erwinaze includes a number of post-marketing commitments related to the manufacture of Erwinaze by PBL.

The current manufacturing capacity for Erwinaze is nearly completely absorbed by demand for the product. We are working with PBL to evaluate potential expansion of its production capacity to increase the supply of Erwinaze over the longer term. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build an excess level of product inventory that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues, and we have experienced, and expect to continue to experience, manufacturing and inventory challenges that have resulted in disruptions in our ability to supply certain markets. If capacity constraints continue, whether as a result of continued quality or other manufacturing issues or otherwise, we may be unable to build a desired excess level of product inventory, and our ability to supply the market may continue to be compromised. Additional Erwinaze supply interruptions and/or our inability to expand production capacity could materially adversely affect our sales of and revenues from Erwinaze and our potential future maintenance and growth of the market for this product.

Defitelio/defibrotide. We are our sole supplier of, and we believe that we are currently the sole worldwide producer of, the defibrotide drug compound. We manufacture the defibrotide compound in a single facility located in Villa Guardia, near Como, Italy. Patheon currently processes the defibrotide compound into its finished vial form, and Patheon is the sole provider of our commercial supply of the finished product in the EU and of our clinical supply. We anticipate that Patheon will also be the sole provider of our commercial supply of the finished product for the U.S. market if the product is approved by the FDA.

Part of the process to obtain FDA approval for defibrotide is to obtain certification from the FDA that the facilities we and Patheon operate are in compliance with the FDA's cGMP requirements. The FDA may deny approval if the FDA determines that either our facility or Patheon's facility does not meet applicable manufacturing and quality requirements. In December 2015, the FDA performed a pre-approval inspection of our manufacturing facility in connection with our NDA submission for defibrotide. The inspection passed, and the FDA did not issue a Form FDA 483 at the conclusion of the inspection. In 2015, the FDA issued a Form FDA 483 to Patheon Italia S.p.A., or Patheon Italia, that included observations related to the Ferentino, Italy facility that manufactures the defibrotide finished product. Failure by Patheon Italia to timely remediate the observations to the FDA's satisfaction or the discovery of issues that impact the defibrotide finished product could have an adverse impact on the potential approval of our NDA for defibrotide, including the timing thereof. Even after a manufacturing facility is approved, the FDA will continue to inspect and evaluate facilities for ongoing compliance with applicable requirements. If Patheon does not or is not able to supply us with finished defibrotide product for any reason, it may take time and resources to implement and execute the necessary technology transfer to another processor, and such delay could negatively impact our product launch in the U.S. market if the product is approved by the FDA and our anticipated revenues from defibrotide and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

JZP-110. In order to conduct any of our clinical trials for JZP-110, we need to have sufficient quantities of clinical product manufactured. While we believe that we will be able to obtain sufficient supplies of JZP-110 for our clinical trials, there can be no assurance that our suppliers will be able to produce sufficient clinical supplies of JZP-110 in a timely manner. Any delay in receiving adequate supplies of JZP-110 for our clinical trials could negatively impact our development program.

For further discussion of the challenges we face with respect to supply of our products and product candidates, see the risk factor under the heading "*We depend on single source suppliers for each of our products and product candidates and their active pharmaceutical ingredients. The loss of any of these suppliers , or delays or problems in the manufacture of our products for commercial sale or our product candidates for use in our clinical trials, could materially and adversely affect our business, financial condition, results of operations and growth prospects"* in Part I, Item 1A of this Annual Report on Form

10-K.

Patents and Proprietary Rights

We actively seek to patent, or to obtain licenses to or to acquire third party patents, to protect our products and related inventions and improvements that we consider important to our business. We own a portfolio of U.S and non-U.S. patents and patent applications and have licensed rights to a number of issued patents and patent applications. Our owned and licensed patents and patent applications cover or relate to our products and product candidates, including certain formulations, uses to treat particular conditions, distribution methods and methods of administration, drug delivery technologies and delivery profiles and methods of production. Patents extend for varying periods according to the date of the patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The patent laws of non-U.S. countries differ from those in U.S., and the degree of protection afforded by non-U.S. patents may be different from the protection offered by U.S. patents.

The patents and patent applications that relate to our lead marketed products include:

- *Xyrem.* Xyrem is covered by 20 U.S. patents that expire at various times from December 2019 to March 2033, of which 16 are listed in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or Orange Book. These patents relate to Xyrem's stable and microbially resistant formulation, its manufacturing process, its method of use, including its restricted distribution system, and its method of administration. Of the patents listed in the Orange Book, four are formulation patents expiring between December 2019 and July 2020; seven are method of use patents covering the distribution of Xyrem expiring between December 2022 and June 2024; three are method of use patents covering Xyrem's use in narcolepsy, which expire in December 2019; and two are method of administration patents expiring in March 2033. Four patents are not listed in the Orange Book but also relate to Xyrem: two for methods for making the formulation expiring December 2019, one for a distribution system expiring June 2024 and one for method of administration expiring March 2033. A Xyrem formulation patent has issued in multiple non-U.S. countries and will expire in December 2019. In addition to our issued patents, we have patent applications relating to Xyrem pending in the U.S. and other countries.

  Seven companies have sent us notices that they have filed ANDAs with the FDA seeking FDA approval to market a generic version of Xyrem. We have filed lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and the litigation proceedings are ongoing. Some of the ANDA filers have also filed petitions for IPR with respect to the validity of certain distribution, method of use and formulation patents covering Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to petitions related to certain patents covering the Xyrem distribution system, and

we expect the PTAB to issue final decisions on the validity of those patents in July 2016. For a description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

- *Defitelio*. The unique process of deriving defibrotide from porcine DNA is extensive and uses both chemical and biological processes that rely on complex characterization methods. We have a portfolio of U.S. and non-U.S. patents and patent applications relating to various compositions, methods of use and methods of characterization, which will expire at various times between April 2017 and June 2035.

Erwinaze has no patent protection. It was awarded orphan drug exclusivity for the treatment of ALL in the U.S. until November 2018, and we believe that it is protected by exclusivity that prevents approval of a biosimilar in the U.S. through late 2023 under the BPCIA. For more details, see "Business—Government Regulation—Orphan Drug and Other Exclusivities" in Part I, Item 1 of this Annual Report on Form 10-K.

The patents and patent applications that relate to our product candidates include:

- *JZP-110*. JZP-110 and its associated uses are claimed in multiple U.S. and non-U.S. patents and patent applications. We acquired rights to JZP-110 from Aerial in January 2014, including Aerial's patent rights relating to JZP-110, other than in certain jurisdictions in Asia where SK retains rights. One of the U.S. composition of matter patents expired on September 2015. Two U.S. method of use patents covering treatment of sleep-related conditions will expire in June 2026 and August 2027, respectively, subject to any patent term extension.
- *JZP-386.* Two U.S. patents cover the composition of deuterated analogs of sodium oxybate, including JZP-386, and their methods for treating certain diseases and disorders, including narcolepsy. The first patent expires in August 2030, and the second patent expires in February 2032. A European patent that corresponds to the first U.S. patent expires in April 2030. Further, patent applications corresponding to the second U.S. patent were filed in the U.S., Europe and Japan, and, if issued, would expire in February 2032. We were granted exclusive licenses to these patent rights by Concert.

We cannot be certain that any of our patent applications, or those of our licensors, will result in issued patents, that the patents we own and license, or any additional patents we may own or license, will prevent other companies from developing similar or therapeutically equivalent products, or that others will not be issued patents that may prevent the sale of our products or require licensing and the payment of significant fees or royalties.

We also rely on our trade secrets and those of our licensors, as well as other unpatented proprietary information, to protect our products and commercial position, particularly with respect to our products with limited or no patent protection, such as Erwinaze and Defitelio. To the extent that our products have a competitive edge as a result of our reliance on trade secrets and unpatented know-how, our competitive position may be compromised if others independently develop products using the same or similar technologies or trade secrets.

We seek to protect our trade secrets and proprietary knowledge in part through confidentiality agreements with our employees, consultants, advisors and collaboration partners. Nevertheless, these agreements may not effectively prevent disclosure of our confidential information and may not provide us with an adequate remedy in the event of unauthorized disclosure of our confidential information. In addition, if our employees, consultants, advisors or collaboration partners develop inventions or processes independently or jointly with us that may be applicable to our products under development, disputes may arise about ownership or proprietary rights to those inventions and processes. Such inventions and processes will not necessarily become our property, but may remain the property of those third parties or their employers. Protracted and costly litigation could be necessary to enforce and determine the scope of our proprietary rights. In addition, courts outside of the United States are sometimes less willing to protect trade secrets.

Failure to obtain or maintain patent and trade secret protection, for any reason, could have a material adverse effect on our business. See the risk factors under the heading "Risks Related to Our Intellectual Property" in Part I, Item 1A of this Annual Report on Form 10-K.

In addition, we have a number of trademarks and service marks to further protect the proprietary position of our products. We also have pending trademark and service mark applications in the U.S. and elsewhere in the world.

Government Regulation

The manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, sale, distribution, record keeping, importing and exporting of our products and our research and development activities are subject to extensive regulation by the FDA, the EC, the competent authorities of the EU member states and other regulatory authorities. Regulations differ from country to country. As a result of these regulations, product development, approval and commercialization processes are expensive and time-consuming.

Approval of Pharmaceutical Products

We are not permitted to market a pharmaceutical product in the U.S. or in the EU member states until we receive approval from the FDA, the EC or the competent authorities of the EU member states, as applicable. An application for marketing approval must contain information demonstrating the quality, safety and efficacy of the pharmaceutical product, including data from preclinical and clinical trials, information pertaining to the preparation and manufacture of the drug or biologic, analytical methods, product formulation, details on the manufacture and stability of the finished pharmaceutical product, proposals concerning fulfillment of pharmacovigilance obligations, and proposed product packaging and labeling.

In the U.S., the FDA, under the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations, regulates the review, approval, manufacturing and marketing of our products. Our failure, or the failure of any of our third party partners, to comply with applicable requirements could subject us to administrative or judicial sanctions or other negative consequences, such as delays in approval or refusal to approve a product candidate, withdrawal of product approval, notices of violation, untitled letters, warning letters, fines and other monetary penalties, unanticipated expenditures, product recall or seizure, total or partial suspension of production or distribution, interruption of manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, civil penalties and/or criminal prosecution.

To obtain FDA approval of a product candidate, an applicant, also called a sponsor, must, among other things, submit the data and information described above in the form of an NDA or BLA, as applicable, and pay a user fee. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming, and the outcomes are uncertain. The steps required before a drug or biologic may be approved for marketing in the U.S. generally include: preclinical laboratory tests and animal tests; submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials commence; adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug or biologic for each indication; the submission to the FDA of the NDA or BLA; satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made, analyzed and stored to assess compliance with cGMP; potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the application; and FDA review and approval of the application.

Human clinical trials conducted before approval of a product for a specific indication generally proceed in three sequential phases, although the phases may overlap. Clinical trials must be conducted in accordance with general investigational plans and protocols, as well as the FDA's requirements, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to ensure that the data and results are credible and accurate and that the trial participants are adequately protected. The FDA enforces good clinical practices through periodic inspections of trial sponsors, principal investigators and trial sites. In Phase 1, the initial introduction of the drug into human subjects, frequently healthy volunteers, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence of effectiveness. Phase 2 usually involves clinical trials in a limited patient population to determine the effectiveness of the drug for a particular indication or indications, dosage tolerance and optimum dosage and to identify common adverse effects and safety risks. If a drug demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2, Phase 3 clinical trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites. In addition, Phase 4, or post-approval, clinical trials may be required by the FDA and are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of products approved under accelerated approval regulations.

The FDA reviews a submitted NDA or BLA before it accepts it for filing and may refuse to file an application and/or request additional information before acceptance. Once an NDA or BLA submission is accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the PDUFA, for a new molecular entity, the FDA has twelve months from submission in which to complete its initial review of a standard application and respond to the applicant, and eight months for a priority application for a new molecular entity. The FDA does not always meet its PDUFA goal dates, and in certain circumstances the PDUFA goal date may be extended. The FDA may not act quickly or favorably in reviewing applications, and we may encounter significant difficulties or costs in any efforts to obtain FDA approvals, which could delay or preclude us from marketing our product candidates.

If the FDA determines that a REMS is necessary to ensure that the benefits of the drug outweigh the risks, a sponsor may be required to include a proposed REMS (as part of the application or after approval), which may include a patient package insert or a medication guide to provide information to consumers about the product's risks and benefits; a plan for communication to healthcare providers; and restrictions on the product's distribution referred to as elements to assure safe use, or ETASU. For example, Xyrem is required to have a REMS. See the discussion regarding REMS, particularly in the context of potential generic competition, under "Business—Government Regulation—*The Hatch-Waxman Act*" below and in the risk factor in Part I, Item 1A of this Annual Report on Form 10-K under the heading "*The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation*

strategy, and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem."

After the FDA evaluates a marketing application, including a REMS when applicable, it also evaluates any manufacturing and nonclinical and clinical trial facilities for the proposed product. When the FDA's evaluation is complete, it issues an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the application, the FDA will issue an approval letter. The FDA may also refer an application to the appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee.

The FDA has and has used various programs, including fast track, priority review, breakthrough therapy and accelerated approval (Subpart H and E), that are intended to expedite or simplify the process for reviewing certain applications and/or provide for approval on the basis of surrogate endpoints or restricted distribution. Generally, drugs and biologics may be eligible for one or more of these programs if they are intended for serious or life-threatening diseases or conditions, have potential to address unmet medical needs, or may provide meaningful benefit over existing treatments.

Outside of the U.S., our ability to market a medicinal product generally depends upon receiving a marketing authorization from the appropriate regulatory authority. The requirements governing the conduct of clinical trials, obtaining marketing authorization, fulfillment of pharmacovigilance obligations, obtaining pricing and reimbursement and related matters vary widely from country to country. In any country, however, we will generally be permitted to commercialize our products if the appropriate regulatory authority is satisfied that we have presented adequate evidence of safety, quality and efficacy. The time needed to secure approval for medicinal products may be longer or shorter than that required for FDA approval. The regulatory approval and oversight process in other countries includes all of the risks associated with regulation by the FDA and certain state regulatory agencies as described below.

In the EU, marketing authorization for medicinal products can be obtained through several different procedures. These are through a centralized, mutual recognition procedure, decentralized procedure, or national procedure (single country). The centralized procedure allows a company to submit a single application to the EMA, which will provide a positive opinion regarding the application if it meets certain safety, quality and efficacy requirements. The EC will, based on a positive opinion of the EMA, grant a centralized marketing authorization that is valid in all EU member states and three of the four European Free Trade Association, or EFTA, countries (Iceland, Liechtenstein and Norway). The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products and biologic products, and optional for certain other products. The decentralized procedure allows companies to file identical applications for authorization to several EU member states simultaneously for medicinal products that have not yet been authorized in any EU member state. The competent authority of one EU member state, selected by the applicant, assesses the application for marketing authorization. The competent authorities of the other EU member states are subsequently required to grant marketing authorization for their territories on the basis of this assessment except where grounds of potential serious risk to public health require this authorization to be refused. The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU member state to apply for this authorization to be recognized by the competent authorities in other EU member states.

The initial marketing authorization granted in the EU is valid for five years. Once renewed, the authorization is usually valid for an unlimited period unless the national competent authority or the EMA decides, on justified grounds relating to pharmacovigilance, which could include exposure of an insufficient number of patients to the product concerned, to proceed with one additional five-year renewal. The renewal of a marketing authorization is subject to a re-evaluation of the risk-benefit balance of the product by the national competent authorities or the EMA.

In addition, products may be eligible for grant of marketing authorization under exceptional circumstances if an applicant for marketing authorization can demonstrate that comprehensive data on the efficacy and safety of the product under normal conditions of use cannot be provided due to certain specified objective and verifiable reasons. A marketing authorization granted under exceptional circumstances is valid for five years, but is subject to an annual reassessment of conditions imposed by the competent authorities, including conditions relating to the safety of the product, notification to the national competent authorities of any incident relating to its use, and actions to be taken. In October 2013, the EC granted marketing authorization under exceptional circumstances for Defitelio for the treatment of severe VOD in adults and children undergoing HSCT.

The making available or placing on the EU market of unauthorized medicinal products is prohibited. However, the competent authorities of the EU member states may exceptionally and temporarily allow the supply of such products, either on a named patient basis or through a compassionate use process, to individual patients or a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorized medicinal product.

Clinical studies must currently be conducted in accordance with the requirements of the EU Clinical Trials Directive and applicable good clinical practice standards, as implemented into national legislation by EU member states. All entities conducting clinical trials in the EU will be required to comply with the requirements of the new EU Clinical Trials Regulation, which will take effect after May 28, 2016. The new EU Clinical Trials Regulation, which will replace the EU Clinical Trials Directive, introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU, including a new coordinated procedure for authorization of clinical trials that is reminiscent of the mutual recognition procedure for marketing authorization of medicinal products, and an obligation on sponsors to publish clinical trial results.

The Hatch-Waxman Act

The approval process described above for the U.S. is premised on the applicant being the owner of, or having obtained a right of reference to, all of the data required to prove the safety and effectiveness of a drug product. This type of marketing application, sometimes referred to as a "full" or "stand-alone" NDA, is governed by Section 505(b)(1) of the FDCA. A Section 505(b)(1) NDA contains full reports of investigations of safety and effectiveness, which includes the results of preclinical and clinical trials, together with detailed information on the manufacture and composition of the product, in addition to other information as described above.

Alternatively, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which updated certain sections of the FDCA, establishes two abbreviated approval pathways for drug products that are in some way follow-on versions of products already covered by an approved NDA. The first path, under Section 505(b)(2), is for the approval of a product that is similar, but not identical, to a previously-approved brand-name product, which is referred to as the "referenced drug." Under this path, the applicant is permitted to rely to some degree on the FDA's finding that the referenced drug is safe and effective, and must submit its own product-specific data of safety and effectiveness to the extent necessary because of the differences between the products. The FDA may then approve the new drug product for all or some of the label indications for which the referenced product has been approved, or for a new indication sought by the Section 505(b)(2) applicant.

The second path established under the Hatch-Waxman Act is for the approval of generic drugs. Section 505(j) of the FDCA permits the submission of an ANDA for a generic version of an approved, brand-name drug. Generally, an ANDA must contain data and information showing that the proposed generic product and the approved referenced drug (1) have the same active ingredient, in the same strength and dosage form, to be delivered via the same route of administration, (2) are intended for the same uses, and (3) are bioequivalent. This data and information are provided instead of independently demonstrating the proposed generic product's safety and effectiveness, which are inferred from the fact that the generic product is the same as the referenced drug the FDA previously found to be safe and effective. To date, seven potential generic drug manufacturers have filed ANDAs with the FDA requesting approval to market a generic version of Xyrem. Additional ANDAs may be filed seeking approval to market generic forms of Xyrem and/or other products. For a description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

To the extent that an ANDA or a Section 505(b)(2) NDA applicant is relying on the FDA's findings for an already-approved product, the applicant is required to certify that there are no patents listed for that product in the Orange Book, or that for each Orange Book-listed patent the listed patent has expired, or will expire on a particular date and approval is sought after patent expiration, or the listed patent is invalid or will not be infringed by the manufacture, use or sale of the new product. A certification that the new product will not infringe the referenced product's Orange Book-listed patents or that such patents are invalid is called a "Paragraph IV Patent Certification," or Paragraph IV Certification. If the patent is for an approved method of use, an ANDA or Section 505(b)(2) applicant can also file a statement, called a "section viii statement," that the application does not seek approval of the use covered by the listed patent. If the applicant does not challenge the listed patents, the ANDA or the Section 505(b)(2) NDA will not be approved until all the listed patents claiming the referenced product have expired, as well as any additional period of exclusivity that might be obtained for completing pediatric studies pursuant to the FDA's written request. The ANDA or the Section 505(b)(2) NDA may also be subject to delay in review or approval based on applicable non-patent exclusivities, such as exclusivity that results from obtaining approval of a new chemical entity or of a new use of a previously approved active ingredient.

If the applicant has provided a Paragraph IV Certification to the FDA, the applicant must also send a notice of such certification to the holder of the NDA and the relevant patent holders once the ANDA or the Section 505(b)(2) NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a legal challenge to the proposed generic product for infringing the patent. The filing of a patent infringement lawsuit within 45 days of receipt of a notice of Paragraph IV Certification automatically prevents the FDA from approving the ANDA or the Section 505(b)(2) NDA until the earliest of 30 months after the NDA holder's receipt of the notice of Paragraph IV Certification, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant. The 30-month stay period may also be shortened or lengthened upon order of the court in the infringement lawsuit. For drugs with five-year exclusivity, if an action for patent infringement is initiated after year four of that exclusivity period, then the 30-month stay period is extended by such amount of time so that 7.5 years has elapsed since the approval of the NDA for the referenced drug.

This period could be extended by six months if the NDA sponsor obtains pediatric exclusivity. Alternatively, if the listed patent holder does not file a patent infringement lawsuit within the required 45-day period, the applicant will not be subject to the 30-month stay. The FDA may issue tentative approval of an ANDA if the generic applicant meets all conditions for approval but cannot receive effective approval because the 30-month stay or a period of statutory exclusivity has not expired.

We intend to vigorously defend any patents for our approved products, including our Orange Book-listed patents. Seven companies have sent us notices of Paragraph IV Certification that they have filed ANDAs with the FDA seeking approval to market a generic version of Xyrem before the expiration of the Orange Book-listed patents relating to Xyrem. We have filed lawsuits seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents. For a description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K. If an ANDA is approved after the 30-month stay and before conclusion of any relevant patent litigation at the district, and potentially appellate, court, a generic manufacturer could nonetheless choose to commercialize the generic product, also known as a "launch at risk." In the event of such commercialization, the generic manufacturer generally would be liable to us for damages if we ultimately prevail in the patent litigation.

Section 505-1(i)(1) of the FDCA generally provides that (i) an ANDA with a referenced drug subject to the REMS requirements is required to have a REMS with the same elements as the referenced drug, such as a medication guide, a patient package insert and other ETASU, and (ii) the ANDA drug and the referenced drug shall use a single shared system to assure safe use. However, the FDA may waive this requirement for a single shared system and permit the ANDA holder to submit separate but comparable REMS documents if the FDA either determines that the burden of creating a single shared system outweighs its benefit, or if the ANDA applicant certifies that it has been unable to obtain a license to any aspects of the REMS for the referenced drug product that are covered by a patent or a trade secret. The FDCA provides that the FDA may seek to negotiate a license between the ANDA sponsor and the sponsor of the listed product before granting a waiver of the single shared system requirement. The FDCA further states that a REMS shall not be used by an NDA holder to block or delay generic drugs from entering the market.

The FDA has stated that it expects the negotiation of a single shared REMS between an NDA holder and any ANDA applicant or applicants to proceed concurrently with the FDA's review of the ANDAs. The FDA has further stated that it typically monitors the progress of industry working groups attempting to develop shared REMS, and that it has acted to help ensure that sponsors were cooperating and that there were no obstacles to developing a single shared system. In January 2014, the FDA held an initial meeting with us and the three then-current sodium oxybate ANDA applicants to facilitate the development of a single shared REMS for sodium oxybate. In October 2015, the FDA held a telephonic meeting with us and the seven current sodium oxybate ANDA applicants to discuss the status of the development of a single shared REMS for sodium oxybate. The parties had regular interactions with respect to developing a single shared REMS prior to this meeting, and we are seeking to continue the interactions with the goal of developing a single shared REMS. However, we are aware that, separate from the discussions with us, the FDA and ANDA applicants have exchanged communications regarding the potential development of a single shared REMS for sodium oxybate. We cannot predict whether, or to what extent, interactions among the parties will continue or whether we will develop a single shared REMS. If we do not develop a single shared REMS or license or share intellectual property pertinent to our Xyrem REMS with generic competitors within a time frame or on terms that the FDA considers acceptable, the FDA may assert that its waiver authority permits it to approve the ANDA of one or more generic competitors with a separate REMS that differs from our approved Xyrem REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the development of a single shared REMS for sodium oxybate, licensing or sharing intellectual property pertinent to our Xyrem REMS, or the FDA's response to a request by one or more ANDA applicants for a waiver of the requirement for a single shared REMS, including in connection with a certification that the applicant had been unable to obtain a license. For more information, see the risk factors under the headings "*We have incurred and expect to continue to incur substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products*" and "*The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy, and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem*" in Part I, Item 1A of this Annual Report on Form 10-K.

We expect that the approval of an ANDA that results in the launch of a generic version of Xyrem would have a material adverse effect on our business, financial condition, results of operations and growth prospects. For more information, see the risk factor under the heading "*We have incurred and expect to continue to incur substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products*" in Part I, Item 1A of this Annual Report on Form 10-K.

Under the Hatch-Waxman Act, newly approved drugs and indications may benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act provides five-year marketing exclusivity to the first applicant to gain approval

of an NDA for a new chemical entity, meaning that the FDA has not previously approved any other new drug containing the same active moiety. The Hatch-Waxman Act prohibits the FDA from accepting for review an ANDA or a Section 505(b)(2) NDA for another version of such drug during the five-year exclusive period; however, as explained above, submission of an ANDA or Section 505(b)(2) NDA containing a Paragraph IV Certification is permitted after four years, which may trigger litigation leading to a 30-month stay of approval of the ANDA or Section 505(b)(2) NDA that could extend to 7.5 years after approval of the referenced drug. Protection under the Hatch-Waxman Act will not prevent the submission or approval of another "full" NDA; however, the applicant would be required to conduct its own preclinical and adequate and well-controlled clinical trials to demonstrate safety and effectiveness. The Hatch-Waxman Act also provides three years of marketing exclusivity for the approval of new and supplemental NDAs, including Section 505(b)(2) NDAs, for, among other things, new indications, dosages, or strengths of an existing drug, if new clinical investigations that were conducted or sponsored by the applicant are determined by the FDA to be essential to the approval of the application.

The Hatch-Waxman Act also permits a patent term extension of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years after the FDA approves a marketing application. The patent term extension period is generally equal to the sum of one-half the time between the effective date of an IND and the submission date of an NDA, and all of the time between the submission date of an NDA and the approval of that application, up to a total of five years. Only one patent applicable to a product or its use may be extended, and only if the regulatory review leads to the first commercial marketing of that drug, and the extension must be applied for prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves applications for patent term extension. We will consider applying for a patent term extension for some of our patents to add patent life beyond the expiration date, if we meet the legal requirements permitting an extension and depending on the expected length of clinical trials and other factors involved in the submission of an NDA.

Orphan Drug and Other Exclusivities

Some jurisdictions, including the U.S., may designate drugs or biologics for relatively small patient populations as orphan drugs. The FDA grants orphan drug designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. if there is no reasonable expectation that the cost of developing and making available in the U.S. a drug or biologic for this type of disease or condition will be recovered from sales in the U.S. for that product. In the U.S., in order to obtain orphan drug designation, the designation must be requested before submitting an application for marketing approval. An orphan drug designation does not shorten the duration of the regulatory review and approval process. However, if a product that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same product for the same indication for a period of seven years from the time of FDA approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Competitors may receive approval of different drugs or biologics for the indications for which the orphan product has exclusivity.

The FDA approved Xyrem as an orphan drug for the treatment of EDS and cataplexy in patients with narcolepsy, but those periods of orphan drug exclusivity have expired. Erwinaze has orphan drug exclusivity for the treatment of ALL until November 2018, seven years from its FDA approval. Defibrotide has orphan drug designation to treat and prevent VOD.

Separately, Erwinaze, as a biologic product approved under a BLA, is subject to the BPCIA. The BPCIA authorizes the FDA to license a biological product that is biosimilar to an FDA-licensed biologic through an abbreviated pathway. The BPCIA establishes criteria for determining whether a product is biosimilar to an already-licensed biologic, or reference product, and establishes a process for an abbreviated BLA for a biosimilar product to be submitted, reviewed and approved. The BPCIA provides periods of exclusivity that protect a reference product from competition by biosimilars. Under the BPCIA, the FDA may not accept a biosimilar application for review until four years after the date of first licensure of the reference product, and the biosimilar cannot be licensed until 12 years after the reference product was first licensed. Because the BPCIA is a relatively new law, we anticipate that its impact on both reference product sponsors and biosimilar applicants will evolve over a period of years. Its implementation likely will be shaped by a variety of factors, including FDA issuance of guidance documents, proposed regulations, and decisions in the course of considering specific applications. Erwinaze is expected to receive exclusivity that prevents approval of a biosimilar in the U.S. through late 2023 under the BPCIA.

Products also may be eligible for six months of additional exclusivity and patent protection if the sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within statutory time limits, whatever statutory or regulatory periods of exclusivity or listed patent protection cover the drug are extended by six months. This is not a patent term extension, but it effectively extends the period during which, because of regulatory exclusivity or listed patents, the FDA cannot approve an ANDA or 505(b)(2) NDA. We will consider seeking

pediatric exclusivity if we meet the legal requirements and believe it will be commercially beneficial. For example, in the fourth quarter of 2014, in response to a written request from the FDA to generate additional data, we initiated a Phase 3 clinical trial to assess the safety and efficacy of Xyrem in children and adolescents aged seven to 17 who have narcolepsy with cataplexy.

In the EU, orphan drug designation may be granted to products that can be used to treat life-threatening diseases or chronically debilitating conditions with an incidence of no more than five in 10,000 people or that, for economic reasons, would be unlikely to be developed without incentives. In order to receive orphan drug designation, there must also be no satisfactory method of diagnosis, prevention or treatment of the condition, or if such a method exists, the medicine must potentially be of a significant benefit to those affected by the condition. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU member states and a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, access to the centralized marketing authorization procedure 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 the similar product is deemed 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 it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity. Defibrotide received orphan drug designation to treat and prevent VOD from the EMA prior to grant of marketing authorization in the EU and from the Korean Ministry of Food and Drug Safety. The Commonwealth of Australia-Department of Health has granted defibrotide orphan drug designation for the treatment of VOD. In addition, the EMA also granted orphan drug designation to defibrotide for the prevention of GvHD, another potentially fatal complication of HSCT.

Post-Approval Regulation

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes, modifying a REMS or making certain additional labeling claims, are subject to further regulatory review and approval. Obtaining approval for a new indication generally requires that additional clinical studies be conducted.

Often, even after a drug or biologic has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies and trials. If such post-approval conditions are not satisfied, the FDA may impose civil monetary penalties, declare the product misbranded or prohibit the introduction of the drug in interstate commerce. Holders of an approved NDA or BLA are required to: report certain adverse reactions to the FDA; comply with certain requirements concerning advertising and promotional labeling for their products; submit drug safety or adverse event reports; and continue to have quality control and manufacturing procedures conform to cGMP after approval. For example, the FDA's approval of the BLA for Erwinaze includes a number of post-marketing commitments related to the manufacture of Erwinaze by us and PBL.

Similarly, outside of the U.S., we are subject to a variety of post-authorization regulations, including with respect to clinical studies, product manufacturing, advertising and promotion, distribution, and safety reporting. For example, the marketing authorization in the EU for Defitelio was granted under exceptional circumstances and requires us to comply with a number of post-marketing obligations, including obligations relating to the manufacturing of the drug substance and finished product, the submission of data concerning patients treated with the product collected through a third-party patient registry and the establishment of a multi-center, multinational and prospective observational patient registry.

We monitor adverse events resulting from the use of our commercial products, as do the regulatory authorities, and we file periodic reports with the authorities concerning adverse events. The FDA also periodically inspects our records related to safety reporting. Following such inspections, the FDA may issue notices on Form FDA 483 and warning letters that could cause us to modify certain activities. A Form FDA 483 notice, if issued at the conclusion of an FDA inspection, can list conditions the FDA investigators believe may have violated relevant FDA regulations or guidance. Failure to adequately and promptly correct the observation(s) can result in further regulatory enforcement action.

The authorities review these events and reports, and if they determine that any events and/or reports indicate a trend or signal, they can require a change in a product label, restrict sales and marketing and/or require or conduct other actions, potentially including withdrawal or suspension of the product from the market. From time to time, the FDA issues drug safety communications on its adverse event reporting system based on its review of reported adverse events. For example, we changed our Xyrem label in 2012 in connection with an FDA drug safety communication reminding physicians and patients that the use of Xyrem with alcohol or central nervous system depressants can impair consciousness and lead to severe breathing problems. For more information, see the risk factor under the heading "*The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy,*

and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem" in Part I, Item 1A of this Annual Report on Form 10-K.

The holder of an EU marketing authorization for a medicinal product must also comply with the EU's recent pharmacovigilance legislation, which includes requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. This legislation enhanced the authority of the EMA and the competent authorities of the EU member states to require companies to conduct additional post-approval clinical efficacy and safety studies and increased the burden on companies with respect to additional monitoring, adverse event management and reporting. As part of the legislation and its related regulations and guidelines, marketing authorization holders may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time consuming and expensive and could impact profitability. The EMA reviews periodic safety update reports submitted by marketing authorization holders. If the EMA has concerns that the risk benefit profile of a product has varied, it can adopt an opinion advising that the existing marketing authorization for the product be varied and requiring the marketing authorization holder to conduct post-authorization safety studies. The opinion is then submitted for approval by the EC. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

The manufacturing process for pharmaceutical products is highly regulated, and regulators may shut down manufacturing facilities that they believe do not comply with regulations. We and our third party suppliers are subject to cGMP, which are extensive regulations governing manufacturing processes, stability testing, record keeping and quality standards as defined by the FDA, the EMA, the competent authorities of EU member states and other regulatory authorities. The FDA also periodically inspects the sponsor's records related to manufacturing facilities, which effort includes assessment of compliance with cGMP. Following such inspections, the FDA may also issue notices on Form FDA 483 and warning letters. We and our third party suppliers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. In addition to Form FDA 483 notices and warning letters, failure to comply with the statutory and regulatory requirements may result in suspension of manufacturing, product seizure, withdrawal of the product from the market and criminal penalties, among other enforcement remedies.

In addition, various requirements apply to the manufacturing and placing on the EU market of medicinal products. The manufacturing of medicinal products in the EU requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance. These requirements include compliance with EU equivalent cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU member states. Marketing authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU member states' requirements applicable to the manufacturing of medicinal products.

U.S. Healthcare Reform

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, together the Healthcare Reform Act, is a sweeping measure intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. This law substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, benefits for patients within a coverage gap in the Medicare Part D prescription drug program (commonly known as the "donut hole"), rules regarding prescription drug benefits under the health insurance exchanges, changes to the Medicaid Drug Rebate program, expansion of the Public Health Service's 340B drug pricing discount program, or 340B program, fraud and abuse and enforcement. These changes impact existing government healthcare programs and are resulting in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. Details of the changes to the Medicaid Drug Rebate program and the 340B program are discussed under the risk factor *"If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects"* in Part I, Item 1A of this Annual Report on Form 10-K.

Some states have elected not to expand their Medicaid programs by raising the income limit to 133% of the federal poverty level, as is permitted under the Healthcare Reform Act. For each state that does not choose to expand its Medicaid

program, there may be fewer insured patients overall, which could impact our sales, business and financial condition. Where Medicaid patients receive insurance coverage under any of the new options made available through the Healthcare Reform Act, the possibility exists that manufacturers may be required to pay Medicaid rebates on drugs used under these circumstances, a decision that could impact manufacturer revenues. In addition, the federal government has announced delays in the implementation of key provisions of the Healthcare Reform Act, including the employer mandate. The implications of these delays for our sales, business and financial condition, if any, are not yet clear.

Legislative changes to the Healthcare Reform Act remain possible. We expect that the Healthcare Reform Act, as currently enacted or as it may be amended, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of our existing products or to successfully commercialize our product candidates, if approved.

Other Regulatory Requirements

We are also subject to regulation by other regional, national, state and local agencies, including the DEA, the U.S. Department of Justice, or DOJ, the Federal Trade Commission, or FTC, the U.S. Department of Commerce, or DOC, the Office of Inspector General, or OIG, of the U.S. Department of Health and Human Services, or HHS, and other regulatory bodies. In addition to the FDCA, other statutes and regulations govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including preclinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information, promotion, marketing, and pricing to government purchasers and government healthcare programs. Our partners, including our suppliers and distributors and the central pharmacy for Xyrem, are subject to many of the same requirements.

Controlled Substance Regulations

The DEA imposes various quota, registration, record keeping and reporting requirements, labeling and packaging requirements, importing, exporting, security controls and a restriction on prescription refills on certain pharmaceutical products that meet the definition of a controlled substance of listed chemical under the CSA. The states also impose similar requirements for handling controlled substances. Sodium oxybate, in the form of an active pharmaceutical ingredient, is regulated by the DEA as a Schedule I controlled substance, a category reserved for products believed to present the highest risk of substance abuse and with no approved medicinal use. When contained in Xyrem, sodium oxybate is regulated as a Schedule III controlled substance.

The DEA limits the quantity of certain Schedule I controlled substances that may be produced in the U.S. in any given calendar year through a quota system. DEA quotas are required for our sodium oxybate supplier to supply us with sodium oxybate and for our Xyrem supplier to obtain sodium oxybate in order to supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, our sodium oxybate supplier and our Xyrem supplier are required to request and justify allocation of sufficient annual DEA quotas as well as additional DEA quotas if our commercial or clinical requirements exceed the allocated quotas throughout the year. In the past, we have had to engage in lengthy efforts to obtain the needed quotas after the original annual quotas had first been allocated. For 2016, both our active pharmaceutical ingredient supplier and our Xyrem supplier have been allocated most, but not all, of their respective requested quotas. If, in the future, we and our third party suppliers cannot obtain the quotas that are needed on a timely basis, or at all, our business, financial condition, results of operations and growth prospects could be materially and adversely affected.

As a Schedule III drug, Xyrem is also subject to DEA and state regulations relating to manufacturing, storage, distribution and physician prescription procedures, including limitations on prescription refills.

The third parties who perform our clinical and commercial manufacturing, distribution, dispensing and clinical studies for Xyrem are required to maintain necessary DEA registrations and state licenses. The DEA periodically inspects facilities for compliance with its rules and regulations. Failure to comply with current and future regulations of the DEA or relevant state authorities could lead to a variety of sanctions, including revocation or denial of renewal of DEA registrations, fines, injunctions, or civil or criminal penalties, and could have an adverse effect on our business and financial condition.

The U.S. and the EU member states are parties to the Convention on Psychotropic Substances (1971), or the 1971 Convention. Sodium oxybate is a derivative of GHB. GHB is controlled in Schedule II under the 1971 Convention. While the DEA imposes its own scheduling requirements in the U.S. under the CSA, the U.S. is obligated as a signatory to the 1971 Convention to ensure that drug scheduling in the U.S. is consistent with its obligations under the international treaties. Failure by us or any of our partners, including suppliers and distributors, to comply with international or domestic requirements could result in, among other things, additional operating costs to us, delays in shipments outside or into the U.S. and adverse regulatory actions. For more information, see the risk factor under the heading *"We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products"* in Part I, Item 1A of this Annual Report on Form 10-K.

Sales and Marketing Regulations

We are also subject to various U.S. federal and state laws restricting certain marketing practices in the pharmaceutical industry, including anti-kickback laws and false claims laws. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Liability under the federal anti-kickback statute may be established without a person or entity having actual knowledge of the statute or specific intent to violate it. Violations of the federal anti-kickback statute may be punished by civil and criminal fines, imprisonment, and/or exclusion from participation in federal healthcare programs. The federal civil False Claims Act, or the False Claims Act, prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of federal funds, or knowingly making, or causing to be made, a false statement to get a false claim paid. Violations of the False Claims Act may result in significant financial penalties and damages. In addition, the Physician Payment Sunshine provisions of the Healthcare Reform Act require extensive tracking of payments and transfers of value to physicians and teaching hospitals and public reporting of the data collected, and government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and the False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. A number of states now require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states restrict when pharmaceutical companies may provide meals to prescribers or engage in other marketing related activities. Some states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Massachusetts and Nevada require pharmaceutical companies to implement compliance programs or marketing codes of conduct. Outside the U.S., we are also subject to similar regulations in those countries where we market and sell products.

The number and complexity of both U.S. federal and state laws continue to increase, and additional governmental resources are being added to enforce these laws and to prosecute companies and individuals who are believed to be violating them. For more information regarding these laws and regulations, see the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products—Other Regulatory Authorities*" in Part I, Item 1A of this Annual Report on Form 10-K.

The FDA, the competent authorities of the EU member states and other governmental authorities require advertising and promotional labeling to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. The FDA routinely provides its interpretations of that authority in informal communications and also in more formal communications such as untitled letters or warning letters, and although such communications may not be considered final agency decisions, companies may decide not to contest the agency's interpretations so as to avoid disputes with the FDA, even if they believe the claims to be truthful, not misleading and otherwise lawful.

The FDA, the competent authorities of the EU member states and other governmental authorities also actively investigate allegations of off-label promotion activities in order to enforce regulations prohibiting these types of activities. A company that is found to have promoted an approved product for off-label uses may be subject to significant liability, including civil and administrative financial penalties and other remedies as well as criminal financial penalties and other sanctions. Even when a company is not determined to have engaged in off-label promotion, the allegation from government authorities or market participants that a company has engaged in such activities could have a significant impact on the company's sales, business and financial condition. The U.S. government has also required companies that have engaged in such activities to enter into complex corporate integrity agreements and deferred- or non-prosecution agreements that impose significant reporting and other burdens on the affected companies. For all of our products, it is important that we maintain a comprehensive compliance program. Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could subject us to a range of regulatory actions that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

In the EU, the advertising and promotion of our products are subject to EU member states' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product

that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

To help patients afford our products, we have various programs to assist them, including patient assistance programs, a Xyrem free product voucher program and co-pay coupon programs for certain products. These programs and related risks are discussed in greater detail in the risk factor under the heading "*Changes in healthcare law and implementing regulations, including those based on recently enacted legislation, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict and these changes could have a material adverse effect on our business and financial condition*" in Part I, Item 1A of this Annual Report on Form 10-K.

Anti-Corruption Legislation

Our business activities outside of the U.S. are subject to the U.S. Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct or rules of other countries in which we operate, including the U.K. Bribery Act of 2010, or the UK Bribery Act. The FCPA and similar anti-corruption laws in foreign countries generally prohibit the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to U.S. or non-U.S. government officials in order to improperly influence any act or decision, secure an improper advantage, or obtain or retain business. Excepted from the FCPA are payments to facilitate or expedite routine government action and bona fide, reasonable reimbursement of expenses. 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 UK Bribery Act prohibits giving, offering, or promising bribes to any person, including U.K. and non-U.K. government officials and private persons, as well as requesting, agreeing to receive, or accepting bribes from any person. In addition, under the UK 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 U.K. and non-U.K. government officials and private persons in any country, 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 UK 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, our dealings with these prescribers and purchasers may be subject to the FCPA. Recently the Securities and Exchange Commission, or SEC, and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, or Dodd-Frank 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 our suppliers 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.

Data Privacy and Protection

We are also subject to laws and regulations covering data privacy and the protection of health-related and other personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which may affect our business. Numerous federal and state laws and regulations, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of personal information. Failure to comply with such laws and regulations could create liability for us (including the imposition of significant penalties), result in adverse publicity and negatively affect our business. In addition, healthcare providers who prescribe our products and research institutions we collaborate with are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA. Although we are not directly subject to HIPAA other than with respect to providing certain employee benefits, we could potentially be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

EU member states and other jurisdictions where we operate have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the EU Data Protection Directive, as implemented into national laws by the EU member states, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. The EU Data Protection Directive prohibits the transfer of personal data to countries outside of the European Economic Area, or EEA, such as the U.S., which are not considered by the EC to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Although there are legal mechanisms to allow for the transfer of personal data from the EEA and Switzerland to the U.S., a recent decision of the European Court of Justice that invalidated the safe harbor framework on which we have relied has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it will no longer be possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the EU to entities in the U.S. In addition, data protection authorities from the different EU member states may interpret the EU Data Protection Directive and national laws differently, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU. If we or our vendors fail to comply with applicable data privacy laws, or if the legal mechanisms we or our vendors rely upon to allow for the transfer of personal data from the EEA or Switzerland to the U.S. (or other countries not considered by the EC to provide an adequate level of data protection) are not considered adequate, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted if our ability to transfer personal data outside of the EEA or Switzerland is restricted, which could adversely impact our operating results. In December 2015, a proposal for an EU General Data Protection Regulation, intended to replace the current EU Data Protection Directive, was agreed between the European Parliament, the Council of the European Union and the EC. The EU General Data Protection Regulation, which will be officially adopted in early 2016, will introduce new data protection requirements in the EU, as well as substantial fines for breaches of the data protection rules. The EU General Data Protection Regulation, which will be applicable two years after the date of its publication in the Official Journal for the European Union, will increase our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules.

Additional requirements and restrictions regarding, among other things, the export and importation of products, intellectual property rights, the environment, taxation and work safety apply in individual countries, and non-compliance with such requirements may result in civil, criminal or administrative sanctions.

Pharmaceutical Pricing and Reimbursement

Our ability to commercialize our products successfully, and to attract commercialization partners for our products, depends in significant part on the availability of adequate financial coverage and reimbursement from third party payors, including, in the U.S., governmental payors such as the Medicare and Medicaid programs, managed care organizations and private health insurers.

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably. We expect to experience pricing pressure in the U.S. in connection with the sale of our products due to managed healthcare, the increasing influence of health maintenance organizations, additional legislative proposals to curb healthcare costs and negative publicity regarding pricing and price increases generally, which could limit the prices that we charge for our products, including Xyrem, limit our commercial opportunity and/or negatively impact revenues from sales of our products. We anticipate that the U.S. Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs, particularly given the current atmosphere of mounting criticism of prescription costs in the U.S. These cost containment measures include controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government health care programs; pharmaceutical cost transparency bills that aim to require drug companies to justify their prices; controls on healthcare providers; challenges to the pricing of drugs or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; changes in drug importation laws; expansion of use of managed care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person; and public funding for cost effectiveness research, which may be used by government and private third party payors to make coverage and payment decisions. For example, much attention has been paid to legislation proposing federal rebates on Medicare Part D and Medicare Advantage utilization for drugs issued to certain groups of lower income beneficiaries and the desire to change the provisions that treat these dual-eligible patients differently from traditional Medicare patients. Any such changes could have a negative impact on revenues from sales of our products.

In addition, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as

amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2025. These cuts reduce reimbursement payments related to our products, which could potentially negatively impact our revenue.

Third party payors decide which drugs they will pay for and establish reimbursement and co-pay levels. Third party payors are increasingly challenging the prices charged for medical products and services and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost effectiveness of our products. Even with studies, our products may be considered less safe, less effective or less cost-effective than other products, and third party payors may not provide coverage and reimbursement for our products or any of our product candidates that we commercialize, in whole or in part. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. For example, third party payors have started to require discounts and/or exclusivity arrangements with some drug manufacturers in exchange for including a specific product on their formularies. Any such requirements could have a negative impact on revenues from sales of our products.

Payors also are increasingly considering new metrics as the basis for reimbursement rates, such as average sales price, average manufacturer price and actual acquisition cost. The existing data for reimbursement based on these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates. Both Medicare and Medicaid are administered by the Centers for Medicare and Medicaid Services, or CMS. CMS surveys and publishes retail community pharmacy acquisition cost information in the form of National Average Drug Acquisition Cost to provide state Medicaid agencies with a basis of comparison for their own reimbursement and pricing methodologies and rates. It is difficult to project the impact of these evolving reimbursement mechanics on the willingness of payors to cover our products.

We participate in and have certain price reporting obligations to the Medicaid Drug Rebate program, several state Medicaid supplemental rebate programs and other governmental pricing programs, and we have obligations to report the average sales price for the Medicare program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Part B of the Medicare program. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. The status of price reporting submissions and potential liability for two radiopharmaceutical products that we divested in December 2013 and May 2015, respectively, is discussed in the risk factor under the heading "*If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects"* in Part I, Item 1A of this Annual Report on Form 10-K. In addition, a significant portion of our revenue from sales of Erwinaze is obtained through government payors, including Medicaid, and any failure to qualify for reimbursement for Erwinaze under those programs would have a material adverse effect on revenues from sales of Erwinaze.

Federal law also requires that a company that participates in the Medicaid rebate program report the average sales price information each quarter to CMS for certain categories of drugs that are paid under Part B of the Medicare program. Manufacturers calculate the average sales price based on a statutorily defined formula and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B for our products and the resulting Medicare payment rate, and could negatively impact our results of operations.

Federal law requires that any company that participates in the Medicaid rebate program also participate in the Public Health Service's 340B drug pricing discount program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B pricing program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid rebate program. Any changes to the definition of average manufacturer price and the Medicaid rebate amount under the Healthcare Reform Act could affect our 340B ceiling price calculations and negatively impact our results of operations. In January 2016, CMS issued a final rule to implement the changes to the Medicaid rebate program under the Healthcare Reform Act, and we are evaluating the impact of the final rule.

We do not currently expect any material change to our calculations under the Medicaid rebate program or our 340B liability based on the recently released final rule. However, our business could be adversely affected if and to the extent our implementation of the final rule impacts our calculations under the Medicaid rebate program or our 340B liability, or if CMS challenges the approach we take in our implementation of the final rule.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies, we participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. Under this program, we are obligated to make our product available for procurement on an FSS contract and charge a price to four federal agencies - the VA, U.S. Department of Defense, or DoD, Public Health Service and U.S. Coast Guard - that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non-federal average manufacturer price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP.

Outside of the U.S., political, economic and regulatory developments are also subjecting the healthcare industry to fundamental changes and challenges. Pressure by governments and other stakeholders on prices and reimbursement levels continue to exist. In various EU member states we expect to be subject to continuous cost-cutting measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states. These EU member states include the U.K., France, Germany, Ireland, Italy, Spain, and Sweden. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost and cost-effectiveness of individual medicinal products, as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states.

In the EU, our products are marketed through various channels and within different legal frameworks. In certain EU member states, reimbursement for unauthorized products is provided through national named patient or compassionate use programs. Such reimbursement may no longer be available if authorization for named patient or compassionate use programs expire or are terminated or if marketing authorization is granted for the product. In other EU member states, authorization and reimbursement policies may also delay commercialization of our products, or may adversely affect our ability to sell our products on a profitable basis. After initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or arbitrage between low-priced and high-priced member states.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted, could have a material adverse effect on our ability to operate profitably in the EU.

Employees

As of February 17, 2016, we had approximately 910 employees worldwide. We consider our employee relations to be good.

Environment, Health and Safety

Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Italy and Ireland where we have manufacturing facilities. Our manufacturing activities in Italy and Ireland involve the controlled storage, use and disposal of chemicals and solvents. Environmental and health and safety authorities in the relevant jurisdictions administer laws that implement EU directives and regulations governing, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. In certain cases, such laws, directives and regulations may impose strict liability for pollution of the environment and contamination resulting

from spills, disposals or other releases of hazardous substances or waste or any migration of such hazardous substances or waste. Costs, damages and/or fines may result from the presence, investigation and remediation of such contamination at properties currently or formerly owned, leased or operated by us or at off-site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination.

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc was formed under the laws of Ireland (registered number 399192) as a private limited liability company in March 2005 under the name Azur Pharma Limited and was subsequently re-registered as a public limited company under the name Azur Pharma Public Limited Company, or Azur Pharma, in October 2011. On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma were combined in a merger transaction, in connection with which Azur Pharma was re-named Jazz Pharmaceuticals plc and we became the parent company of and successor to Jazz Pharmaceuticals, Inc. We refer to this transaction as the Azur Merger.

Our predecessor, Jazz Pharmaceuticals, Inc., was incorporated in California in March 2003 and was reincorporated in Delaware in January 2004. In the Azur Merger, all outstanding shares of Jazz Pharmaceuticals, Inc.'s common stock were canceled and converted into the right to receive, on a one-for-one basis, our ordinary shares.

In June 2012, we acquired EUSA Pharma Inc., or EUSA Pharma, which we refer to as the EUSA Acquisition, and in January 2014, we completed the Gentium Acquisition.

Available Information

We file or furnish pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or Exchange Act, as applicable, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, amendments to those reports, proxy statements and other information electronically with the SEC. Further copies of these reports are located at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding our filings at www.sec.gov.

The mailing address of our headquarters is Fourth Floor, One Burlington Road, Dublin 4, Ireland, and our telephone number at that location is 353-1-634-7800. Our website is www.jazzpharmaceuticals.com. Through a link on our website, we make copies of our periodic and current reports, proxy statements and other information available, free of charge, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. 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.

Item 1A. Risk Factors

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. The risks described below are not the only ones we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Our business could be harmed by any of these risks. The trading price of our ordinary shares could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and accompanying notes.

Risks Related to Xyrem and the Significant Impact of Xyrem Sales

Xyrem is our largest selling product, and our inability to maintain or increase sales of Xyrem would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Xyrem is our largest selling product and our financial results are significantly influenced by sales of Xyrem, which accounted for 72.5% and 67.0% of our net product sales for the years ended December 31, 2015 and 2014. Our future plans assume that sales of Xyrem will increase. While Xyrem product sales grew from 2014 to 2015, we cannot assure you that we can maintain sales of Xyrem at or near current levels, or that Xyrem sales will continue to grow. We have periodically increased the price of Xyrem, most recently in February 2016, and we cannot assure you that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes.

In addition to other risks described herein, our ability to maintain or increase Xyrem product sales is subject to a number of risks and uncertainties, the most important of which are discussed in more detail below, including those related to:

- the potential introduction of a generic version of Xyrem or an alternative sodium oxybate product for treating cataplexy and/or EDS in narcolepsy;
- changed or increased regulatory restrictions, including changes to our Xyrem REMS, the development of a single shared REMS for sodium oxybate with potential generic competitors or other regulatory actions by the FDA;
- our suppliers' ability to obtain sufficient quotas from the DEA to satisfy our needs for Xyrem;
- any supply, manufacturing or distribution problems arising with any of our suppliers or distributors, all of whom are sole source providers for us;
- any increase in pricing pressure from or restrictive conditions for reimbursement required by, and the availability of reimbursement from, third party payors;
- changes in healthcare laws and policy, including changes in requirements for rebates, reimbursement and coverage by federal healthcare programs;
- continued acceptance of Xyrem by physicians and patients, even in the face of negative publicity that surfaces from time to time;
- changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell Xyrem; and
- operational disruptions at the central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA.

These and the other risks described below related to Xyrem product sales and protection of our proprietary rights could have a material adverse effect on our ability to maintain or increase sales of Xyrem.

If sales of Xyrem were to decline significantly, we might need to reduce our operating expenses or seek to raise additional funds, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects, or we might not be able to acquire, in-license or develop new products in the future to grow our business.

If generic versions of Xyrem or other sodium oxybate products that compete with Xyrem are approved and launched, sales of Xyrem would be adversely affected.

Although Xyrem is covered by patents covering its manufacture, formulation, distribution system and method of use, seven third parties have filed ANDAs seeking FDA approval of generic versions of Xyrem, and additional third parties may also seek to introduce generic versions of Xyrem or other sodium oxybate products for treatment of cataplexy and/or EDS in narcolepsy. If one or more companies receive FDA approval of an ANDA for a generic version of Xyrem or an NDA for other sodium oxybate products, it is possible that such company or companies could introduce generic versions of Xyrem or other sodium oxybate products before our patents expire if they do not infringe our patents, if it is determined that our patents are invalid or unenforceable, or if such company or companies decide, before applicable ongoing patent litigation is concluded, to launch a sodium oxybate product at risk of potentially being held liable for damages for patent infringement.

Seven companies have sent us notices that they have filed ANDAs with the FDA seeking approval to market a generic version of Xyrem. We have filed lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, but we cannot assure you that any of the lawsuits will prevent the introduction of a generic version of Xyrem for any particular length of time, or at all. Additional ANDAs could also be filed requesting approval to market generic versions of Xyrem. If any of these applications is approved, and a generic version of Xyrem is introduced, our sales of Xyrem would be adversely affected. Although no trial date has been set in any of the ANDA suits, we anticipate that trial on some of the patents in the Roxane case could occur as early as the second quarter of 2016. However, the actual timing of events may be significantly earlier or later than we currently anticipate, and we cannot predict the timing or outcome of events in this or the other ANDA litigation.

In January 2015, certain of the ANDA filers filed petitions for IPR with respect to the validity of six patents covering the distribution system for Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to these petitions, and we expect the PTAB to issue final decisions on the validity of the patents in July 2016. In September and October 2015, certain of the ANDA filers filed petitions for IPR by the PTAB with respect to the validity of an additional patent covering the distribution system for Xyrem and with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. In December 2015, one of the ANDA filers filed a petition for IPR with respect to the validity of a patent covering the formulation of Xyrem. In February 2016, one of the ANDA filers filed a petition for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

In accordance with the Hatch-Waxman Act, as a result of our having filed a timely lawsuit against Roxane, FDA approval of Roxane's ANDA was stayed until April 18, 2013, but that stay has expired. We do not know the status of Roxane's ANDA and cannot predict what actions the FDA or Roxane may take with respect to Roxane's ANDA. If Roxane's ANDA is approved by the FDA, Roxane may seek to launch a generic version of Xyrem prior to a District Court, or potential appellate court, decision in our ongoing patent litigation. While, in the event of such commercialization, Roxane would be liable to us for damages in the event we ultimately prevail in the patent litigation, we expect that the introduction of generic competition for Xyrem would have a material adverse effect on our business, financial condition, results of operations and growth prospects. For more information, see the risk factor under the heading "*The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy, and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem"* in Part I, Item 1A of this Annual Report on Form 10-K.

Other companies could also develop products that are similar, but not identical, to Xyrem, such as an alternative formulation or an alternative formulation combined with a different delivery technology, and seek approval in the U.S. by referencing Xyrem and relying, to some degree, on the FDA's approval of Xyrem and related determinations of safety and efficacy. For example, a company that is using its proprietary technology for delivery of a sodium oxybate formulation to eliminate second nighttime dosing for narcolepsy patients has stated that it anticipates commencing a Phase 3 pivotal trial in 2016 that is expected to run through early 2017. If this company is successful in developing a sodium oxybate formulation that could be effectively used with its delivery technology and is able to obtain FDA or other regulatory approval for its product to treat narcolepsy patients, we expect the launch of such a product would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

A generic manufacturer or manufacturer of an alternative sodium oxybate product would need to obtain quotas from the DEA in order to manufacture in the U.S. both the active pharmaceutical ingredient and the finished product to compete with Xyrem. The DEA limits the quantity of certain Schedule I controlled substances that may be produced in the U.S. in any given calendar year through a quota system. DEA quotas are required for our sodium oxybate supplier to supply us with sodium oxybate and for our Xyrem supplier to obtain sodium oxybate in order to supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, our sodium oxybate supplier and our Xyrem supplier are required to request and justify allocation of sufficient annual DEA quotas as well as additional DEA quotas if our commercial or clinical requirements exceed the allocated quotas throughout the year. For the last few years, our suppliers were allocated only a portion of the published annual aggregate quota for the active pharmaceutical ingredient. Consequently, a generic manufacturer or manufacturer of an alternative sodium oxybate product may be able to obtain a portion of the annual aggregate active pharmaceutical ingredient quota. In the past, we have also had to engage in lengthy efforts to obtain the needed quotas after the original annual quotas had first been allocated. For 2016, both our active pharmaceutical ingredient supplier and our Xyrem supplier have been allocated most, but not all, of their respective requested quotas. If, in the future, we and our suppliers cannot obtain the quotas that are needed on a timely basis, or at all, our business, financial condition, results of operations and growth prospects could be materially and adversely affected.

After any introduction of a generic competitor, a significant percentage of the prescriptions written for Xyrem may be filled with the generic version, resulting in a loss in sales of Xyrem. Generic competition often also results in decreases in the prices at which branded products can be sold, particularly when there is more than one generic available in the marketplace. In addition, certain U.S. state laws allow for, and in a few instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products where a generic version is available. We expect that generic competition for Xyrem would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy, and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem.

As a condition of approval of Xyrem, the FDA mandated that we maintain a risk management and controlled distribution system, or Xyrem Risk Management Program, in conjunction with Xyrem's approval by the FDA to ensure the safe distribution of Xyrem and minimize the risk of misuse, abuse and diversion of sodium oxybate. The Xyrem Risk Management Program included a number of elements, including patient and physician education, a database of information to track and report certain information, and the use of a single central pharmacy to distribute Xyrem. The Xyrem Risk Management Program, adopted in 2002 before the FDA had authority to require REMS, was deemed to be an approved REMS pursuant to the FDAAA. The FDAAA, which amended the FDCA, required that deemed REMS and related documents be updated to comply with the current requirements for REMS documents. Pursuant to the FDCA, we engaged with the FDA starting in 2008 to finalize our REMS documents for Xyrem, including initiating dispute resolution procedures with the FDA in February 2014. On February 27, 2015, the FDA notified Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, of (i) the FDA's approval of the REMS for Xyrem in the form submitted by us in November 2014, which includes provisions requiring distribution through a single pharmacy, and (ii) the FDA's denial of our dispute resolution appeal as moot as a result of approval of the Xyrem REMS.

The Xyrem REMS approval notice included statements from the FDA that (i) the approval action should not be construed or understood as agreement with us that dispensing through a single pharmacy is the only way to ensure that the benefits of Xyrem outweigh its risks, and that the FDA has continuing concerns that limiting the distribution of Xyrem to one pharmacy imposes burdens on patient access and the healthcare delivery system, and (ii) as with all REMS, the FDA intends to evaluate the Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. We cannot predict whether the FDA will seek to require or ultimately require modifications to the Xyrem REMS, including with respect to the distribution system, or seek to otherwise impose or ultimately impose additional requirements to the Xyrem REMS, or the potential timing, terms or propriety thereof. Any such modifications or additional requirements could potentially make it more difficult or expensive for us to distribute Xyrem, make it easier for future generic competitors, and/or negatively affect sales of Xyrem.

In late August 2015, we implemented the final approved Xyrem REMS. The process under which enrolled patients receive Xyrem is complex and includes multiple mandatory steps taken by the central pharmacy. The transition to the final approved REMS necessitated significant operational changes at the central pharmacy and revised documentation requirements for patients and prescribers. In the third quarter of 2015, Xyrem product sales were impacted by operational disruption and resulting delays in prescription fills and refills. As physicians and patients familiarized themselves with the new REMS process and documentation requirements, the central pharmacy experienced a significantly increased volume of calls from patients and physicians' offices that the pharmacy was not able to timely address, resulting in a backlog of prescription fills and refills that were delayed. We may experience further disruptions and resulting adverse impacts on Xyrem product sales. In addition, we cannot guarantee that our implementation of the Xyrem REMS will meet FDA requirements, that the ongoing assessments that we submit in accordance with the FDA's Xyrem REMS approval will be satisfactory to the FDA, or that the Xyrem REMS will satisfy the FDA's expectations in its anticipated evaluation of the Xyrem REMS on an ongoing basis. Any failure to comply with the REMS obligations could result in enforcement action by the FDA; lead to changes in our Xyrem REMS obligations; continue to negatively affect sales of Xyrem; result in additional costs and expenses for us; and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

While we have an exclusive agreement with Express Scripts, the central pharmacy for Xyrem, through June 2017, if the central pharmacy does not fulfill its contractual obligations to us, fails to meet the requirements of the Xyrem REMS applicable to the central pharmacy, provides timely notice that it wants to terminate our agreement, refuses or fails to adequately serve patients, or fails to promptly and adequately address operational challenges, whether expected or unexpected, the fulfillment of Xyrem prescriptions and our sales would be adversely affected. If we change to a new central pharmacy, new contracts might be required with government and other insurers who pay for Xyrem, and the terms of any new contracts could be less favorable to us than current agreements. In addition, any new central pharmacy would need to be registered with the DEA and would also need to implement the particular processes, procedures and activities necessary to distribute Xyrem under the Xyrem REMS. Transitioning to a new pharmacy could result in product shortages, which would negatively affect sales of Xyrem,

result in additional costs and expenses for us and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Section 505-1(i)(1) of the FDCA generally provides that (i) an ANDA that references a drug subject to a REMS with elements to assure safe use, or ETASU, is required to have a REMS with the same elements as the referenced drug, and (ii) the ANDA drug and the referenced drug shall use a single shared system to assure safe use. However, the FDA may waive this requirement for a single shared system and permit the ANDA holder to submit a separate but comparable REMS if the FDA either determines that the burden of creating a single shared system outweighs its benefit, or if the ANDA applicant certifies that it has been unable to obtain a license to any aspects of the REMS for the referenced drug that are covered by a patent or a trade secret. The FDCA provides that the FDA may seek to negotiate a license between the ANDA applicant and the sponsor of the referenced drug before granting a waiver of the single shared system requirement. Accordingly, we may face pressure to develop a single shared REMS with potential generic competitors for Xyrem that is different from the approved Xyrem REMS or to license or share intellectual property pertinent to the Xyrem REMS, or elements of the Xyrem REMS, including proprietary data required for safe distribution of sodium oxybate, with generic competitors.

The FDA has stated that it expects the negotiation of a single shared REMS between an NDA holder and any ANDA applicant or applicants to proceed concurrently with the FDA's review of the ANDAs. The FDA has further stated that it typically monitors the progress of industry working groups attempting to develop shared REMS, and that it has acted to help ensure that sponsors were cooperating and that there were no obstacles to developing a single shared system. In January 2014, the FDA held an initial meeting with us and the three then-current sodium oxybate ANDA applicants to facilitate the development of a single shared REMS for sodium oxybate. In October 2015, the FDA held a telephonic meeting with us and the seven current sodium oxybate ANDA applicants to discuss the status of the development of a single shared REMS for sodium oxybate. The parties had regular interactions with respect to developing a single shared REMS prior to this meeting, and we are seeking to continue the interactions with the goal of developing a single shared REMS. However, we are aware that, separate from the discussions with us, the FDA and ANDA applicants have exchanged communications regarding the potential development of a single shared REMS for sodium oxybate. We cannot predict whether, or to what extent, interactions among the parties will continue or whether we will develop a single shared REMS. If we do not develop a single shared REMS or license or share intellectual property pertinent to our Xyrem REMS with generic competitors within a time frame or on terms that the FDA considers acceptable, the FDA may assert that its waiver authority permits it to approve the ANDA of one or more generic competitors with a separate REMS that differs from our approved Xyrem REMS. The FDA has exercised this waiver authority in two instances of which we are aware, including most recently in connection with the May 2015 approval of Roxane Laboratories' ANDA for alosetron hydrochloride tablets as generic versions of Lotronex tablets. This waiver was subject to the condition that the waiver-granted REMS system be open to all current and future sponsors of ANDAs or NDAs for alosetron hydrochloride products, and the FDA limited the grant of the waiver to a term of three years, subject to potential extension by the FDA. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the development of a single shared REMS for sodium oxybate, licensing or sharing intellectual property pertinent to our Xyrem REMS or elements of the Xyrem REMS, or the FDA's response to a request by one or more ANDA applicants for a waiver of the requirement for a single shared REMS, including in connection with a certification that the applicant had been unable to obtain a license. For more information, see the risk factor under the heading "*We have incurred and expect to continue to incur substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products"* in Part I, Item 1A of this Annual Report on Form 10-K.

The FTC has been paying increasing attention to the use of REMS by companies selling branded products, in particular to whether a REMS may be deliberately being used to reduce the risk of competition from generic drugs in a way that may be deemed to be anticompetitive. It is possible that the FTC, other governmental authorities or others could claim or determine that we are using the Xyrem REMS in an anticompetitive manner (including in light of the FDA's statement in the Xyrem REMS approval notice that the Xyrem REMS could be used in an anticompetitive manner inconsistent with applicable provisions of the FDCA) or have engaged in other anticompetitive practices. The FDCA further states that a REMS shall not be used by an NDA holder to block or delay generic drugs from entering the market. Several of the ANDA applicants have asserted that our patents covering the distribution system for Xyrem should not have been listed in the Orange Book and that the Xyrem REMS is blocking competition. We cannot predict the outcome of these claims in the ongoing litigation, or the impact of any similar claims that may be made in the future.

As required by the FDA and other regulatory agencies, the adverse event information that we collect for Xyrem is regularly reported to the FDA and could result in the FDA requiring changes to the Xyrem label or taking or requiring us to take other actions that could have an adverse effect on Xyrem's commercial success. Our Xyrem REMS includes unique features that provide more extensive information about adverse events, including deaths, than is generally available for other products that are not subject to similar REMS requirements.

Any failure to demonstrate our substantial compliance with applicable regulatory requirements to the satisfaction of the FDA or any other regulatory authority could result in such regulatory authorities taking actions in the future, which could have a material adverse effect on Xyrem sales and therefore on our business, financial condition, results of operations and growth prospects. For more information, see the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products*" in Part I, Item 1A of this Annual Report on Form 10-K.

The FDA has required that Xyrem's label include a boxed warning regarding the risk of central nervous system depression and misuse and abuse. A boxed warning is the strongest type of warning that the FDA can require for a drug product and warns prescribers that the drug carries a significant risk of serious or even life-threatening adverse effects. A boxed warning also means, among other things, that the product cannot be advertised through reminder ads, or ads that mention the pharmaceutical brand name but not the indication or medical condition it treats. We cannot predict whether the FDA will require additional warnings, including boxed warnings, to be included on Xyrem's label. Warnings in the Xyrem label and any limitations on our ability to advertise and promote Xyrem may have affected, and could in the future negatively affect, Xyrem sales and therefore our business, financial condition, results of operations and growth prospects.

Risks Related to Our Business

While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products. Our inability to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition to Xyrem, we are commercializing a portfolio of products, including our other lead marketed products, Erwinaze and Defitelio.

Erwinaze (called Erwinase in markets outside the U.S.), a biologic product, is used in conjunction with chemotherapy to treat patients with ALL with hypersensitivity to *E. coli*-derived asparaginase. Erwinaze was approved by the FDA under a BLA and was launched in the U.S. in November 2011. It is also being sold under marketing authorizations, named patient programs, temporary use authorizations or similar authorizations in multiple countries in Europe and elsewhere.

Erwinaze represents an important part of our strategy to grow sales of our existing products. However, our ability to successfully and sustainably maintain or grow sales of Erwinaze is subject to a number of challenges, including the limited population of patients with ALL and the incidence of hypersensitivity reactions to *E. coli*-derived asparaginase within that population and our need to apply for and receive marketing authorizations, through the EU's mutual recognition procedure or otherwise, in certain additional countries so we can launch promotional efforts in those countries. Another significant challenge to our ability to maintain the current sales level and to increase sales is our limited inventory of Erwinaze and our need to avoid supply interruptions of Erwinaze due to capacity constraints, production delays, quality or regulatory challenges or other manufacturing difficulties. See the discussion regarding Erwinaze supply issues in the risk factor under the heading "*We depend on single source suppliers for each of our products, product candidates and their active pharmaceutical ingredients. The loss of any of these suppliers, or delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in Part I, Item 1A of this Annual Report on Form 10-K.

We also face numerous other risks that may impact Erwinaze sales, including regulatory risks, the development of new asparaginase treatments or treatment protocols that could reduce the rate of hypersensitivity in patients with ALL, the development of new treatment protocols for ALL that may not include asparaginase-containing regimens, difficulties with obtaining and maintaining favorable pricing and reimbursement arrangements, and potential competition from future biosimilar products. In addition, if we fail to comply with our obligations under our agreement with the licensor and supplier of Erwinaze or lose exclusive rights to Erwinaze, or otherwise fail to maintain or grow sales of Erwinaze, our growth prospects could be negatively affected.

We made a significant investment in Defitelio/defibrotide in 2014, adding the product to our portfolio as a result of the Gentium Acquisition, and then securing worldwide rights to the product by acquiring rights to defibrotide in the Americas in August 2014. Our ability to realize the anticipated benefits from this investment is subject to a number of risks and uncertainties, including our ability to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval of defibrotide in other countries, including the U.S., so that we can commercialize the product in those countries. For more information, see the risk factor under the heading "*We may not be able to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval of defibrotide in other countries, including the U.S., which could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in Part I, Item 1A of this Annual Report on Form 10-K.

In the event we are able to obtain U.S. marketing approval, we will also face other challenges that could impact the anticipated value of Defitelio/defibrotide, including the limited size of the population of VOD patients who are indicated for treatment with Defitelio/defibrotide (particularly if the FDA requires more narrow or restricted labeling than we have proposed or if changes in HSCT treatment protocols reduce the incidence of VOD); U.S. market acceptance of defibrotide at its commercial price, particularly in light of past access to defibrotide free of charge through an expanded access treatment protocol; the need to establish U.S. pricing and reimbursement support for defibrotide, including through acceptance by hospital pharmacy and therapeutics committees; the possibility that we may be required to conduct time-consuming and costly clinical trials as a condition of any U.S. marketing approval for the product; the lack of experience of U.S. physicians in diagnosing and treating VOD; and challenges to our ability to develop the product for additional indications. If sales of Defitelio/defibrotide do not reach the levels we expect, our anticipated revenue from the product would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Failure to maintain or increase prescriptions and revenue from sales of our products, including Erwinaze and Defitelio, could have a material adverse effect on our business, financial condition, results of operations and growth prospects. We may choose to increase the price of our products, and we cannot assure you that price adjustments will not negatively affect our sales volumes. In addition, sales of Erwinaze may fluctuate significantly from quarter to quarter, depending on the number of patients receiving treatment, the availability of supply to meet the demand for the product, the dosing requirements of treated patients and other factors. The market price of our ordinary shares may decline if sales of our products do not continue or grow at the rates anticipated by financial analysts or investors.

In addition, if we fail to obtain approvals for certain of our products in new indications or formulations, we will be unable to commercialize our products in new indications or formulations, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We may not be able to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval of defibrotide in other countries, including the U.S., which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We launched Defitelio in certain European countries in 2014 and continued to launch in additional European countries on a rolling basis through 2015. We are in the process of making pricing and reimbursement submissions with respect to Defitelio in those European countries where Defitelio is not yet launched, including in countries where pricing and reimbursement approvals are required for launch. We cannot predict the timing of Defitelio's launch in countries where we are engaged in pricing and reimbursement submissions. If we experience delays or unforeseen difficulties in obtaining favorable pricing and reimbursement approvals, planned launches in the affected countries would be delayed, which could negatively impact anticipated revenue from Defitelio. The process for obtaining pricing and reimbursement approvals is complex and can vary from country to country. In addition, orphan products that have significant impact on patient survival, such as Defitelio, may be budgeted on a local rather than national level. The balance of all of these factors will determine our ability to ultimately obtain favorable pricing and reimbursement approvals. In addition, many European countries periodically review their reimbursement classes, which could have an adverse impact on the reimbursement status of Defitelio. If we are unable to obtain and maintain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country's reimbursed price influences other countries, our growth prospects in Europe could be negatively affected.

We have developed estimates of anticipated pricing, which are based on our research and understanding of the product and target market. However, due to efforts to provide for containment of health care costs, one or more countries may not support our estimated level of governmental pricing and reimbursement for Defitelio, particularly in light of the budget crises faced by a number of countries in Europe, which would negatively impact anticipated revenue from Defitelio. Furthermore, after initial pricing and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or arbitrage between low-priced and high-priced countries. If any of these events occurs, our anticipated revenue from Defitelio would be negatively affected.

Due to the limited amount of historical sales data from commercialization of Defitelio in Europe, our Defitelio sales will be difficult to predict from period to period, particularly since we may experience delays and unforeseen difficulties in obtaining favorable pricing and reimbursement approvals in additional countries. As a result, you should not rely on Defitelio sales results or trends in any period as being indicative of future performance. In addition, if sales of Defitelio do not reach the levels we expect, our anticipated revenue from Defitelio would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Defitelio was authorized under "exceptional circumstances" because it was not possible to obtain complete information about the product due to the rarity of the disease and because ethical considerations prevented conducting a study directly comparing Defitelio with best supportive care or a placebo. A marketing authorization granted under exceptional circumstances is subject to approval conditions and an annual reassessment of the risk-benefit balance by EMA. As a result, if

we fail to meet the approval condition for Defitelio, which requires that we set up a patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use, or if it is determined that the balance of risks and benefits of using Defitelio changes materially, the EMA could vary, suspend or withdraw the marketing authorization for Defitelio. This could negatively impact our anticipated revenue from Defitelio and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The marketing authorization application that Gentium initially filed with the EMA in 2011 sought approval for defibrotide for the treatment and prevention of VOD in adults and children. The approval Gentium received in October 2013 was for the narrower indication of treatment of severe VOD in adults and children undergoing HSCT. The scope of any future approvals we receive may negatively affect defibrotide's growth prospects.

At the time of the Gentium Acquisition, Gentium had licensed to Sigma-Tau the rights to defibrotide for the treatment and prevention of VOD in North America, Central America and South America. We acquired these rights from Sigma-Tau in August 2014. Defibrotide has been, and continues to be, made available as an investigational drug to patients diagnosed with VOD in the U.S. through an expanded access treatment protocol open under an investigational new drug application. We are engaged in activities related to the potential approval of defibrotide in the U.S. In September 2015, the FDA accepted for filing with priority review our NDA for defibrotide for the treatment of VOD with evidence of multi-organ dysfunction following HSCT. Based on timelines established by the PDUFA, we expect FDA review of the NDA to be completed by March 31, 2016. However, the FDA does not always meet the timelines established by PDUFA, and it is possible that the FDA's review of our NDA will not be completed by the PDUFA date, in which case our plans for commercialization of defibrotide in the U.S. may be delayed. Even if the FDA approves our NDA, the FDA may require more narrow or restricted labeling than we have proposed, and/or we may be required to conduct time-consuming and costly clinical trials as a condition of approval, which could negatively affect our business, financial condition, results of operations and growth prospects. In addition, approval of our NDA is dependent on our and our supplier's ability to obtain FDA certification of cGMP in connection with the manufacturing of the defibrotide drug compound and the processing of defibrotide into finished product for the U.S. market and on the outcome of FDA inspections of clinical sites and potentially other entities involved in the development of defibrotide. In 2015, the FDA issued a Form FDA 483 to Patheon Italia that included observations related to the Ferentino, Italy facility that manufactures the defibrotide finished product. Failure by Patheon Italia to timely remediate the observations to the FDA's satisfaction or the discovery of issues that impact the defibrotide finished product could have an adverse impact on the potential approval of our NDA for defibrotide, including the timing thereof. Also, although the FDA has granted Fast Track designation to defibrotide to treat severe VOD in HSCT recipients, this designation does not increase the likelihood that defibrotide will receive marketing approval. In any event, we cannot predict whether our NDA will be approved in a timely manner, if at all.

We are also assessing the potential for approval of defibrotide in other countries and for development of defibrotide in additional indications. We cannot know when, if ever, defibrotide will be approved in any other country or under what circumstances, and what, if any, additional clinical or other development activities will be required in order to potentially obtain such regulatory approval and the cost associated with such required activities, if any. If we fail to obtain approval for defibrotide in other countries or for new indications, our anticipated revenue from defibrotide and our growth prospects would be negatively affected.

We cannot predict whether historical revenues from named patient programs for our hematology/oncology products will continue or whether we will be able to continue to distribute those products on a named patient basis.

In certain European countries, reimbursement for products that have not yet received marketing authorization may be provided through national named patient programs. Erwinase and defibrotide are available on a named patient basis in many countries where they are not commercially available. Such reimbursement may cease to be available if authorization for a named patient program expires or is terminated. While we generate revenue from the distribution of these products through named patient programs, we cannot predict whether historical revenues from these programs will continue, whether we will be able to continue to distribute our products on a named patient basis in these countries, whether we will be able to commercialize our products in countries where the products have historically been available on a named patient basis, or whether commercial revenues will exceed revenues historically generated from sales on a named patient basis. Any failure to maintain revenues from sales of Erwinase and/or defibrotide on a named patient basis and/or to generate revenues from commercial sales of these products exceeding historical sales on a named patient basis could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We depend on single source suppliers for each of our products, product candidates and their active pharmaceutical ingredients. The loss of any of these suppliers, or delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, could materially and adversely affect our business, financial condition, results of operations and growth prospects.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of process controls required to consistently produce the active pharmaceutical ingredient and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, process controls, quality control and quality assurance, including testing of stability, impurities and impurity levels and other product specifications by validated test methods, and compliance with strictly enforced U.S., state and non-U.S. regulations. If we or any of our third party suppliers encounter these or any other manufacturing, quality or compliance difficulties with respect to any of our products, particularly Xyrem and Erwinaze since we maintain limited inventories for these products, we may be unable to meet commercial demand for such products, which could adversely affect our business, financial condition, results of operations and growth prospects.

We have completed construction of a manufacturing and development facility in Ireland and expect to begin commercial operations at the facility in 2016. Currently, however, other than the manufacturing plant in Italy where we produce some active pharmaceutical ingredients, including the defibrotide drug substance, we do not currently have our own commercial manufacturing capability for our products or product candidates, or their active pharmaceutical ingredients, or the capability to package our products. The availability of our products for commercial sale depends upon our ability to procure the ingredients, raw materials, packaging materials and finished products we need from third parties. In part due to the limited market size for our products and product candidates, we have entered into supply and manufacturing agreements with suppliers, each of which is currently our single source for each of our marketed products and for the active pharmaceutical ingredients used in some of these products. These single source arrangements put us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties at our suppliers.

We maintain limited inventories of Xyrem and Erwinaze, as well as the ingredients or raw materials used to make them. Our limited inventory puts us at significant risk of not being able to meet product demand. In addition, the DEA limits the quantity of certain Schedule I controlled substances that may be produced in the U.S. in any given calendar year through a quota system. The active pharmaceutical ingredient of Xyrem, sodium oxybate, is a Schedule I controlled substance, production quantities of which are limited by the DEA through a quota system. The DEA limits the quantity of certain Schedule I controlled substances that may be produced in the U.S. in any given calendar year through a quota system. DEA quotas are required for our sodium oxybate supplier to supply us with sodium oxybate and for our Xyrem supplier to obtain sodium oxybate in order to supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, our sodium oxybate supplier and our Xyrem supplier are required to request and justify allocation of sufficient annual DEA quotas as well as additional DEA quotas if our commercial or clinical requirements exceed the allocated quotas throughout the year. In the past, we have had to engage in lengthy efforts to obtain the needed quotas after the original annual quotas had first been allocated. For 2016, both our active pharmaceutical ingredient supplier and our Xyrem supplier have been allocated most, but not all, of their respective requested quotas. If, in the future, we and our third party suppliers cannot obtain the quotas that are needed on a timely basis, or at all, our business, financial condition, results of operations and growth prospects could be materially and adversely affected.

Siegfried (USA) Inc., subsequently renamed Siegfried USA, LLC, or Siegfried, has been our sole supplier of sodium oxybate since 2012. We expect that Siegfried will continue to be our sole supplier of sodium oxybate for the foreseeable future, and we cannot assure you that Siegfried can or will continue to supply on a timely basis, or at all, sufficient quantities of active pharmaceutical ingredient to enable the manufacture of the quantities of Xyrem that we need.

Erwinaze is licensed from and manufactured by a single source, which was Public Health England, or PHE, through March 31, 2015. As of April 1, 2015, the facility at which Erwinaze is manufactured was transferred to PBL, which is wholly owned by the U.K. Secretary of State for Health. The FDA's approval of the BLA for Erwinaze includes a number of post-marketing commitments related to the manufacture of Erwinaze. Inability to comply with regulatory requirements, including compliance with manufacturing-related post-marketing commitments that are part of the BLA approval, as well as other requirements monitored by the FDA, could adversely affect Erwinaze supply and could result in FDA approval being revoked or product recalls, either of which could have a material adverse effect on our sales of and revenues from Erwinaze and limit our potential future maintenance and growth of the market for this product. In addition, if the FDA or any non-U.S. regulatory authority mandates any changes to the specifications for Erwinaze, we may face challenges having product produced to meet such specifications, and our supplier may increase its price to supply Erwinaze meeting such specifications, which may result in additional costs to us and may decrease any profit we would otherwise achieve with Erwinaze.

The current manufacturing capacity for Erwinaze is nearly completely absorbed by demand for the product. We are working with PBL to evaluate potential expansion of its production capacity to increase the supply of Erwinaze over the longer

term. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build an excess level of product inventory that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues, and we have experienced, and expect to continue to experience, manufacturing and inventory challenges that have resulted in disruptions in our ability to supply certain markets. If capacity constraints continue, whether as a result of continued quality or other manufacturing issues or otherwise, we may be unable to build a desired excess level of product inventory, and our ability to supply the market may continue to be compromised. If production difficulties occur and result in a disruption to supply or capacity constraints, we do not have the right to engage a backup supplier for Erwinaze except in very limited circumstances, such as following the termination of the agreement by us due to the uncured material breach or the cessation of manufacturing by our supplier. If we are required to engage a backup or alternative supplier, the transfer of technical expertise and manufacturing process to the backup or alternative supplier would be difficult, costly and time-consuming, might not be successful and would increase the likelihood of a delay or interruption in manufacturing or a shortage of supply of Erwinaze. If we fail to obtain a sufficient supply of Erwinaze, our sales of and revenues from Erwinaze, our potential future maintenance and growth of the market for this product, and/or our business, financial condition, results of operations and growth prospects could be materially adversely affected.

We are our sole supplier of, and we believe that we are currently the sole worldwide producer of, the defibrotide drug compound. We manufacture the defibrotide drug compound in a single facility located in Villa Guardia, near Como, Italy. Patheon currently processes the defibrotide compound into its finished vial form, and Patheon is the sole provider of our commercial supply of the finished product in the EU and of our clinical supply. We anticipate that Patheon will also be the sole provider of our commercial supply of the finished defibrotide product for the U.S. market if the product is approved by the FDA. Part of the process to obtain FDA approval for defibrotide is to obtain certification from the FDA that the facilities we and our third party provider operate are in compliance with the FDA's cGMP requirements. The FDA may deny approval to manufacture defibrotide if the FDA determines that either our facility or our third party provider's facility does not meet applicable manufacturing and quality requirements. In 2015, the FDA issued a Form FDA 483 to Patheon Italia that included observations related to the Ferentino, Italy facility that manufactures the defibrotide finished product. Failure by Patheon Italia to timely remediate the observations to the FDA's satisfaction or the discovery of issues that impact the defibrotide finished product could have an adverse impact on the potential approval of our NDA for defibrotide, including the timing thereof. Even after a manufacturing facility is approved, the FDA will continue to inspect and evaluate facilities for ongoing compliance with applicable requirements. If Patheon does not or is not able to supply us with finished defibrotide product for any reason, it may take time and resources to implement and execute the necessary technology transfer to another processor, and such delay could negatively impact our planned product launch in the U.S. market if the product is approved by the FDA and our anticipated revenues from defibrotide and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

In addition, defibrotide is derived from porcine DNA. Our supplier of porcine materials may also be evaluated and inspected by the FDA in connection with our application for approval of defibrotide in the U.S. If our supplier experiences safety or other issues that impact its ability to supply porcine materials to us as needed, we may not be able to find alternative suppliers in a timely fashion, which could negatively impact our supply of defibrotide.

In order to conduct and complete our clinical program for JZP-110 or to potentially conduct future clinical trials for other product candidates, if any, we need to have sufficient quantities of clinical product manufactured and available for use. There can be no assurance that our suppliers will be able to produce or provide sufficient clinical supplies of JZP-110 or other product candidates in a timely manner. Any delay in receiving adequate supplies of JZP-110 or other product candidates for our studies could negatively impact our development programs.

Failure by us or our third party suppliers to comply with regulatory requirements could adversely affect our or their ability to supply products or ingredients. All facilities and manufacturing techniques used for the manufacture of pharmaceutical products must be operated in conformity with applicable current cGMP requirements. DEA regulations also govern facilities where controlled substances such as Xyrem's active pharmaceutical ingredient are manufactured. Our manufacturing facilities and manufacturing facilities of our suppliers have been and are subject to periodic unannounced inspection by the FDA, the EMA, the DEA, the Italian Health Authority and other regulatory authorities, including state authorities and similar authorities in other jurisdictions, to confirm compliance with cGMP and other requirements. We and our third party suppliers must continually expend time, money and effort in production, record keeping and quality assurance and control to ensure that our products and product candidates meet applicable specifications and other requirements for product safety, efficacy and quality. Failure to comply with applicable legal and regulatory requirements subjects us and our suppliers to possible legal or regulatory action, including restrictions on supply or shutdown, which may adversely affect our or a supplier's ability to supply the ingredients or finished products we need. Moreover, our or our third party suppliers' facilities could be damaged by fire, flood, earthquake, power loss, telecommunication and information system failure, terrorism or similar events. Any of these events could cause a delay or interruption in manufacturing and potentially a supply shortage of our products, which could negatively impact our anticipated revenues.

If, for any reason, our suppliers, including any new suppliers, do not continue to supply us with our products or product candidates in a timely fashion and in compliance with applicable quality and regulatory requirements, or otherwise fail or refuse to comply with their obligations to us under our supply and manufacturing arrangements, we may not have adequate remedies for any breach, and their failure to supply us could result in a shortage of our products or product candidates, which could adversely affect our business, financial condition, results of operations and growth prospects.

In addition, if one of our suppliers fails or refuses to supply us for any reason, it would take a significant amount of time and expense to qualify a new supplier. The FDA and similar international regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and certain packaging materials used in our products. The loss of one of our suppliers could require us to obtain regulatory clearance in the form of a "prior approval supplement" and to incur validation and other costs associated with the transfer of the active pharmaceutical ingredient or product manufacturing process. We believe that it could take up to two years, or longer in certain cases, to qualify a new supplier, and we may not be able to obtain active pharmaceutical ingredients or finished products from new suppliers on acceptable terms and at reasonable prices, or at all. If there are delays in qualifying new suppliers or facilities or a new supplier is unable to obtain a sufficient quota from the DEA, if required, or to otherwise meet FDA or similar international regulatory body's requirements for approval, there could be a shortage of the affected products for the marketplace or for use in clinical studies, or both, particularly since we do not have secondary sources for supply and manufacture of the active pharmaceutical ingredients for our products or backup suppliers for our finished products.

Our ability to develop and deliver products in a timely and competitive manner depends on our third party suppliers being able to continue to meet our ongoing commercial needs. Any delay in supplying, or failure to supply, products or product candidates by any of our suppliers could result in our inability to meet the commercial demand for our products, or our needs for use in clinical trials, and could adversely affect our business, financial condition, results of operations and growth prospects.

We have substantially expanded our international footprint and operations, and we may expand further in the future, but we do not yet have substantial historical experience in international markets and may not achieve the results that we, our shareholders or analysts who cover our business expect.

We are headquartered in Dublin, Ireland and have multiple offices in the U.S., the United Kingdom, Italy and other countries in Europe. Our headcount has grown to approximately 910 in February 2016. This includes employees in 14 countries in North America and Europe, a European commercial presence, a complex distribution network for products in Europe and additional territories, and manufacturing facilities in Italy and Ireland. In addition, we may expand our international operations into other countries in the future, either organically or by acquisition. While we have acquired significant management and other personnel with substantial international experience, conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- applicable trade laws, tariffs, export quotas, custom duties or other trade restrictions and any changes to them;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations, as well as maintaining positive interactions with unionized employees in one of our international locations;
- liabilities for activities of, or related to, our international operations, products or product candidates;
- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

As a result of our rapid growth, our business and corporate structure has become substantially more complex. There can be no assurance that we will effectively manage the increased complexity without experiencing operating inefficiencies or control deficiencies. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In recent years, the global economy has been impacted by the effects of an ongoing global financial crisis, including the European sovereign debt crisis, which has caused extreme disruption in the financial markets, including severely diminished liquidity and credit availability. In addition, we expect to continue to grow our product sales in Europe. Continuing worldwide economic instability, including challenges faced by the Eurozone and certain of the countries in Europe and the ongoing

budgetary difficulties faced by a number of EU member states, including Greece and Spain, has led and may continue to lead to substantial delays in payment and payment partially with government bonds rather than cash for medicinal drug products, which could negatively impact our revenues and profitability.

The commercial success of our products depends upon their market acceptance by physicians, patients, third party payors and the medical community.

Physicians may not prescribe our products, in which case we would not generate the revenues we anticipate from product sales. Market acceptance of any of our products by physicians, patients, third party payors and the medical community depends on:

- the clinical indications for which a product is approved, including any restrictions placed upon the product in connection with its approval, such as a REMS, patient registry or labeling restrictions;
- the prevalence of the disease or condition for which the product is approved and the severity of side effects;
- acceptance by physicians and patients of each product as a safe and effective treatment;
- perceived advantages over alternative treatments;
- relative convenience and ease of administration;
- physician and patient assessment of the burdens associated with obtaining or maintaining the certifications required under the Xyrem REMS;
- the cost of treatment in relation to alternative treatments, including generic products;
- the extent to which the product is approved for inclusion on formularies of hospitals and managed care organizations; and
- the conditions for reimbursement required by, and appropriate pricing and availability of reimbursement from, third party payors.

Because of our dependence upon market acceptance of our products, any adverse publicity associated with harm to patients or other adverse events resulting from the use or misuse of our products or any similar products distributed by other companies, including generic versions of our products, could materially and adversely affect our business, financial condition, results of operations and growth prospects. For example, from time to time, there is negative publicity about illicit GHB and its effects, including with respect to illegal use, overdoses, serious injury and death. Because sodium oxybate, the active pharmaceutical ingredient in Xyrem, is a derivative of GHB, Xyrem sometimes also receives negative mention in publicity relating to GHB. Patients, physicians and regulators may therefore view Xyrem as the same as or similar to illicit GHB. In addition, there are regulators and some law enforcement agencies that oppose the prescription and use of Xyrem generally because of its connection to GHB. Xyrem's label includes information about adverse events from GHB.

In addition, we have periodically increased the price of Xyrem and may do so again in the future. We also have made and may in the future make similar price increases on our other products. Price increases on our products and negative publicity regarding pricing and price increases generally, whether on our products or products distributed by other pharmaceutical companies, could negatively affect market acceptance of our products.

For additional discussion about payor acceptance, see the risk factor under the heading "*Price approvals and reimbursement may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably"* in Part I, Item 1A of this Annual Report on Form 10-K.

We may not be able to successfully identify and acquire, in-license or develop additional products or product candidates to grow our business, and, even if we are able to do so, we may not be able to successfully manage the risks associated with integrating any products or product candidates we may acquire in the future into our product portfolio, or we may otherwise fail to realize the anticipated benefits of these acquisitions.

We intend to grow our business over the long term by acquiring or in-licensing and developing additional products and product candidates that we believe have significant commercial potential. Future growth through acquisition or in-licensing will depend upon the availability of suitable products and product candidates for acquisition or in-licensing on acceptable prices, terms and conditions. Any growth through development will depend upon our identifying and obtaining product candidates, our ability to develop those product candidates and the availability of funding to complete the development of, obtain regulatory approval for and commercialize these product candidates. Even if appropriate opportunities are available, we may not be able to successfully identify them, or we may not have the financial resources necessary to pursue them. Other companies, many of which may have substantially greater financial, marketing and sales resources, compete with us for these opportunities. In order to compete successfully to acquire attractive products or product candidates in the current business

climate, we may have to pay higher prices for assets than may have been paid historically, which may make it more difficult for us to realize an adequate return on any acquisition.

Even if we are able to successfully identify and acquire, in-license or develop additional products or product candidates, we cannot assure you that we will be able to successfully manage the risks associated with integrating any products or product candidates or the risks arising from anticipated and unanticipated problems in connection with an acquisition or in-licensing. In any event, we may not be able to realize the anticipated benefits of any acquisition or in-licensing for a variety of reasons, including the possibility that a product candidate proves not to be safe or effective in later clinical trials, a product fails to reach its forecasted commercial potential as a result of pricing pressures, negative publicity regarding actual or potential future price increases for that product or otherwise, or the integration of a product or product candidate gives rise to unforeseen difficulties and expenditures. Any failure in identifying and managing these risks and uncertainties effectively would have a material adverse effect on our business.

In addition, product and product candidate acquisitions create other uncertainties and risks, particularly when the acquisition takes the form of a merger or other business consolidation. Our business acquisitions have required, and any similar future transactions will also require, significant efforts and expenditures, including with respect to transition activities and integrating the acquired business with our historical business. We may encounter unexpected difficulties, or incur unexpected costs, in connection with potential acquisitions and similar transactions, which include:

- high acquisition costs;
- the need to incur substantial debt or engage in dilutive issuances of equity securities to pay for acquisitions;
- the potential disruption of our historical core business;
- the strain on, and need to continue to expand, our existing operational, technical, financial and administrative infrastructure;
- the difficulties in assimilating employees and corporate cultures;
- the failure to retain key managers and other personnel;
- the challenges in controlling additional costs and expenses in connection with and as a result of any acquisition;
- the need to write down assets or recognize impairment charges;
- the diversion of our management’s attention to integration of operations and corporate and administrative infrastructures; and
- any unanticipated liabilities for activities of or related to the acquired business or its operations, products or product candidates.

If any of these or other factors impair our ability to integrate any acquired business efficiently and successfully, we may be required to spend time or money on integration activities that otherwise would be spent on the development and expansion of our business. If we fail to integrate or otherwise manage an acquired business successfully and in a timely manner, resulting operating inefficiencies could increase costs and expenses more than we planned, could negatively impact the market price of our ordinary shares and could otherwise distract us from execution of our strategy. Failure to maintain effective financial controls and reporting systems and procedures during and after integration of an acquired business could also impact our ability to produce timely and accurate financial statements.

Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Since 2014, we have made significant investments into expanding our product development pipeline and expect to continue to increase our research and development organization. Significant clinical, development and financial resources will be required to progress product candidates through clinical trials and the regulatory approval process to develop them into commercially viable products. We have a number of product candidates under development. We also intend to pursue clinical development of other product candidates that we may acquire or in-license in the future. Any failure or delay in completing clinical trials for our product candidates would prevent or delay the commercialization of our product candidates, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

As a condition to regulatory approval, each product candidate must undergo extensive and expensive preclinical studies and clinical trials to demonstrate to a statistically significant degree that the product candidate is safe and effective. The results at any stage of the development process may lack the desired safety, efficacy or pharmacokinetic characteristics. Results of limited preclinical studies, including studies of our product candidates in animal models, may not predict the results of human

clinical trials of those product candidates. Similarly, results from early clinical trials may not be predictive of results obtained in later and larger clinical trials, and product candidates in later clinical trials may fail to show the desired safety and efficacy despite having progressed successfully through initial clinical testing. In that case, the FDA or any equivalent non-U.S. regulatory agency may determine our data is not sufficiently compelling to warrant marketing approval and may require us to engage in additional clinical trials or provide further analysis which may be costly and time-consuming. A number of companies in the pharmaceutical industry, including us, have suffered significant setbacks in clinical trials, even in advanced clinical trials after showing positive results in preclinical studies or earlier clinical trials. For example, in the second quarter of 2015, we initiated patient enrollment in three Phase 3 clinical trials for JZP-110, a late-stage investigational compound being developed for potential treatment of EDS in patients with narcolepsy and EDS in patients with OSA. We expect to receive preliminary data results from these trials in the fourth quarter of 2016. However, these results may not be positive, and we may be unable to complete these clinical trials in a timely manner, or at all. If a product candidate, including JZP-110, fails at any stage of development, it will not receive regulatory approval, we will not be able to commercialize it, and we will not receive any return on our investment in that product candidate.

Our development pipeline projects may not be successful, and any adverse events or other information generated during the course of studies related to existing products could result in action by the FDA or any non-U.S. regulatory agency which may restrict our ability to sell, or sales of, currently marketed products, or such events or other information could otherwise have a material adverse effect on a related commercial product. Any failure or delay in completing clinical trials for line extensions or the generation of additional clinical data could materially and adversely affect the maintenance and growth of the markets for the related marketed products, which could adversely affect our business, financial condition, results of operations and overall growth prospects.

In addition to issues relating to the results generated in clinical trials, clinical trials can be delayed or halted for a variety of reasons, including:

- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;
- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidate for use in trials;
- delays or failures in reaching agreement on acceptable terms with prospective study sites;
- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board, also known as Ethics Committees in Europe, to conduct a clinical trial at a prospective study site;
- delays or failures in recruiting patients to participate in a clinical trial;
- failure of our clinical trials and clinical investigators to be in compliance with the FDA and other regulatory agencies' good clinical practice guidelines;
- unforeseen safety issues, including negative results from ongoing preclinical studies and clinical trials and adverse events associated with product candidates;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites;
- failure of our third party clinical trial managers to satisfactorily perform their contractual duties, comply with regulations or meet expected deadlines; or
- insufficient funds to complete the trials.

We rely on third parties to conduct our clinical trials, and if they do not properly and successfully perform their legal and regulatory obligations, as well as their contractual obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We rely on contract research organizations and other third parties to assist us in designing, managing, monitoring and otherwise carrying out our clinical trials, including with respect to site selection, contract negotiation and data management. We do not control these third parties and, as a result, they may not treat our clinical studies as a high priority, or in the manner in which we would prefer, which could result in delays. We are responsible for confirming that each of our clinical trials is conducted in accordance with its general investigational plan and protocol, as well as the FDA's and non-U.S. regulatory agencies' requirements, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to ensure that the data and results are credible and accurate and that the trial participants are adequately protected. The FDA and non-U.S. regulatory agencies enforce good clinical practices through periodic inspections of trial sponsors,

principal investigators and trial sites. If we, contract research organizations or other third parties assisting us or our study sites fail to comply with applicable good clinical practices, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or its non-U.S. counterparts may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA or non-U.S. regulatory agencies will determine that any of our clinical trials comply with good clinical practices. In addition, our clinical trials must be conducted with product produced under the FDA's cGMP regulations and similar regulations outside of the U.S. Our failure, or the failure of our product suppliers, to comply with these regulations may require us to repeat or redesign clinical trials, which would delay the regulatory approval process.

If third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain is compromised due to failure to adhere to our clinical protocols, including dosing requirements, or regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may not meet regulatory requirements. If our clinical trials do not meet regulatory requirements or if these third parties need to be replaced, our clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates or succeed in our efforts to create approved line extensions for certain of our existing products or generate additional useful clinical data in support of these products.

We face substantial competition from other companies, including companies with greater resources, including larger sales organizations and more experience working with large and diverse product portfolios, than we have.

The commercial potential of our current products and any future products may be reduced or eliminated if our competitors develop or acquire and commercialize generic or branded products that are safer or more effective, have fewer side effects, are easier to administer or are less expensive than our products. The pharmaceutical industry is highly competitive and dominated by a number of large, established pharmaceutical companies, as well as specialty pharmaceutical companies that market products and develop product candidates in sleep, hematology/oncology, pain and other therapeutic areas. Many of our competitors, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources than we do. They can spend more on, and have more expertise in, research and development, regulatory, manufacturing, distribution and sales activities. As a result, our competitors may obtain FDA or other regulatory approvals for their product candidates more rapidly than we may and may market their products more effectively than we do. Smaller or earlier stage companies may also prove to be significant competitors, particularly through focused development programs and collaborative arrangements with large, established companies. While there is currently no direct competition to Erwinaze to treat ALL patients with hypersensitivity to *E. coli*-derived asparaginase, other companies have developed or are developing new treatments for ALL, including new asparaginase treatments that could reduce the rate of hypersensitivity in patients with ALL, and new treatment protocols are being developed for ALL that may not include asparaginase-containing regimens. For example, a number of companies are developing new immunotherapy treatments for relapsed or refractory ALL patients, including one treatment that was recently approved, and a company recently announced positive efficacy and safety results from its completed Phase 2/3 pivotal trial in Europe for an alternative asparaginase treatment consisting of L-asparaginase encapsulated inside donor-derived red blood cells. The development of these new treatments could negatively impact our ability to maintain and grow sales of Erwinaze in patient populations where the benefit of an asparaginase-containing regime is not well established.

In addition, many of our competitors are able to deploy more personnel to market and sell their products than we do. We currently have a relatively small number of sales representatives compared with the number of sales representatives of most other pharmaceutical companies with marketed products. Each of our sales representatives is responsible for a territory of significant size. The continued growth of our current products and the launch of any future products may require expansion of our sales force and sales support organization, and we may need to commit significant additional funds, management and other resources to the growth of our sales organization. We may not be able to achieve any necessary growth in a timely or cost-effective manner or realize a positive return on our investment, and we may not have the financial resources to achieve the necessary growth in a timely manner or at all. In particular, we compete with a significant number of pharmaceutical and life sciences companies with extensive sales, marketing and promotional experience in hematology/oncology markets, and our failure to compete effectively in this area could negatively affect our sales of Erwinaze, Defitelio and other products. We also have to compete with other pharmaceutical and life sciences companies to recruit, hire, train and retain sales and marketing personnel, and turnover in our sales force and marketing personnel could negatively affect sales of our products. If our specialty sales force and sales organization are not appropriately sized to adequately promote any current or potential future products, the commercial potential of our current products and any future products may be diminished.

We also face competition, and may in the future face additional competition, from manufacturers of generic drugs. Generic competition often results in decreases in the prices at which branded products can be sold, particularly when there is more than one generic available in the marketplace. In addition, legislation enacted in the U.S. allows for, and in a few instances in the absence of specific instructions from the prescribing physician mandates, the dispensing of generic products rather than branded products where a generic version is available. Other companies could also develop products that are

similar, but not identical, to our marketed products, such as an alternative formulation of our product or an alternative formulation combined with a different delivery technology, and seek approval in the U.S. by referencing our products and relying, to some degree, on the FDA's finding that our products are safe and effective. For more information, see the risk factor under the heading *"If generic versions of Xyrem or other sodium oxybate products that compete with Xyrem are approved and launched, sales of Xyrem would be adversely affected"* in Part I, Item 1A of this Annual Report on Form 10-K.

Our products and product candidates may also compete in the future with new products currently under development by others. Any products that we develop are likely to be in a highly competitive market, and many of our competitors may succeed in developing products that may render our products obsolete or noncompetitive.

Our ability to continue to grow further requires that we compete successfully with specialty pharmaceutical companies for product and product candidate acquisition and in-licensing opportunities. These competitors include established companies that may have a competitive advantage over us due to their size and financial resources.

If we fail to attract, retain and motivate key personnel or to retain the members of our executive management team, our operations and our future growth may be adversely affected.

Our success and our ability to grow depend in part on our continued ability to attract, retain and motivate highly qualified personnel and on our ability to develop and maintain important relationships with leading academic institutions, clinicians and scientists. We are highly dependent upon our executive management team and other critical personnel, all of whom work on many complex matters that are essential to our success. We do not carry "key person" insurance. The loss of services of one or more members of our executive management team or other key personnel could delay or prevent the successful completion of some of our vital activities. Any employee may terminate his or her employment at any time without notice or with only short notice and without cause or good reason. The resulting loss of institutional knowledge may negatively impact our operations and future growth.

In addition, to grow our company we will need additional personnel. Competition for qualified personnel in the pharmaceutical industry is very intense. If we are unable to attract, retain and motivate quality individuals, including in our research and development operations, which are continuing to expand, our business, financial condition, results of operations and growth prospects could be adversely affected.

We also depend on the unique abilities, industry experience and institutional knowledge of the members of our board of directors to efficiently set company strategy and effectively guide our executive management team. We cannot be certain that future board turnover will not negatively affect our business.

Significant disruptions of information technology systems or data security breaches could adversely affect our business.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result we manage a number of third party vendors who may or could have access to our confidential information. The size and complexity of our information technology systems, and those of third party vendors with whom we contract, and the large amounts of confidential information stored on those systems, make such systems potentially vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third party vendors, and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity. Cyber-attacks could include the deployment of harmful malware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. From time to time, our systems have been subject to cyber-attacks.

Significant disruptions of our information technology systems or security breaches could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), and could result in financial, legal, business and reputational harm to us. Any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, 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 the privacy and security of personal information, which could disrupt our business, result in increased costs or loss of revenue, and/or result in significant legal and financial exposure. In addition, security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices to access confidential information increases the risk of security breaches. While we have implemented security measures to protect our information

technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business.

Risks Related to Our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

Our commercial success depends in part on obtaining and maintaining patent protection of our products and product candidates and their use and the methods used to manufacture and distribute them, as well as successfully defending these patents against third party challenges, and successfully protecting our trade secrets. Our ability to protect our products and product candidates from unauthorized making, using, selling, offering to sell or importation by third parties depends on the extent to which we have rights under valid and enforceable patents or have trade secrets that cover these activities. We cannot be certain that any of our patent applications, or those of our licensors, will result in issued patents, that the patents we own and license, or any additional patents we may own or license, will prevent other companies from developing similar or therapeutically equivalent products, or that others will not be issued patents that may prevent the sale of our products or require licensing and the payment of significant fees or royalties.

The patent position of pharmaceutical companies can be highly uncertain and involve complex legal, regulatory and factual questions. We own a portfolio of U.S. and non-U.S. patents and patent applications and have licensed rights to a number of issued patents and patent applications that cover or relate to our products and product candidates, including Xyrem and Defitelio. Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Even if we are able to obtain patents covering our products and product candidates, any patent may be challenged, invalidated, held unenforceable or circumvented, potentially including by FDA approval of an ANDA that avoids infringement of our intellectual property.

On September 16, 2011, the Leahy-Smith America Invents Act, or the America Invents Act, was signed into law. The final substantive provisions of the America Invents Act, including the first to file system, became effective on March 16, 2013. The America Invents Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are being filed, prosecuted and litigated. For example, the America Invents Act enacted proceedings involving post-issuance patent review procedures, such as IPR and other post grant reviews. These proceedings are conducted before the PTAB. Each proceeding has different eligibility criteria and different patentability challenges that can be raised. The IPR process permits any person (except a party who has sued on the patent for more than a year) to challenge the validity of the patent on the grounds that it was anticipated or made obvious by prior art. The America Invents 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, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. We cannot predict what impact, if any, amendments to the America Invents Act or other patent-related legislation, or judicial decisions interpreting such legislation, will have on such uncertainties and costs.

Although Xyrem is covered by patents covering its formulation, distribution system and method of use, third parties are seeking to introduce generic versions of Xyrem, and additional third parties may also attempt to invalidate or design around the patents, or assert that they are invalid or otherwise unenforceable, and seek to introduce generic versions of Xyrem or other sodium oxybate products for treatment of cataplexy and/or EDS in narcolepsy. If one or more companies receive FDA approval of an ANDA for generic versions of Xyrem or an NDA for other sodium oxybate products, it is possible that such company or companies could introduce generic versions of Xyrem or other sodium oxybate products before our patents expire, if it is determined that our patents are invalid, unenforceable or non-infringed, or if such company or companies decide, before applicable ongoing patent litigation is concluded, to launch competition to Xyrem at risk of potentially being held liable for damages for patent infringement.

Seven ANDAs have been filed with the FDA by third parties seeking to market generic versions of Xyrem. We have filed lawsuits seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, but we cannot assure you that any of the lawsuits will prevent the introduction of a generic version of Xyrem for any particular length of time, or at all. Additional ANDAs could also be filed requesting approval to market generic versions of Xyrem. If any of these applications is approved, and a generic version of Xyrem is introduced, our sales of Xyrem would be adversely affected. Although no trial date has been set in any of the ANDA suits, we anticipate that trial on some of the patents in the Roxane case could occur as early as the second quarter of 2016. However, the actual timing of events may be significantly earlier or later than we currently anticipate, and we cannot predict the timing or outcome of events in this or the other ANDA litigation.

In addition, certain of the ANDA filers have challenged the validity of six patents covering the distribution system for Xyrem by filing petitions for IPR. In July 2015, the PTAB issued decisions instituting IPR trials with respect to these petitions, and we expect the PTAB to issue final decisions on the validity of the patents by July 2016. In September and October 2015,

certain of the ANDA filers filed petitions for IPR with respect to the validity of an additional patent covering the distribution system for Xyrem and with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. In December 2015, one of the ANDA filers filed a petition for IPR with respect to the validity of a patent covering the formulation of Xyrem. In February 2016, one of the ANDA filers filed a petition for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

A company that is using its proprietary technology for delivery of a sodium oxybate formulation to eliminate second nighttime dosing for narcolepsy patients has stated that it anticipates commencing a Phase 3 pivotal trial in 2016 that is expected to run through early 2017. For more information, see the risk factor under the heading "*If generic versions of Xyrem or other sodium oxybate products that compete with Xyrem are approved and launched, sales of Xyrem would be adversely affected*" in Part I, Item 1A of this Annual Report on Form 10-K.

The existence of a patent will not necessarily prevent other companies from developing similar or therapeutically equivalent products or protect us from claims of third parties that our products infringe their issued patents, which may require licensing and the payment of significant fees or royalties. Competitors may successfully challenge our patents, produce similar products that do not infringe our patents, or manufacture products in countries where we have not applied for patent protection or that do not respect our patents. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents, our licensed patents or in third party patents.

The degree of future protection to be afforded by our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates but that are not covered by the claims of our patents, or for which we are not licensed under our license agreements;
- we or our licensors or partners might not have been the first to invent or file, as appropriate, subject matters covered by our issued patents or pending patent applications or the pending patent applications or issued patents of our licensors or partners;
- others may independently develop similar or alternative products without infringing our intellectual property rights;
- our pending patent applications may not result in issued patents;
- our issued patents and the issued patents of our licensors or partners may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges by third parties;
- our issued patents may not cover our competitors' products;
- our issued patents and the issued patents of our licensors or partners may be vulnerable to legal challenges as a result of changes in applicable law;
- we may not develop additional proprietary products that are patentable; or
- the patents of others may have an adverse effect on our business.

We also may rely on trade secrets and other unpatented proprietary information to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets and other unpatented proprietary information, our employees, consultants, advisors and partners may unintentionally or willfully disclose our proprietary information to competitors, and we may not have adequate remedies for such disclosures.

If our employees, consultants, advisors and partners develop inventions or processes independently, or jointly with us, that may be applicable to our products under development, disputes may arise about ownership or proprietary rights to those inventions and processes. Enforcing a claim that a third party illegally obtained and is using any of our inventions or trade secrets is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside of the U.S. are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Certain of the products we sell have no patent protection and, as a result, potential competitors face fewer barriers in introducing competing products. We rely on trade secrets and other unpatented proprietary information to protect our commercial position with respect to such products, which we may be unable to do. In some instances, we also rely on

regulatory exclusivity. For example, Erwinaze has no patent protection. In addition to protection using trade secrets, Erwinaze has orphan drug exclusivity in the U.S. for a seven-year period from its FDA approval, which precludes approval of another product with the same principal molecular structure for the same indication until November 2018. Erwinaze, as a biologic product approved under a BLA, is also subject to the BPCIA. We believe that Erwinaze is protected by exclusivity that prevents approval of a biosimilar in the U.S. through late 2023 under the BPCIA. Because the BPCIA is a relatively new law, we anticipate that its impact on both reference product sponsors and biosimilar applicants will evolve over a period of years. Its implementation likely will be shaped by a variety of factors, including FDA issuance of guidance documents, proposed regulations, and decisions in the course of considering specific applications. As a result, it is possible that a potential competing drug product might obtain FDA approval before the orphan drug and expected BCPIA exclusivity periods have expired, which would adversely affect sales of Erwinaze. In the EU, the regulatory data protection and thus regulatory exclusivity period for Erwinase has lapsed. This also means that any new marketing authorizations for Erwinase in other EU member states will not receive any regulatory data protection. If a biosimilar product to Erwinaze is approved as interchangeable to Erwinaze in the U.S. or in other countries where Erwinaze is sold, a significant percentage of the prescriptions that would have been written for Erwinaze may be filled with the biosimilar version, resulting in a loss in sales of Erwinaze, and there may be a decrease in the price at which Erwinaze can be sold. Competition from a biosimilar product to Erwinaze could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our research and development collaborators may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research that may be relevant to our business. While the ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to contractual limitations, these contractual provisions may be insufficient or inadequate to protect our trade secrets and may impair our patent rights. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our innovations and other confidential information, then our ability to obtain patent protection or protect our proprietary information may be jeopardized. Moreover, a dispute may arise with our research and development collaborators over the ownership of rights to jointly developed intellectual property. Such disputes, if not successfully resolved, could lead to a loss of rights and possibly prevent us from pursuing certain new products or product candidates.

We have incurred and expect to continue to incur substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products.

Our ability, and that of our partners, to commercialize any approved products will depend, in part, on our ability to obtain patents, enforce those patents and operate without infringing the proprietary rights of third parties. The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions. We have filed multiple U.S. patent applications and non-U.S. counterparts, and may file additional U.S. and non-U.S. patent applications. There can be no assurance that any issued patents we own or control will provide sufficient protection to conduct our business as presently conducted or as proposed to be conducted. Moreover, for a variety of reasons, including the existence of relevant prior research performed and the existence of conflicting patent applications submitted in the same manner or similar fields, there can be no assurance that any patents will issue from the patent applications owned by us, or that we will remain free from infringement claims by third parties.

If we choose to go to court to stop a third party from infringing our patents, our licensed patents or our partners' patents, that third party has the right to ask the court, or to argue in front of an administrative agency, to rule that these patents are invalid and/or should not be enforced. These lawsuits and administrative proceedings are expensive and consume time and other resources, and we may not be successful in these proceedings or in stopping infringement. There is also a risk that a court will decide that these patents are not valid or infringed, or that the PTAB will decide that certain patents are not valid, and that we do not have the right to stop a third party from using the patented subject matter. Litigation involving patent matters is frequently settled between the parties, rather than continuing to a court ruling. If we were to settle a patent lawsuit with a generic pharmaceutical company, we could be subject to investigations by the FTC or other antitrust enforcement agencies or government or private-party lawsuits. The FTC has publicly stated that, in its view, certain types of agreements between brand and generic pharmaceutical companies related to the settlement of patent litigation or the manufacture, marketing and sale of generic versions of branded drugs violate the antitrust laws and has commenced investigations and brought actions against some companies that have entered into such agreements. In particular, the FTC has expressed its intention to take aggressive action to challenge settlements that include an alleged transfer of value from the brand company to the generic company (so-called "pay for delay" patent litigation settlements) and to call on legislators to pass stronger laws prohibiting such settlements. Because there is currently no precise legal standard with respect to the lawfulness of such settlements, there could be extensive litigation over whether any settlement that we might enter into constitutes a reasonable and lawful patent settlement. Any such investigations or lawsuits, and the outcome thereof, could have a material adverse effect on our business.

Seven companies have sent us notices that they have filed ANDAs with the FDA seeking approval to market a generic version of Xyrem. We have filed lawsuits seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and the litigation proceedings are ongoing. In addition, certain of the ANDA filers have challenged the validity of six patents covering the distribution system for Xyrem by filing petitions for IPR. In July 2015, the PTAB issued decisions instituting IPR with respect to these six petitions, and we expect the PTAB to issue final decisions on the validity of the patents by July 2016. In September and October 2015, certain of the ANDA filers filed petitions for IPR with respect to the validity of an additional patent covering the distribution system for Xyrem and with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. In December 2015, one of the ANDA filers filed a petition for IPR with respect to the validity of a patent covering the formulation of Xyrem. In February 2016, one of the ANDA filers filed a petition for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. In addition, the IPR process under the America Invents Act permits any person, whether they are accused of infringing the patent at issue or not, to challenge the validity of certain patents. As a result, entities associated with hedge funds have challenged valuable pharmaceutical patents through the IPR process. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business. For more information, see the risk factor under the heading "*It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection*" in Part I, Item 1A of this Annual Report on Form 10-K. We cannot assure you that our pending lawsuits, other lawsuits or proceedings we may file in the future, or our defense against any lawsuits or other proceeding that have been or will be brought against us will be successful in stopping the infringement of our patents, that any such litigation or other proceedings will be cost-effective, or that any of them will have a satisfactory result for us.

A third party may claim that we or our manufacturing or commercialization partners are using inventions covered by the third party's patent rights, or that we or such partners are infringing, misappropriating or otherwise violating other intellectual property rights, and may go to court to stop us from engaging in our normal operations and activities, including making or selling our products. Such lawsuits are costly and could affect our results of operations and divert the attention of management and development personnel. There is a risk that a court could decide that we or our partners are infringing, misappropriating or otherwise violating third party patent or other intellectual property rights, which could be very costly to us and have a material adverse effect on our business.

In the pharmaceutical and life sciences industry, like other industries, it is not always clear to industry participants, including us, which patents cover various types of products or methods. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our products or methods do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid or unenforceable, which we may not be able to do.

Because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, because patent applications in the U.S. and many non-U.S. jurisdictions are typically not published until 18 months after their priority date, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for inventions covered by our or our licensors' issued patents or pending applications, or that we or our licensors were the first inventors. Our competitors may have filed, and may in the future file, patent applications covering subject matter similar to ours. Any such patent application may have priority over our or our licensors' patents or applications and could further require us to obtain rights to issued patents covering such subject matter. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our U.S. patent position with respect to such inventions. Patent interferences are limited or unavailable for patent applications filed after March 16, 2013.

Some of our competitors may be able to sustain the costs of complex patent and other intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

We own patents that cover, among other things, the formulation and method of use covering the administration for Xyrem. In July 2014, the USPTO issued us a new method of use patent relating to the safe and effective use of Xyrem by decreasing the dose of Xyrem when used concomitantly with divalproex sodium. In June 2015, the USPTO issued us another new method of use patent relating to decreasing the dose of Xyrem when used concomitantly with divalproex sodium. Both of these patents have been listed in the Orange Book. We have filed lawsuits against each of the Xyrem ANDA filers alleging infringement of these patents and seeking a permanent injunction to prevent these Xyrem ANDA filers from introducing a generic version of Xyrem that would infringe these patents. In April 2015, Roxane moved to dismiss claims involving the July

2014 patent on the grounds that it does not cover patentable subject matter. In October 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of IPR proceedings before the PTAB relating to the patent that was the subject of Roxane's motion. While we believe the additional safety information is critical for the safe use of Xyrem and should be required to be included in the label for any proposed generic form of Xyrem, we do not know whether the FDA will require any proposed generic form of Xyrem to include this information in its product label or whether we will be successful in maintaining the validity of the applicable patents and protecting the patents from infringement.

We also own method of use patents and trade secrets that cover elements of the Xyrem REMS, including patents that cover the use of a single central pharmacy to distribute Xyrem. The Xyrem REMS approval notice includes statements from the FDA that (i) the approval action should not be construed or understood as agreement with us that dispensing through a single pharmacy is the only way to ensure that the benefits of Xyrem outweigh its risks, and that the FDA has continuing concerns that limiting the distribution of Xyrem to one pharmacy imposes burdens on patient access and the healthcare delivery system and (ii) as with all REMS, the FDA intends to evaluate the Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. We cannot predict whether the FDA will seek to require or ultimately require modifications to the Xyrem REMS, including with respect to the Xyrem distribution system, or seek to otherwise impose or ultimately impose additional requirements to the Xyrem REMS, or the potential timing, terms or propriety thereof. Any such modifications or additional requirements could potentially make it easier for future generic competitors, make it more difficult or expensive for us to distribute Xyrem and/or negatively affect sales of Xyrem. In particular, depending on the nature of any such modifications or additional requirements, the ability of our existing patents to protect our Xyrem distribution system from generic competitors may be reduced. In addition, the extent of protection provided by our method of use patents covering the distribution of Xyrem depends on the nature of the distribution system that may be used by any generic competitor, including whether the distribution system is as restricted as the distribution system set forth in the Xyrem REMS. If a generic competitor is able to obtain ANDA approval for a generic version of Xyrem based on a REMS that does not fall within the scope of any of the claims of our distribution patents, those patents will not be a barrier to the generic version's entry into the market. We cannot be certain whether our existing distribution patents or patents that may be granted in the future will be construed to cover any generic REMS or risk management plan that might be approved by the FDA. The interpretation of intellectual property protections and the effect of these protections are extremely complex, and we cannot predict the impact of any of these matters on our business.

Risks Related to Our Industry

The regulatory approval process is expensive, time-consuming and uncertain and may prevent us or our partners from obtaining approvals for the commercialization of some or all of our product candidates.

The manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, sale, distribution, record keeping, importing and exporting of our products and our research and development activities are subject to extensive regulation by the FDA, the EC the competent authorities of the EU member states and other regulatory authorities. Regulations differ from country to country. As a result of these regulations, product development, approval and commercialization processes are expensive and time-consuming. For example, we are not permitted to market a pharmaceutical product in the U.S. or in the EU member states until we receive approval from the FDA, the EC or the competent authorities of the EU member states, as applicable. An application for marketing approval must contain information demonstrating the quality, safety and efficacy of the pharmaceutical product, including data from preclinical and clinical trials, information pertaining to the preparation and manufacture of the active pharmaceutical ingredient, analytical methods, product formulation, details on the manufacture and stability of the finished pharmaceutical product and proposed product packaging and labeling. Submission of an application for marketing authorization does not assure approval for marketing in any jurisdiction, and we may encounter significant difficulties or costs in our efforts to obtain approval to market products. If we are unable to obtain regulatory approval of our product candidates, we will not be able to commercialize them and recoup our research and development costs. Any delay or failure in obtaining approval of a drug candidate, or receipt of approval for narrower indications than sought, can have a negative impact on our financial performance.

If the FDA, the EC or the competent authorities of the EU member states determine that a REMS or the imposition of post-marketing obligations is necessary to ensure that the benefits of the drug outweigh the risks, we may be required to include a proposed REMS as part of an NDA or BLA or to propose post-marketing obligations to be included in the marketing authorization for our products in the EU. We may also be required to include a patient package insert or a medication guide to provide information to consumers about the product's risks and benefits, a plan for communication to healthcare providers, and restrictions on the product's distribution. For example, the FDA requires a REMS for Xyrem, discussed in detail in the risk factor under the heading "*The manufacture, distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy, and these restrictions and requirements, as well*

as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem" in Part I, Item 1A of this Annual Report on Form 10-K , and other products that we sell are or may become subject to a REMS specific to our product or shared with other products in the same class of drug. We cannot predict the impact that any new REMS requirements applicable to any of our products would have on our business.

As another example, the marketing authorization in the EU for Defitelio requires us to comply with a number of post-marketing obligations, including obligations relating to the establishment of a patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use. If we fail to meet the post-marketing obligations imposed as part of the marketing authorization for Defitelio or if it is determined that the balance of risks and benefits of using Defitelio changes materially, the EMA could propose to the EC that the marketing authorization for Defitelio be varied, suspended or withdrawn.

Changes in healthcare law and implementing regulations, including those based on recently enacted legislation, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and these changes could have a material adverse effect on our business and financial condition.

The Healthcare Reform Act is a sweeping measure intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. This law substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, benefits for patients within a coverage gap in the Medicare Part D prescription drug program (commonly known as the "donut hole"), rules regarding prescription drug benefits under the health insurance exchanges, changes to the Medicaid Drug Rebate program, expansion of the Public Health Service's 340B drug pricing discount program, fraud and abuse and enforcement. These changes will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.

Details of the changes to the Medicaid Drug Rebate program and the 340B program are discussed in the risk factor under the heading "*If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in Part I, Item 1A of this Annual Report on Form 10-K. Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate program. The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program has and will continue to increase our costs and the complexity of compliance, has been and will be time-consuming, and could have a material adverse effect on our results of operations.

Some states have elected not to expand their Medicaid programs by raising the income limit to 133% of the federal poverty level, as is permitted under the Healthcare Reform Act. For each state that does not choose to expand its Medicaid program, there may be fewer insured patients overall, which could impact our sales, business and financial condition. Where Medicaid patients receive insurance coverage under any of the new options made available through the Healthcare Reform Act, the possibility exists that manufacturers may be required to pay Medicaid rebates on drugs used under these circumstances, a decision that could impact manufacturer revenues. In addition, the federal government has also announced delays in the implementation of key provisions of the Healthcare Reform Act, including the employer mandate. The implications of these delays for our sales, business and financial condition, if any, are not yet clear.

Moreover, legislative changes to the Healthcare Reform Act remain possible. We expect that the Healthcare Reform Act, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of our existing products or to successfully commercialize our product candidates, if approved.

In addition to the Healthcare Reform Act, there will continue to be proposals by legislators at both the federal and state levels, regulators and third party payors to keep healthcare costs down while expanding individual healthcare benefits. Likewise, in the countries in the EU, legislators, policymakers and healthcare insurance funds continue to propose and implement cost-containing measures to keep healthcare costs down, due in part to the attention being paid to healthcare cost containment and other austerity measures in the EU. Certain of these changes could impose limitations on the prices we will be able to charge for our products and any approved product candidates or the amounts of reimbursement available for these products from governmental agencies or third party payors, may increase the tax obligations on pharmaceutical companies such as ours, or may facilitate the introduction of generic competition with respect to our products. Further, an increasing number of EU member states and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere. In addition, the ongoing budgetary

difficulties faced by a number of EU member states, including Greece and Spain, have led and may continue to lead to substantial delays in payment and payment partially with government bonds rather than cash for medicinal drug products, which could negatively impact our revenues and profitability. Moreover, in order to obtain reimbursement for our products in some countries, including some EU member states, we may be required to conduct clinical trials that compare the cost-effectiveness of our products to other available therapies. There can be no assurance that our products will obtain favorable reimbursement status in any country.

To help patients afford our products, we have various programs to assist them, including patient assistance programs, a Xyrem free product voucher program and co-pay coupon programs for Xyrem and certain other products. Additionally, we make grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations. Co-pay coupon programs, including our program for Xyrem, have received some negative publicity related to their use to promote branded pharmaceutical products over other less costly alternatives. In recent years, other pharmaceutical manufacturers were named in class action lawsuits challenging the legality of their co-pay programs under a variety of federal and state laws. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar lawsuits or insurer actions. In addition, in November 2013, CMS issued guidance to the issuers of qualified health plans sold through the Healthcare Reform Act's marketplaces encouraging such plans to reject patient cost-sharing support from third parties and indicating that CMS intends to monitor the provision of such support and may take regulatory action to limit it in the future. In September 2014, the OIG of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Medicare Part D beneficiaries from using co-pay coupons. In 2015, the OIG refined existing guidance with respect to manufacturer grants to independent charitable foundations that provide financial support to financially needy patients, and has issued new or revised advisory opinions containing updated guidance on the government's view of such programs. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, including Xyrem, and therefore could have a material adverse effect on our sales, business and financial condition.

We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products.

Oversight by FDA and Equivalent Non-U.S. Regulatory Authorities

We are subject to significant ongoing regulatory obligations with respect to our marketed products, such as safety reporting requirements and additional post-marketing obligations, including regulatory oversight of the promotion and marketing of our products. In addition, research, testing, manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, sale, distribution, record keeping, importing and exporting of our products are, and any of our product candidates that may be approved by the FDA, the EC, the competent authorities of the EU member states and other non-U.S. regulatory authorities will be, subject to extensive and ongoing regulatory requirements. These requirements apply both to us and to third parties we contract with to perform services and supply us with products. Failure by us or any of our third party partners, including suppliers, distributors and our respective central pharmacies for Xyrem and for Prialt, to comply with applicable requirements could subject us to administrative or judicial sanctions or other negative consequences, such as delays in approval or refusal to approve a product candidate, withdrawal, suspension or variation of product approval, untitled letters, warning letters, fines and other monetary penalties, unanticipated expenditures, product recall, withdrawal or seizure, total or partial suspension of production or distribution, interruption of manufacturing or clinical trials, operating restrictions, injunctions; suspension of licenses, civil penalties and/or criminal prosecution, any of which could have a significant impact on our sales, business and financial condition.

We monitor adverse events resulting from the use of our commercial products, as do the regulatory authorities, and we file periodic reports with the authorities concerning adverse events. The authorities review these events and reports, and if they determine that any events and/or reports indicate a trend or signal, they can require a change in a product label, restrict sales and marketing and/or require or conduct other actions, potentially including withdrawal or suspension of the product from the market, any of which could result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The FDA and the EMA's Pharmacovigilance Risk Assessment Committee, or the PRAC, also periodically inspects the company records related to safety reporting. Following such inspections, the FDA may issue notices on Form FDA 483 and warning letters that could cause us to modify certain activities. The PRAC may propose to the Committee on Human medicinal Products, or the CHMP, that the marketing authorization holder be required to take specific steps or advise that the existing marketing authorization be varied, suspended, or withdrawn. A Form FDA 483 notice, if issued at the conclusion of an FDA inspection, can list conditions the FDA investigators believe may have violated relevant FDA regulations or guidance. Failure

to adequately and promptly correct the observation(s) can result in further regulatory enforcement action. For example, in April 2014, we received a Form FDA 483 at the conclusion of a pharmacovigilance inspection conducted by the FDA. The Form FDA 483 included observations relating to certain aspects of our adverse drug experience, or ADE, reporting system for all of our products, including Xyrem. We responded to the Form FDA 483 with a description of the corrective actions and improvements we had implemented before or shortly following the inspection and additional improvements that we planned to implement, and have now implemented, to address the observations in the Form FDA 483. In August 2014, the FDA issued an Establishment Inspection Report to us, which indicates that the inspection is closed. Although we have implemented improvements to our ADE reporting system, there can be no assurance that the FDA or other regulatory agencies will not identify additional matters in future pharmacovigilance inspections or that we will be able to adequately address any matters identified by the FDA or other regulatory agencies in the future, and the failure to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If we receive regulatory approvals to sell our products, the FDA, the EC, the competent authorities of the EU member states and other non-U.S. regulatory authorities where our products are approved may impose significant restrictions on the indicated uses or marketing of our products, or impose requirements for burdensome post-approval study commitments. The terms of any product approval, including labeling, may be more restrictive than we desire and could affect the commercial potential of the product. If we become aware of problems with any of our products in the U.S., the EU or elsewhere in the world or at our third party suppliers' facilities, a regulatory agency may impose restrictions on our products, our suppliers, our other partners or us. In such an instance, we could experience a significant drop in the sales of the affected products, our product revenues and reputation in the marketplace may suffer, and we could become the target of lawsuits. For example, in April 2015, Medtronic Inc., or Medtronic, announced a consent decree with the FDA related to Medtronic's SynchroMed® II implantable infusion pump systems. Our product Prialt is approved for administration to patients via that pump. While the Medtronic consent decree does not impact existing patients with the pump, physicians who want to implant the pump in new patients are required to complete a certification process to document medical necessity. While the approved indication for Prialt is one of the conditions eligible to support a showing of medical necessity provided by the consent decree, we cannot predict the impact of this new certification requirement on sales of Prialt.

The EU has adopted new legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, and this new legislation enhanced the authority of the EMA and the competent authorities of the EU member states to require companies to conduct additional post-approval clinical efficacy and safety studies and increased the burden on companies with respect to additional monitoring, adverse event management and reporting. Under the legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

The FDA approved the BLA for Erwinaze in the U.S. in November 2011, subject to certain post-marketing requirements, which have been completed, and compliance with multiple post-marketing commitments, including certain commitments that must be met by the product's manufacturer with respect to product manufacturing, which are outside of our control. While activities are underway to complete the post-marketing commitments, any inability to comply with regulatory requirements, including compliance with manufacturing-related post-marketing commitments that are part of the BLA approval, as well as other requirements monitored by the FDA, could adversely affect Erwinaze supply and could result in FDA approval being revoked or product recalls, either of which could have a material adverse effect on our sales of and revenues from Erwinaze and limit our potential future maintenance and growth of the market for this product.

The marketing authorization in the EU for Defitelio requires us to comply with a number of post-marketing obligations. These include obligations relating to the establishment of a patient registry. We may be unable to comply with this or other post-marketing obligations imposed as part of the marketing authorization for Defitelio. Failure to comply with these requirements may lead to the suspension, variation or withdrawal of the marketing authorization for Defitelio in the EU.

Erwinase and defibrotide are available on a named patient basis in many countries where they are not commercially available. While we believe we have satisfied the regulations regarding our communications and medical affairs activities in those countries, if any such country's regulatory authorities determine that we are promoting Erwinase or defibrotide without proper authorization, we could be found to be in violation of pharmaceutical advertising law or the regulations permitting sales under named patient programs. In that case, we may be subject to financial or other penalties.

The FDA, the competent authorities of the EU member states and other governmental authorities require advertising and promotional labeling to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. The FDA routinely provides its interpretations of that authority in informal communications and also in more formal communications such as untitled letters or warning letters, and although

such communications may not be considered final agency decisions, companies may decide not to contest the agency's interpretations so as to avoid disputes with the FDA, even if they believe the claims to be truthful, not misleading and otherwise lawful.

The FDA, the competent authorities of the EU member states and other governmental authorities also actively investigate allegations of off-label promotion activities in order to enforce regulations prohibiting these types of activities. A company that is found to have promoted an approved product for off-label uses may be subject to significant liability, including civil and administrative financial penalties and other remedies as well as criminal financial penalties and other sanctions. Even when a company is not determined to have engaged in off-label promotion, the allegation from government authorities or market participants that a company has engaged in such activities could have a significant impact on the company's sales, business and financial condition. The U.S. government has also required companies to enter into complex corporate integrity agreements and/or non-prosecution agreements that impose significant reporting and other burdens on the affected companies. For all of our products, it is important that we maintain a comprehensive compliance program. Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could subject us to a range of regulatory actions that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

Other Regulatory Authorities

We are also subject to regulation by other regional, national, state and local agencies, including the DEA, the DOJ, the FTC, the DOC, the OIG and other regulatory bodies, as well as governmental authorities in those non-U.S. countries in which we commercialize our products. In addition to the FDCA, other federal, state and non-U.S. statutes and regulations govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including preclinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information, promotion, marketing, and pricing to government purchasers and government healthcare programs. Our partners, including our suppliers and distributors and the central pharmacy for Xyrem, are subject to many of the same requirements.

These requirements include obtaining sufficient quotas from the DEA each year to manufacture sodium oxybate and Xyrem in the U.S. In addition to quota requirements, the DEA imposes various registration, importing, exporting, record keeping and reporting requirements, labeling and packaging requirements, security controls and a restriction on prescription refills on certain pharmaceutical products under the CSA. The states also impose similar requirements for handling controlled substances. The U.S. and the EU member states are parties to the Convention on Psychotropic Substances (1971), or the 1971 Convention. In October 2012, the World Health Organization sent a recommendation to the United Nations Commission on Narcotic Drugs, or CND, to reschedule GHB under the 1971 Convention from Schedule IV status to Schedule II status. In March 2013, the CND voted to reschedule GHB from Schedule IV to Schedule II under the 1971 Convention. While the DEA imposes its own scheduling requirements in the U.S. under the CSA, the U.S. is obligated as a signatory to the 1971 Convention to ensure that drug scheduling in the U.S. is consistent with its obligations under the international treaties. The change in international scheduling did not result in a change in the U.S. control of GHB. Failure by us or any of our partners, including suppliers and distributors, to comply with the requirements of the CSA and other regulatory bodies could result in, among other things, additional operating costs to us, delays in shipments outside or into the U.S. and adverse regulatory actions.

The U.S. federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Liability may be established without a person or entity having actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. The Healthcare Reform Act amended the Social Security Act to provide 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 federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common manufacturer business arrangements and activities from prosecution and administrative sanction, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations of our products may be subject to scrutiny if they do not qualify for an exemption or safe harbor. We seek to comply with the exemptions and safe harbors whenever possible, but our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability, and therefore would be subject to a facts and circumstances analysis.

The False Claims Act prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of federal funds, or knowingly making, or causing to be made, a false statement to get a false claim paid. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf

of the federal government alleging violations of the statute and to share in any monetary recovery. Many pharmaceutical and other healthcare companies have been investigated or subject to lawsuits by whistleblowers and have reached substantial financial settlements with the federal government under the False Claims Act for a variety of alleged improper marketing activities, including providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees, grants, free travel, and other benefits to physicians to induce them to prescribe the company's products; and inflating prices reported to private price publication services, which are used to set drug reimbursement rates under government healthcare programs. In addition, in recent years the government and private whistleblowers have pursued False Claims Act cases against a number of pharmaceutical companies for causing false claims to be submitted as a result of the marketing of their products for unapproved uses. Pharmaceutical and other healthcare companies also are subject to other federal false claim laws, including federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

In addition, the Sunshine provisions require extensive tracking of payments and transfers of value to physicians and teaching hospitals and public reporting of the data collected. On September 30, 2014, CMS published the first set of data collected under the Sunshine provisions. On or before the 90th day of each calendar year starting in 2015, manufacturers covered under the Sunshine provisions are required to submit a report disclosing payments and transfers of value made in the preceding calendar year, and CMS then will publish the reported data on or before June 30 of the reporting year. It is widely anticipated that public reporting under the Sunshine provisions will result in increased scrutiny of the financial relationships between industry, teaching hospitals and physicians, and such scrutiny may negatively impact our ability to engage with physicians on matters of importance to us. In addition, if the data reflected in our reports are found to be in violation of any of the Sunshine provisions or any other U.S. federal, state or local laws or regulations that may apply, we may be subject to significant civil, criminal and administrative penalties, damages or fines.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. A number of states require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states restrict when pharmaceutical companies may provide meals to prescribers or engage in other marketing related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Massachusetts and Nevada require pharmaceutical companies to implement compliance programs or marketing codes of conduct. Outside the U.S., we are subject to similar regulations in those countries where we market and sell products.

In the EU, the advertising and promotion of our products are subject to EU member states' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

Interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct in the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of the EU member states. One example is the U.K. Bribery Act. As further discussed below, the U.K. Bribery Act applies to any company incorporated in or "carrying on business" in the U.K., irrespective of where in the world the alleged bribery activity occurs, which could have implications for our interactions with physicians both in and outside of the U.K. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states require that payments made to physicians must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her competent professional organization, and/or the competent authorities of the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Our business activities outside of the U.S. 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 U.K. Bribery Act. The FCPA and similar anti-

corruption laws generally prohibit the 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 both U.K. and non-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, in another country 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 having in place adequate procedures designed to prevent bribery is an available defense. 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, our dealings with these prescribers and purchasers may be subject to regulation under the FCPA. Recently the U.S. Securities and Exchange Commission, or SEC, and the DOJ 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 suppliers 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.

We are also subject to laws and regulations covering data privacy and the protection of health-related and other personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which may affect our business. Numerous federal and state laws and regulations, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of personal information. Failure to comply with such laws and regulations, could create liability for us (including the imposition of significant penalties), result in adverse publicity and negatively affect our business. In addition, healthcare providers who prescribe our products and research institutions we collaborate with are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA other than with respect to providing certain employee benefits, we could potentially be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In addition, EU member states and other jurisdictions where we operate have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the EU Data Protection Directive, as implemented into national laws by the EU member states, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. The EU Data Protection Directive prohibits the transfer of personal data to countries outside of the European Economic Area, or EEA, such as the U.S., which are not considered by the EC to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Although there are legal mechanisms to allow for the transfer of personal data from the EEA and Switzerland to the U.S., a recent decision of the European Court of Justice that invalidated the safe harbor framework on which we have relied has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it will no longer be possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the EU to entities in the U.S. In addition, data protection authorities from the different EU member states may interpret the EU Data Protection Directive and national laws differently, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU. If we or our vendors fail to comply with applicable data privacy laws, or if the legal mechanisms we or our vendors rely upon to allow for the transfer of personal data from the EEA or Switzerland to the U.S. (or other countries not considered by the EC to provide an adequate level of data protection) are not considered adequate, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted if our ability to transfer personal data outside of the EEA or Switzerland is restricted, which could adversely impact our operating results. In December 2015, a proposal for an EU General Data Protection Regulation, intended to replace the current EU Data Protection Directive, was agreed between the European Parliament, the Council of the European Union and the European Commission. The EU General Data Protection Regulation, which will be officially adopted in early 2016, will introduce new data protection requirements in the EU, as well as substantial fines for breaches of the data protection rules. The EU General Data Protection Regulation, which will be applicable two years after the date of its publication in the Official Journal for the European Union, will increase

our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules.

The number and complexity of both U.S. federal and state laws continue to increase, and additional governmental resources are being added to enforce these laws and to prosecute companies and individuals who are believed to be violating them. In addition, we expect private plaintiffs to continue to file lawsuits against pharmaceutical manufacturers under the whistleblower provisions of the False Claims Act and state equivalents and to seek out new theories of liability under those statutes. We also expect government enforcement agencies to continue to "intervene" in private whistleblower lawsuits, effectively converting the private lawsuit into a lawsuit by the government, which typically increases the likelihood that the lawsuit will result in increased expense for the company and/or a burdensome settlement. For example, federal enforcement agencies recently have shown interest in pharmaceutical companies' product and patient assistance programs, including manufacturer reimbursement support services and relationships with specialty pharmacies. Some of these investigations have resulted in government enforcement authorities intervening in related whistleblower lawsuits and obtaining significant civil and criminal settlements. Other private whistleblowers have proceeded without government invention, causing considerable expense to targeted companies.

Recent changes in the law have reinforced and facilitated these trends. In particular, the Healthcare Reform Act includes a number of provisions aimed at strengthening the government's ability to pursue anti-kickback and false claims cases against pharmaceutical manufacturers and other healthcare entities, including substantially increased funding for healthcare fraud enforcement activities, enhanced investigative powers, and amendments to the False Claims Act that make it easier for the government and whistleblowers to pursue cases for alleged kickback and false claim violations, such as defining a "false" claim to include any claim based on a violation of the anti-kickback statute. While we cannot say with certainty what effect these changes have had or will have on our business, we anticipate that increased enforcement and litigation, including through government intervention in whistleblower lawsuits and private whistleblowers proceeding on their own, will continue for the foreseeable future. Responding to a whistleblower lawsuit, government investigation or enforcement action, defending any claims raised, and paying any resulting fines, damages, penalties or settlement amounts would be expensive and time-consuming, and could have a material adverse effect on our reputation, business, financial condition, results of operations and growth prospects.

Compliance with U.S. federal and state, EU and EU member state national laws that apply to pharmaceutical manufacturers is difficult and time-consuming, and companies that violate these laws may face substantial penalties. The potential sanctions include civil monetary penalties, exclusion of a company's products from reimbursement under government programs, criminal fines and imprisonment. Because of the breadth of these laws and, in some cases, the lack of extensive legal guidance in the form of regulations or court decisions, it is possible that some of our business activities could be subject to challenge under one or more of these laws. For example, the FTC has been paying increasing attention to the use of REMS by companies selling branded products, in particular to whether REMS may be being deliberately used to reduce the risk of competition from generic drugs in a way that may be deemed to be anticompetitive. It is possible that the FTC, other governmental authorities or others could claim or determine that we are using the Xyrem REMS in an anticompetitive manner (including in light of the FDA's statement in the Xyrem REMS approval notice that the Xyrem REMS could be used in an anticompetitive manner inconsistent with applicable provisions of the FDCA) or have engaged in other anticompetitive practices. The FDCA further states that a REMS shall not be used by an NDA holder to block or delay generic drugs from entering the market. Several of the ANDA applicants have asserted that our patents covering the distribution system for Xyrem should not have been listed in the Orange Book, and that the Xyrem REMS is blocking competition. We cannot predict the outcome of these claims in the ongoing litigation, or the impact of any similar claims that may be made in the future. Such a challenge or any other challenge that we or our business partners have failed to comply with applicable laws and regulations could have a material adverse effect on our business, financial condition, results of operations and growth prospects. If we or the other parties with whom we work fail to comply with applicable regulatory requirements, we or they could be subject to a range of regulatory actions that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business.

We manufacture certain active pharmaceutical ingredients, including the defibrotide drug substance, at our manufacturing facilities in Italy. In addition, we have engaged a third party supplier to process defibrotide into the finished product in Italy. Our manufacturing facilities and those of our third party manufacturer are subject to continuing regulation by the Italian Health Authority and other Italian regulatory authorities with respect to the manufacturing of active pharmaceutical ingredients and drug products, including the defibrotide drug substance and its finished form. These facilities are also subject to inspection and regulation by the EMA. Also, part of the process to obtain approval for defibrotide is to pass a pre-approval inspection by the EMA, Italian Health Authority and the FDA to ensure that these facilities are in compliance with cGMP. Following initial approval in a jurisdiction, the applicable authorities will continue to inspect our manufacturing facilities and those of our third party supplier, in some cases, unannounced, to confirm ongoing compliance with cGMP. The cGMP requirements govern

quality control of the manufacturing process and documentation policies and procedures, and we and our third party suppliers will need to ensure that all of our processes, methods and equipment are compliant with cGMP. If these authorities determine that either our facilities or our third party supplier's facility in Italy do not meet the standards of compliance required under applicable regulations, they may deny approval to manufacture our products, require us to stop manufacturing our products, deny approval to the sale of our products or suspend the sale of our products.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in and have certain price reporting obligations to the Medicaid Drug Rebate program, several state Medicaid supplemental rebate programs and other governmental pricing programs, and we have obligations to report average sales price under the Medicare program.

Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Such data previously have not been submitted for Quadramet® (samarium sm 153 lexidronam injection) and ProstaScint® (capromab pendetide), which are radiopharmaceutical products. We engaged in interactions with CMS and a trade group, the Council on Radionuclides and Radiopharmaceuticals, or CORAR, regarding the reporting of Medicaid pricing data and paying Medicaid rebates for radiopharmaceutical products. In addition to the discussions with CMS as part of CORAR, we have had separate discussions with CMS directly regarding Quadramet. We sold Quadramet to a third party in December 2013, but we retained any liabilities related to sales of the product during prior periods. Similarly, we sold ProstaScint to a third party in May 2015, but we retained any liabilities related to sales of the product during prior periods. We are currently unable to predict whether price reporting and rebates will be required for Quadramet and ProstaScint and, if so, for what period they will be required. We are currently unable to reasonably estimate an amount or range of a potential contingent loss related to the payment of rebates for Quadramet or ProstaScint. Any material liability resulting from radiopharmaceutical price reporting and rebates would negatively impact our financial results.

The Healthcare Reform Act made significant changes to the Medicaid Drug Rebate program, such as expanding rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well and changing the definition of average manufacturer price. The Healthcare Reform Act also increased the minimum Medicaid rebate; changed the calculation of the rebate for certain innovator products that qualify as line extensions of existing drugs; and capped the total rebate amount for innovator drugs at 100% of the average manufacturer price. Finally, the Healthcare Reform Act requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government.

In January 2016, CMS issued a final rule to implement the changes to the Medicaid rebate program under the Healthcare Reform Act, and we are evaluating the impact of the final rule. We do not currently expect any material change to our calculations under the Medicaid rebate program or our 340B liability based on the recently released final rule. However, our business could be adversely affected if and to the extent our implementation of the final rule impacts our calculations under the Medicaid rebate program or our 340B liability, or if CMS challenges the approach we take in our implementation of the final rule. In addition, Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate program. The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program has and will continue to increase our costs and the complexity of compliance, has been and will be time-consuming, and could have a material adverse effect on our results of operations.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B drug pricing discount program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B pricing program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The Healthcare Reform Act expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and

rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program. In January 2016, CMS issued a final rule to implement the changes to the Medicaid rebate program under the Healthcare Reform Act, and we are evaluating the impact of the final rule. We do not currently expect any material change to our calculations under the Medicaid rebate program or our 340B liability based on the recently released final rule. However, our business could be adversely affected if and to the extent our implementation of the final rule impacts our calculations under the Medicaid rebate program or our 340B liability, or if CMS challenges the approach we take in our implementation of the final rule. For example, the initiation of any reporting of Medicaid pricing data for ProstaScint and Quadramet could result in retroactive 340B ceiling price liability for these two products. We are currently unable to reasonably estimate an amount or range of a contingent loss. Any material liability resulting from radiopharmaceutical price reporting would negatively impact our financial results. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the Healthcare Reform Act could affect our 340B ceiling price calculations and negatively impact our results of operations.

The Healthcare Reform Act obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340B program and to update the agreement that manufacturers must sign to participate in the 340B program to obligate a manufacturer to offer the 340B price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. HRSA recently issued a proposed regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, as well as proposed omnibus guidance that addresses many aspects of the 340B program, including a proposed expansion of manufacturer record keeping requirements and 340B ceiling price restatement and refund obligations. HRSA is currently expected to issue additional proposed regulations in 2016. Any final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Federal law also requires that a company that participates in the Medicaid Drug Rebate program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Statutory or regulatory changes or CMS binding guidance could affect the average sales price calculations for our products and the resulting Medicare payment rate, and could negatively impact our results of operations.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B drug discount program.

Civil monetary penalties can be applied if we are found to have knowingly submitted any false price information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we participate in the VA, FSS pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory FCP to four federal agencies (VA, U.S. Department of Defense, DoD, Public Health Service, and U.S. Coast Guard). The FCP is based on the Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to penalties of $100,000 for each item of false information. These obligations also contain extensive disclosure and certification requirements.

We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our covered products on a Tricare Agreement in order for these products to be eligible for DoD formulary inclusion.

If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations.

Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Price approvals and reimbursement may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably.

In both U.S. and non-U.S. markets, our ability to commercialize our products successfully, and to attract commercialization partners for our products, depends in significant part on the availability of adequate financial coverage and reimbursement from third party payors, including, in the U.S., governmental payors such as the Medicare and Medicaid programs, managed care organizations and private health insurers. In many countries, price approvals must be obtained before products can be placed on the market or submitted for reimbursement. Third party payors, including government payors, decide which drugs can be reimbursed and establish reimbursement and co-pay levels and conditions for reimbursement. Third party payors are increasingly challenging the prices charged for medical products and services and examining their cost effectiveness, in addition to their safety and efficacy. In some cases, for example, third party payors try to encourage the use of less expensive generic products through their prescription benefits coverage and reimbursement and co-pay policies. We may need to conduct expensive pharmacoeconomic and/or clinical studies in order to demonstrate the cost-effectiveness of our products. Even with such studies, our products may be considered less safe, less effective or less cost-effective than other products, and third party payors may not provide and maintain price approvals, coverage and reimbursement for our products or any of our product candidates that we commercialize, in whole or in part.

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably. We anticipate that the U.S. Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies and reforms intended to curb healthcare costs, particularly given the current atmosphere of mounting criticism of prescription costs in the U.S. These cost containment measures may include controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government health care programs; pharmaceutical cost transparency bills that aim to require drug companies to justify their prices; controls on healthcare providers; challenges to the pricing of drugs, or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; changes in drug importation laws; expansion of use of managed care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person; and public funding for cost effectiveness research, which may be used by government and private third party payors to make coverage and payment decisions. Drug pricing by pharmaceutical companies has recently come under close scrutiny, particularly with respect to companies that have increased the price of products after acquiring those products from other companies. For example, in late 2015 the U.S. House of Representatives formed an Affordable Drug Pricing Task Force to advance legislation intended to control pharmaceutical drug costs and investigate pharmaceutical drug pricing. Since then, both the U.S. House of Representatives and the U.S. Senate have conducted numerous hearings with respect to pharmaceutical drug pricing practices, including in connection with the investigation of specific price increases by several pharmaceutical companies. If we become the subject of government investigation with respect to our drug pricing or other business practices, we could incur significant expense and could be distracted from execution of our strategy. Any such investigation could also result in reduced market acceptance and demand for our products, could harm our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. If healthcare policies or reforms intended to curb healthcare costs are adopted or if we experience negative publicity with respect to pricing of our products or the pricing of pharmaceutical drugs generally, the prices that we charge for our products, including Xyrem, may be limited, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted.

In addition, much attention has been paid to legislation proposing federal rebates on Medicare Part D and Medicare Advantage utilization for drugs issued to certain groups of lower income beneficiaries and the desire to change the provisions that treat these dual-eligible patients differently from traditional Medicare patients. Any such changes could have a negative impact on revenues from sales of our products.

Further, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2025. These cuts reduce reimbursement payments related to our products, which could potentially negatively impact our revenue.

Third party payors' practices may affect the conditions required for reimbursement and the availability of reimbursement for our products, including Xyrem and Defitelio. Our business could be materially harmed if the Medicaid program, Medicare program or other third party payors in the U.S. or elsewhere were to deny reimbursement for our products, limit the indications for which our products will be reimbursed, or provide reimbursement only on unfavorable terms. This risk is particularly

significant with respect to Xyrem in the U.S. and to Defitelio in Europe, in part due to payor sensitivity to the price of these products. Third party payors often require prior authorization for, require reauthorization for continuation of, or refuse to provide reimbursement for our products, and others may do so in the future. As a result of such practices, patients may not be able to obtain prescribed medications due to an inability to afford the medication. For example, we are experiencing increasingly restrictive conditions for reimbursement required by some third party payors for Xyrem, which may have a material effect on the overall level of reimbursement coverage for Xyrem. In addition, increases in reimbursement-related activities have extended the time required to fill prescriptions and could continue to do so in the future. Further, increasing consolidation among third party payors has led to fewer and larger third party payors with increased negotiating power. In particular, a small number of third party payors cover a significant portion of Xyrem patients. We have experienced and expect to continue to experience increasing pressure from third party payors to agree to discounts, rebates or other restrictive pricing terms for Xyrem. If we are unsuccessful in maintaining reimbursement for our products in a timely manner and at acceptable levels, if reimbursement for our products by third party payors is subject to restrictive pricing terms or overly restrictive reimbursement conditions, or if third party payors limit the indications for which our products will be reimbursed or refuse to provide reimbursement, the level of reimbursement for our products would be negatively impacted, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In many countries, procedures to obtain price approvals, coverage and reimbursement can take considerable time after the receipt of marketing approval. We launched Defitelio in certain European countries in 2014 and continued to launch in additional European countries on a rolling basis through 2015. We are in the process of making pricing and reimbursement submissions with respect to Defitelio in those European countries where Defitelio is not yet launched, including in countries where pricing and reimbursement approvals are required for launch. We cannot predict the timing of Defitelio's launch in countries where we are engaged in pricing and reimbursement submissions. If we experience delays or unforeseen difficulties in obtaining favorable pricing and reimbursement approvals, planned launches in the affected countries would be delayed, or, if we are unable to ultimately obtain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country's reimbursed price influences other countries, our growth prospects in Europe could be negatively affected. For more information, see the risk factor under the heading "*We may not be able to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval of defibrotide in other countries, including the U.S., which could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in Part I, Item 1A of this Annual Report on Form 10-K.

We cannot predict actions third party payors may take, or whether they will limit the price approvals, coverage and level of reimbursement for our products or refuse to provide and maintain any approvals or coverage at all. For example, because some of our products compete in a market with both branded and generic products, obtaining and maintaining price approvals and reimbursement coverage by government and private payors may be more challenging than for new chemical entities for which no therapeutic alternatives exist. Additionally, in many countries, reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a significant impact on the prescribing physicians' willingness to prescribe our products. For example, the U.S. federal government follows a Medicare severity diagnosis-related group, or MS-DRG, payment system for certain institutional services provided under Medicare, which some states also use for Medicaid. The MS-DRG system entitles a healthcare facility to a fixed reimbursement based on discharge diagnoses rather than actual costs incurred in providing inpatient treatment, thereby increasing the incentive for the facility to limit or control expenditures for many healthcare products. For our products used in the inpatient setting, there may not be sufficient reimbursement under the MS-DRG to fully cover the cost of our products. We cannot be sure that reimbursement amounts, or the lack of reimbursement, will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only at limited levels, we may not be able to effectively commercialize our products.

Third party payors frequently require that drug companies negotiate agreements with them that provide discounts or rebates from list prices or include other restrictive pricing terms. We have experienced increasing pressure from third party payors to agree to discounts, rebates or other restrictive pricing terms for products such as Xyrem. In addition, if our competitors reduce the prices of their products, or otherwise demonstrate that they are better or more cost effective than our products, this may result in a greater level of reimbursement for their products relative to our products, which would reduce our sales and harm our results of operations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Any such requirements could have a negative impact on revenues from sales of our products.

Payors also are increasingly considering new metrics as the basis for reimbursement rates, such as average sales price, average manufacturer price and actual acquisition cost. Certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates. CMS surveys and publishes retail community pharmacy acquisition cost information to provide state Medicaid agencies with a basis of comparison for their own reimbursement and pricing methodologies and rates. It may be difficult to project the impact of these evolving reimbursement mechanics on the

willingness of payors to cover our products. Any failure to cover our products appropriately, in addition to legislative and regulatory changes and others that may occur in the future, could impact our ability to maximize revenues in the federal marketplace. A significant portion of our revenue from sales of Erwinaze is obtained through government payors, including Medicaid, and any failure to qualify for reimbursement for Erwinaze under those programs, including as a result of legislative changes to these programs, would have a material adverse effect on revenues from sales of Erwinaze.

We expect to experience pricing pressure in the U.S. in connection with the sale of our products due to managed healthcare, the increasing influence of health maintenance organizations, additional legislative proposals to curb healthcare costs and negative publicity regarding pricing and price increases generally, which could limit the prices that we charge for our products, including Xyrem, limit our commercial opportunity and/or negatively impact revenues from sales of our products. In various EU member states we expect to be subject to continuous cost-cutting measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed. We have periodically increased the price of Xyrem, most recently in February 2016, and we have made and may in the future make similar price increases on our other products. We cannot assure you that such price adjustments will not negatively affect our ability to secure and maintain reimbursement coverage for our products, which could negatively impact our sales volumes and revenue.

HTA of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states. These EU member states include the United Kingdom, France, Germany, Ireland, Italy, Spain, and Sweden. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products, as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product vary between EU member states and cannot be determined or anticipated in relation to our products at the present time. If we are unable to ultimately obtain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country’s reimbursed price influences other countries, our growth prospects in Europe could be negatively affected.

In the EU, our products are marketed through various channels and within different legal frameworks. In certain EU member states, reimbursement for unauthorized products may be provided through national named patient programs. Such reimbursement may no longer be available if authorization for named patient programs expire or are terminated or when marketing authorization is granted. In other EU member states, authorization and reimbursement policies may also delay commercialization of our products, or may adversely affect our ability to sell our products on a profitable basis. After initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or arbitrage between low-priced and high-priced member states.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted, could negatively affect our growth prospects in Europe.

There also continue to be legislative proposals to amend U.S. laws to allow the importation into the U.S. of prescription drugs, which can be sold at prices that are regulated by the governments of various non-U.S. countries. The potential importation of prescription drugs could pose significant safety concerns for patients, increase the risk of counterfeit products becoming available in the market, and could also have a negative impact on prescription drug prices in the U.S. For example, the potential importation of Xyrem without the safeguard of our Xyrem REMS could harm patients and could also negatively impact Xyrem revenues.

Product liability and product recalls could harm our business.

The development, manufacture, testing, marketing and sale of pharmaceutical products are associated with significant risks of product liability claims or recalls. Side effects or adverse events known or reported to be associated with, or manufacturing defects in, the products sold by us could exacerbate a patient’s condition, or could result in serious injury or impairments or even death. This could result in product liability claims and/or recalls of one or more of our products. Some of our products, including Xyrem and Prialt, have boxed warnings in their labels. In addition, in the EU, Defitelio’s label includes an inverted black triangle that indicates the product is subject to additional monitoring to permit quick identification of new

safety information, as a condition of authorization of Defitelio under “exceptional circumstances.” In many countries, including in EU member states, national laws provide for strict (no-fault) liability which applies even where damages are caused both by a defect in a product and by the act or omission of a third party.

Product liability claims may be brought by individuals seeking relief for themselves or by groups seeking to represent a class of injured patients. Further, third party payors, either individually or as a putative class, may bring actions seeking to recover monies spent on one of our products. The risk of product liability claims may also increase if a company receives a warning letter from a regulatory agency. Product liability claims are an inherent risk in our business, but we cannot predict the frequency, outcome or cost to defend any such claims.

Product liability insurance coverage is expensive, can be difficult to obtain and may not be available in the future on acceptable terms, or at all. Our product liability insurance may not cover all of the future liabilities we might incur in connection with the development, manufacture or sale of our products. In addition, we may not continue to be able to obtain insurance on satisfactory terms or in adequate amounts.

A successful claim or claims brought against us in excess of available insurance coverage could subject us to significant liabilities and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Such claims could also harm our reputation and the reputation of our products, adversely affecting our ability to market our products successfully. In addition, defending a product liability lawsuit is expensive and can divert the attention of key employees from operating our business.

Product recalls may be issued at our discretion or at the discretion of our suppliers, government agencies and other entities that have regulatory authority for pharmaceutical sales. Any recall of our products could materially adversely affect our business by rendering us unable to sell that product for some time and by adversely affecting our reputation. A recall could also result in product liability claims by individuals and third party payors. In addition, product liability claims could result in an investigation of the safety or efficacy of our products, our manufacturing processes and facilities, or our marketing programs conducted by the FDA, the EMA, or the competent authorities of the EU member states. Such investigations could also potentially lead to a recall of our products or more serious enforcement actions, limitations on the indications for which they may be used, or suspension, variation, or withdrawal of approval. Any such regulatory action by the FDA, the EMA or the competent authorities of the EU member states could lead to product liability lawsuits as well.

We use hazardous materials in our manufacturing facilities, and any claims relating to the improper handling, storage, release or disposal of these materials could be time-consuming and expensive.

Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Italy and Ireland where we have manufacturing facilities. Environmental and health and safety authorities in the relevant jurisdictions administer laws, which implement EU directives and regulations governing, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. In certain cases, such laws, directives and regulations may impose strict liability for pollution of the environment and contamination resulting from spills, disposals or other releases of hazardous substances or waste or any migration of such hazardous substances or waste. Costs, damages and/or fines may result from the presence, investigation and remediation of such contamination at properties currently or formerly owned, leased or operated by us or at off-site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination. Our manufacturing activities in Italy and Ireland involve the controlled storage, use and disposal of chemicals and solvents. Our environmental policy is designed to comply with current EU laws and regulations on environmental protection, to provide for continuous improvement of our manufacturing performance, to protect our employees’ health and safety and to respect the safety of people living close to our plant and in the surrounding community. Although we believe that our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by these EU laws and regulations, we cannot completely eliminate the risk of contamination or injury from hazardous materials. If an accident occurs, an injured party could seek to hold us liable for any damages that result and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance on acceptable terms, or at all. We may incur significant costs to comply with current or future EU environmental laws and regulations.

Risks Related to Our Financial Condition

We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position.

As of December 31, 2015, we had total indebtedness of approximately $1.3 billion, which included $740.6 million of outstanding secured indebtedness under a credit agreement that we entered into in June 2015, which we refer to as our credit agreement, and $575.0 million of outstanding indebtedness under our 1.875% exchangeable senior notes due 2021, or the 2021 Notes, which were issued in August 2014. Our debt 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 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;
- result in dilution to our existing shareholders in the event exchanges of our 2021 Notes are settled in our ordinary shares;
- place us at a competitive disadvantage compared to our less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

Our ability to meet our debt service obligations will depend on our future performance, which will be subject to financial, business and other factors affecting our operations, many of which are beyond our control. If we do not have sufficient funds to meet our debt service obligations, we may be required to refinance or restructure all or part of our existing debt, sell assets, borrow more money or sell securities, none of which we can assure you that we would be able to do in a timely manner, or at all.

Covenants in our credit agreement 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.

Our credit agreement provides for a $750.0 million principal amount term loan due in June 2020 and a $750.0 million revolving credit facility, with loans under such revolving credit facility due in June 2020, subject to early mandatory repayments under certain circumstances. Our credit agreement contains various covenants that limit our ability and/or our restricted subsidiaries' ability to, among other things:

- incur or assume liens or additional debt or provide guarantees in respect of obligations of other persons;
- issue redeemable preferred stock;
- pay dividends or distributions or redeem or repurchase capital stock;
- prepay, redeem or repurchase certain debt;
- make loans, investments, acquisitions (including acquisitions of exclusive licenses) and capital expenditures;
- enter into agreements that restrict distributions from our subsidiaries;
- sell assets and capital stock of our subsidiaries;
- enter into certain transactions with affiliates; and
- consolidate or merge with or into, or sell substantially all of our assets to, another person.

Our credit agreement also includes financial covenants that require us to maintain a maximum secured leverage ratio and a minimum interest coverage ratio. Our ability to comply with these financial covenants may be affected by events beyond our control. In addition, the covenants under our credit agreement could restrict our operations, particularly our ability to respond to changes in our business or to take specified actions to take advantage of certain business opportunities that may be presented to us. Our failure to comply with any of the covenants could result in a default under the credit agreement, which could permit the lenders to declare all or part of any outstanding borrowings to be immediately due and payable, or to refuse to permit additional borrowings under the revolving credit facility. A default under our credit agreement could also lead to a default under agreements governing our current or future indebtedness, including the indenture governing our 2021 Notes.

In addition, the holders of our 2021 Notes have the ability to require us to repurchase their notes for cash if we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution, or the delisting of

our ordinary shares from The NASDAQ Global Select Market. Moreover, upon exchange of the 2021 Notes, unless we elect to cause to be delivered solely ordinary shares to settle such exchange, we will be required to make cash payments in respect of the 2021 Notes being exchanged. In this regard, it is our intent and policy to settle the principal amount of the 2021 Notes in cash upon exchange. However, we may not have enough available cash or be able to obtain financing at the time we are required to make any required repurchases of surrendered 2021 Notes or to pay cash upon exchanges of 2021 Notes. Our failure to repurchase 2021 Notes at a time when the repurchase is required by the indenture governing the 2021 Notes or to pay any cash payable on future exchanges of the 2021 Notes as required by the indenture governing the 2021 Notes would constitute a default under that indenture. A default under that indenture could also lead to a default under agreements governing our current or future indebtedness, including our credit agreement. If the repayment of the related indebtedness were to be accelerated, we may not have sufficient funds to repay the related indebtedness, which could have a material adverse effect on our financial condition and our business. In this regard, if we are unable to repay amounts under our credit agreement, the lenders under the credit agreement could proceed against the collateral granted to them to secure that debt, which would seriously harm our business.

We may not be able to generate sufficient cash to service our debt obligations.

Our ability to make payments on and to refinance our debt will depend on our future financial and operating performance, which is subject to prevailing economic and competitive conditions and to certain financial, business and other factors beyond our control. We may be unable to maintain a level of positive cash flows from operating activities sufficient to permit us to pay the principal and interest on our debt.

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay investments and capital expenditures, seek additional capital or restructure or refinance our debt. These alternative measures may not be successful and may not permit us to meet our scheduled debt service obligations. In the absence of such cash flows and resources, we could face substantial liquidity problems and might be required to dispose of material assets or operations to meet our debt service and other obligations. Our credit agreement restricts our ability to dispose of assets, use the proceeds from any disposition of assets and refinance our indebtedness. We may not be able to consummate or obtain proceeds from such dispositions, and any such proceeds may not be adequate to meet any debt service obligations then due.

In addition, our borrowings under our credit agreement are, and are expected to continue to be, at variable rates of interest and expose us to interest rate risk. If interest rates increase, our debt service obligations on the variable rate indebtedness would increase even if the amount borrowed remained the same, and our net income would decrease.

To continue to grow our business, we will need to commit substantial resources, which could result in future losses or otherwise limit our opportunities or affect our ability to operate our business.

The scope of our business and operations has grown substantially since 2012 through a series of transactions, including the Azur Merger, the EUSA Acquisition and the Gentium Acquisition. To continue to grow our business over the longer term, we will need to commit substantial additional resources to in-licensing and/or acquiring new products and product candidates, and to costly and time-consuming product development and clinical trials of our product candidates. We also intend to continue to invest in our commercial operations in an effort to grow sales of our current products. Our future capital requirements will depend on many factors, including many of those discussed above, such as:

- the revenues from our commercial products, which may be affected by many factors, including the extent of generic competition for our products;
- the costs of our commercial operations;
- the costs of integration activities related to any future strategic transactions we may engage in;
- the cost of acquiring and/or in-licensing any new products and product candidates;
- the scope, rate of progress, results and costs of our development and clinical activities;
- the cost and timing of obtaining regulatory approvals and of compliance with laws and regulations;
- the cost of preparing, filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the cost of investigations, litigation and/or settlements related to regulatory oversight and third party claims; and
- changes in laws and regulations, including, for example, healthcare reform legislation.

Our strategy includes the expansion of our business through the acquisition or in-licensing and development of additional marketed products or product candidates that are in late-stage development. We cannot assure you that we will continue to identify attractive opportunities. Even if appropriate opportunities are available, in order to compete successfully to acquire attractive products or product candidates in the current business climate, we may have to pay higher prices for assets than may have been paid historically, and we may not have the financial resources necessary to pursue them. As a result, we may be

unable to expand our business if we do not have sufficient capital or cannot borrow or raise additional capital on attractive terms. In particular, our substantial indebtedness may limit our ability to borrow additional funds for acquisitions or to use our cash flow or obtain additional financing for future acquisitions. In addition, if we use a substantial amount of our funds to acquire or in-license products or product candidates, we may not have sufficient additional funds to conduct all of our operations in the manner we would otherwise choose.

We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

During the past several years, domestic and international financial markets have experienced extreme disruption from time to time, including, among other things, high volatility and significant declines in stock prices and severely diminished liquidity and credit availability for both borrowers and investors. We expect to opportunistically seek access to the capital and credit markets to supplement our existing cash balances, cash we expect to generate from operations and funds available under our revolving credit facility to satisfy our needs for working capital, capital expenditures and debt service requirements or to continue to grow our business over the longer term through product acquisition and in-licensing, product development and clinical trials of product candidates, and expansion of our commercial operations. In the event of adverse capital and credit market conditions, we may not be able to obtain capital market financing or credit on favorable terms, or at all, which could have a material adverse effect on our business and growth prospects. Changes in our credit ratings issued by nationally recognized credit rating agencies could adversely affect our cost of financing and have an adverse effect on the market price of our securities.

We may not be able to successfully maintain our tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries in North America and a number of other foreign jurisdictions. We are able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, together with intra-group service and transfer pricing agreements, each on an arm's length basis. However, changes in tax laws in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the U.S. Internal Revenue Service, or the IRS, actively audit and otherwise challenge these types of arrangements, and have done so in the pharmaceutical industry. We are subject to reviews and audits by the IRS and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure and transfer pricing arrangements through an audit or lawsuit. For example, in December 2015, we received proposed tax assessment notices from the French tax authorities for 2012 and 2013 relating to certain transfer pricing adjustments. The notices propose additional taxes of approximately $41.8 million, including interest and penalties, based on the foreign exchange rate at December 31, 2015 through the date of the assessment. Responding to or defending against this and other challenges from taxing authorities could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We generally 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, 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 products 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 the conclusion that we should be treated as a foreign corporation for U.S. federal tax purposes.

Although we are incorporated in Ireland, the IRS may assert that we should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal tax purposes pursuant to Section 7874 of the Internal Revenue Code of 1986, as amended, or the Code. For U.S. federal tax purposes, a corporation generally is considered a tax resident in the jurisdiction of its organization or incorporation. Because we are an Irish incorporated entity, we would 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 under which a foreign incorporated entity may, in certain circumstances, be treated as a U.S. corporation for U.S. federal tax purposes. Because we indirectly acquired all of Jazz Pharmaceuticals, Inc.'s assets through the acquisition of the shares of Jazz Pharmaceuticals, Inc. common stock in the Azur Merger, the IRS could assert that we should be treated as a U.S. corporation for U.S. federal tax purposes under Section 7874. For us to be treated as a foreign corporation for U.S. federal tax purposes under Section 7874 of the Code, either (1) the former stockholders of Jazz Pharmaceuticals, Inc. must have owned (within the meaning of Section 7874 of the Code) less than 80% (by both vote and value) of our ordinary shares by reason of holding shares in Jazz Pharmaceuticals, Inc. (the "ownership test"), or (2) we must have substantial business activities in Ireland after the Azur Merger (taking into account the activities of our expanded affiliated group). The Jazz Pharmaceuticals, Inc. stockholders owned less than 80% of our share capital immediately after the Azur Merger by reason of their ownership of shares of Jazz Pharmaceuticals, Inc. common stock. As a result, we believe that we should be treated as a foreign corporation for U.S. federal tax purposes under current law. It is possible that the IRS could disagree with the position that the ownership test is satisfied and assert that Section 7874 of the Code applies to treat us as a U.S. corporation following the Azur Merger. There is limited guidance regarding the Code Section 7874 provisions, including the application of the ownership test described

above. The IRS continues to scrutinize transactions that are potentially subject to Section 7874, and issued new final and temporary regulations under Section 7874 in June 2012, January 2014 and June 2015, as well as notices in September 2014 and November 2015 outlining further regulations the IRS plans to issue. We do not expect these regulations to affect the U.S. tax consequences of the Azur Merger. Nevertheless, new statutory and/or regulatory provisions under Section 7874 of the Code or otherwise could be enacted that adversely affect our status as a foreign corporation for U.S. federal tax purposes, and any such provisions could have retroactive application to us, Jazz Pharmaceuticals, Inc., our respective shareholders and/or the Azur Merger. For more information, see the risk factor under the heading "*Future changes to the tax laws under which we expect to be treated as a foreign corporation for U.S. federal tax purposes or in other tax laws relating to multinational corporations could adversely affect us*," in Part I, Item 1A of this Annual Report on Form 10-K.

Section 7874 of the Code limits Jazz Pharmaceuticals, Inc.'s ability to utilize its U.S. tax attributes to offset certain U.S. taxable income, if any, generated by certain taxable transactions.

Following certain acquisitions of a U.S. corporation by a foreign corporation, Section 7874 of the Code can limit the ability of the acquired U.S. corporation and its U.S. affiliates to utilize U.S. tax attributes such as net operating losses, or NOLs, to offset U.S. taxable income resulting from certain transactions. Based on the limited guidance available, this limitation applies to us. As a result, after the Azur Merger, Jazz Pharmaceuticals, Inc. has not been able and will continue to be unable, for a period of time, to utilize its U.S. tax attributes to offset its U.S. taxable income, if any, resulting from certain taxable transactions. Notwithstanding this limitation, we plan to fully utilize Jazz Pharmaceuticals, Inc.'s U.S. NOLs prior to their expiration. As a result of this limitation, however, it may take Jazz Pharmaceuticals, Inc. longer to use its NOLs. Moreover, contrary to these plans, it is possible that the limitation under Section 7874 of the Code on the utilization of U.S. tax attributes could prevent Jazz Pharmaceuticals, Inc. from fully utilizing its U.S. tax attributes prior to their expiration if Jazz Pharmaceuticals, Inc. does not generate sufficient taxable income.

Jazz Pharmaceuticals, Inc.'s ability to use its net operating losses to offset potential taxable income and related income taxes that would otherwise be due could be subject to further limitations if we do not generate taxable income in a timely manner or if the "ownership change" provisions of Sections 382 and 383 of the Code result in further annual limitations.

Jazz Pharmaceuticals, Inc. has a significant amount of NOLs. Our ability to use these NOLs to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the NOLs, and we cannot predict with certainty when, or whether, Jazz Pharmaceuticals, Inc. will generate sufficient taxable income to use all of the NOLs. In addition, realization of NOLs to offset potential future taxable income and related income taxes that would otherwise be due is subject to annual limitations under the "ownership change" provisions of Sections 382 and 383 of the Code and similar state provisions, which may result in the expiration of additional NOLs before future utilization. In general, an "ownership change" occurs if, during a three-year rolling period, there is a change of 50% or more in the percentage ownership of a company by 5% shareholders (and certain persons treated as 5% shareholders), as defined in the Code and the U.S. Treasury Department regulations, or Treasury Regulations, promulgated thereunder. In this regard, we currently estimate that, as a result of these ownership change provisions, we have an annual limitation on the utilization of certain NOLs and credits of $23.5 million, before tax effect, for 2016 and a combined total of $27.5 million, before tax effect, for 2017 to 2026.

However, Sections 382 and 383 of the Code are extremely complex provisions with respect to which there are many uncertainties, and we have not requested a ruling from the IRS to confirm our analysis of the ownership change limitations related to the NOLs generated by Jazz Pharmaceuticals, Inc. Therefore, we have not established whether the IRS would agree with our analysis regarding the application of Sections 382 and 383 of the Code. If the IRS were to disagree with our analysis, or if Jazz Pharmaceuticals, Inc. experiences additional ownership changes in the future, we could be subject to further annual limitations on the use of the NOLs to offset potential taxable income and related income taxes that would otherwise be due.

Future changes to the tax laws under which we expect to be treated as a foreign corporation for U.S. federal tax purposes or in other tax laws relating to multinational corporations could adversely affect us.

As described above, under current law, we believe that we should be treated as a foreign corporation for U.S. federal tax purposes. However, changes to the Code or the Treasury Regulations or other IRS guidance promulgated thereunder, including under Section 7874 of the Code, could adversely affect our status as a foreign corporation for U.S. federal tax purposes or could otherwise affect our effective tax rate, and any such changes could have prospective or retroactive application. In addition, recent legislative proposals have aimed to expand the scope of U.S. corporate tax residence. This legislation, if passed, could adversely affect us.

In addition, the U.S. Congress, the Organization for Economic Co-operation and Development and other government agencies in jurisdictions where we and our affiliates do business have had an extended focus on issues related to the taxation of multinational corporations. One example is in the area of "base erosion and profit shifting," where payments are made between affiliates from a jurisdiction with high tax rates to a jurisdiction with lower tax rates. As a result, the tax laws in the U.S. and

other countries in which we and our affiliates do business could change on a prospective or retroactive basis, and any such changes could adversely affect us.

We have significant intangible assets and goodwill. Consequently, the future impairment of our intangible assets and goodwill may significantly impact our profitability.

Our intangible assets and goodwill are significant. As of December 31, 2015, we had recorded $1.8 billion of intangible assets and goodwill related to our past acquisitions. Intangible assets and goodwill are subject to an impairment analysis whenever events or changes in circumstances indicate the carrying amount of the asset may not be recoverable. Additionally, goodwill and indefinite-lived assets are subject to an impairment test at least annually.

Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. For example, in January 2016, we terminated a pivotal Phase 2 clinical trial of JZP-416 (pegcrisantaspase), a PEGylated recombinant Erwinia chrysanthemi L-asparaginase being developed for the treatment of patients with ALL who are hypersensitive to E. coli-derived asparaginase. As a result, in the fourth quarter of 2015, we recorded an impairment charge of $31.5 million to our acquired in-process research and development. Our results of operations and financial position in future periods could be negatively impacted should similar or other future impairments of intangible assets or goodwill occur.

Our financial results have been and may continue to be adversely affected by foreign currency exchange rate fluctuations.

We have significant operations in Europe as well as in the U.S., but we report revenues, costs and earnings in U.S. dollars. Our primary currency translation exposure relates to our subsidiaries that have functional currencies denominated in the euro. Exchange rates between the U.S. dollar and the euro have fluctuated and are likely to continue to fluctuate from period to period. Because our financial results are reported in U.S. dollars, we are exposed to foreign currency exchange risk as the functional currency financial statements of non-U.S. subsidiaries are translated to U.S. dollars for reporting purposes. To the extent that revenue and expense transactions are not denominated in the functional currency, we are also subject to the risk of transaction losses. For example, because our Defitelio and Erwinase product sales outside of the U.S. are primarily denominated in the euro, our sales of those products have been and may continue to be adversely affected by fluctuations in foreign currency exchange rates. In this regard, when the U.S. dollar strengthens against a foreign currency, the relative value of sales made in the foreign currency decreases. Conversely, when the U.S. dollar weakens against a foreign currency, the relative value of such sales increases. Accordingly, increases in the value of the U.S. dollar relative to foreign currencies, primarily the euro, could adversely affect our foreign revenues, perhaps significantly. In addition, as we continue to expand our international operations, we will conduct more transactions in currencies other than the U.S. dollar, which could increase our foreign currency exchange risk. Given the volatility of exchange rates, continued concerns regarding European sovereign debt and instability of the euro, as well as our expanding operations, we cannot assure you that we will be able to effectively manage currency transaction and/or translation risks. We have not entered into derivative instruments to offset the impact of foreign currency exchange rate fluctuations. Fluctuations in foreign currency exchange rates could have a material adverse effect on our results of operations and financial condition.

Risks Related to Our Ordinary Shares

The market price of our ordinary shares has been volatile and may continue to be volatile in the future, and the value of your investment could decline significantly.

The market price for our ordinary shares has fluctuated significantly from time to time, for example, varying between a high of $194.73 on July 31, 2015 and a low of $117.26 on October 22, 2015 during the period from December 31, 2014 through December 31, 2015. The market price of our ordinary shares is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market, industry and other factors, including the risk factors described above. The stock market in general, including the market for life sciences companies, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. In particular, recent negative publicity regarding pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact, the market for life sciences companies. These broad market and industry factors have harmed, and in the future may seriously harm, the market price of our ordinary shares, regardless of our operating performance.

Our share price may be dependent upon the valuations and recommendations of the analysts who cover our business. If our results do not meet these analysts' forecasts, the expectations of our investors or the financial guidance we provide to investors in any period, the market price of our ordinary shares could decline. In the past, following periods of volatility in the market or significant price decline, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

In addition, the market price of our ordinary shares may decline if the effects of our past transactions, including the Gentium Acquisition and/or potential future acquisitions, on the financial results of our company are not consistent with the expectations of financial analysts or investors. The market price of our ordinary shares could also be affected by possible sales of our ordinary shares by holders of our 2021 Notes who may view the 2021 Notes as a more attractive means of equity participation in our company and by hedging or arbitrage trading activity involving our ordinary shares by the holders of these notes.

Future sales of our ordinary shares in the public market could cause our share price to fall.

Sales of a substantial number of our ordinary shares in the public market, including sales by members of our management or board of directors, or the perception that these sales might occur, could depress the market price of our ordinary shares and could impair our ability to raise capital through the sale of additional equity or equity-related securities. As of February 17, 2016, we had 61,184,623 ordinary shares outstanding, all of which shares are eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale and other requirements under Rule 144. In addition, future issuances by us of our ordinary shares upon the exercise or settlement of equity-based awards and exchanges of our 2021 Notes would dilute existing shareholders' ownership interests in our company, and any sales in the public market of these ordinary shares, or the perception that these sales might occur, could also adversely affect the market price of our ordinary shares.

Moreover, we have in the past and may in the future grant rights to some of our shareholders that require us to register the resale of our ordinary shares on behalf of these shareholders and/or facilitate offerings of ordinary shares held by these shareholders, including in connection with potential future acquisitions of additional products, product candidates or companies. For example, consistent with our obligations under then-existing registration rights agreements, we entered into underwriting agreements with certain underwriters and selling shareholders pursuant to which selling shareholders sold an aggregate of approximately 13 million ordinary shares in two separate registered public offerings in March 2012 and in March 2013. We have also filed registration statements to register the sale of our ordinary shares reserved for issuance under our equity incentive and employee stock purchase plans, and we intend to file additional registration statements to register any shares automatically added each year to the share reserves under these plans.

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

It may not be possible to enforce court judgments obtained in the U.S. 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 Act 2014, which differs 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 U.S.

Provisions of our articles of association, Irish law and the indenture governing our 2021 Notes 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;
- 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; and
- permit our board of directors to issue one or more series of preferred shares with rights and preferences, as our shareholders may determine by ordinary resolution.

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 shares in certain circumstances. Furthermore, the indenture governing our 2021 Notes requires us to repurchase the notes for cash if we undergo certain fundamental changes and, in certain circumstances, to increase the exchange rate for a holder of 2021 Notes. A takeover of us may trigger the requirement that we purchase our 2021 Notes and/or increase the exchange rate, which could make it more costly for a potential acquiror to engage in a business combination transaction with us.

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 other shareholders to elect directors other than the candidates nominated by our board.

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

Other than funds we have allocated for the purposes of supporting our share repurchase program authorized in November 2015, we anticipate that we will retain all earnings, if any, to support our operations and our proprietary drug development programs, acquire or in-license additional products and product candidates, and pursue other opportunities. If we propose to pay dividends in the future, we must do so in accordance with Irish law, which provides that distributions including dividend payments, share repurchases and redemptions be funded from “distributable reserves.” In addition, our ability to pay cash dividends on or repurchase our ordinary shares is restricted under the terms of our credit agreement. 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, compliance with the terms of our credit agreement and other factors our board of directors deems relevant. Accordingly, holders of our ordinary shares must rely on increases in the trading price of their shares for returns on their investment in the foreseeable future.

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% 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 U.S., an exemption of this stamp duty is available to transfers by shareholders who hold our 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 a record holder who holds our 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 Irish Companies Act 2014 or any other applicable law permit, may, or may provide that a subsidiary of ours 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 our 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 our 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 our 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 U.S., 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 us or our 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.

Our auditor, like other independent registered public accounting firms operating in Ireland and a number of other European countries, is not currently permitted to be subject to inspection by the U.S. Public Company Accounting Oversight Board, or the PCAOB, and as such, our investors currently do not have the benefits of PCAOB oversight.

As an auditor of companies that are publicly-traded in the U.S. and as a firm registered with the PCAOB, our independent registered public accounting firm is required by the laws of the U.S. to undergo regular inspections by the PCAOB to assess its

compliance with the laws of the U.S. and the professional standards of the PCAOB. However, because our auditor is located in Ireland, a jurisdiction where the PCAOB is currently unable to conduct inspections, our auditor is not currently inspected by the PCAOB. Inspections of other auditors conducted by the PCAOB outside of Ireland have at times identified deficiencies in those auditor's audit procedures and quality control procedures, which may be addressed as part of the inspection process to improve future audit quality. The lack of PCAOB inspections in Ireland prevents the PCAOB from regularly evaluating our auditor's audits and its quality control procedures. In addition, the inability of the PCAOB to conduct auditor inspections in Ireland makes it more difficult to evaluate the effectiveness of our auditor's audit procedures or quality control procedures as compared to auditors located outside of Ireland that are subject to regular PCAOB inspections. As a result, our investors are deprived of the benefits of PCAOB inspections, and may lose confidence in our reported financial information and procedures and the quality of our financial statements.

Item 1B. Unresolved Staff Comments

There are no material unresolved written comments that were received from the SEC staff 180 days or more before the end of our 2015 fiscal year relating to our periodic or current reports under the Exchange Act.

Item 2. Properties

Our corporate headquarters are located in Dublin, Ireland, and our U.S. operations are located in Palo Alto, California and Philadelphia, Pennsylvania.

We occupy approximately 17,000 square feet of office space in Dublin, Ireland, 12,000 square feet of which is under one lease, or the Dublin Lease, that expires in May 2022, and 5,000 square feet of which is under a second lease that also expires in May 2022. We have options to terminate these leases in May 2017 for the Dublin Lease and in January 2019 for the second lease, with no less than six months' prior written notice and the payment of a termination fee. We recently completed construction of a 54,000 square foot manufacturing and development facility on land owned by us in Athlone, Ireland.

In Palo Alto, California, we occupy a total of approximately 118,000 square feet of office space, 44,000 square feet of which is occupied under a lease, or the Palo Alto Lease, that expires in August 2017; 57,000 square feet of which is occupied under a sublease that expires in December 2017; and 17,000 square feet of which is occupied under a sublease that expires in July 2017. We have the right to extend the term of the Palo Alto Lease for up to an additional two years. In January 2015, we entered into an agreement to lease approximately 100,000 square feet of office space in Palo Alto, California. We expect to occupy this office space by the end of 2017. This lease has a term of 12 years from commencement, and we have an option to extend the term of the lease twice for a period of five years each. We also have an option to terminate this lease 10 years from commencement, with no less than one year's prior written notice and the payment of a termination fee.

We occupy approximately 19,000 square feet of office space in Philadelphia, Pennsylvania under a lease that expires in April 2019. In addition, we have offices in Oxford, United Kingdom, Lyon, France, Villa Guardia (Como), Italy and elsewhere in Europe. We occupy approximately 14,000 square feet of office space in Oxford, United Kingdom under a lease that expires in August 2024. We have an option to terminate this lease in August 2019, with no less than six months' prior written notice and the payment of a termination fee. We also occupy office space in Lyon, France. In July 2015, we entered into an agreement to lease approximately 1,566 square feet of office space to replace our lease of approximately 9,000 square feet of office space that expires in March 2016. The new lease expires in July 2024. We have an option to terminate this lease in July 2018 and in July 2021, with no less than six months' prior written notice. We expect to occupy the new reduced office space in the second quarter of 2016. We own a manufacturing facility in Villa Guardia (Como), Italy. The manufacturing facility is 25,295 square feet. We also lease approximately 51,667 square feet of office and laboratory space in Villa Guardia (Como), Italy under a lease that expires in December 2017.

We believe that our existing properties are in good condition and suitable for the conduct of our business. As we continue to expand our operations, we may need to lease additional or alternative facilities.

Item 3. Legal Proceedings

Xyrem ANDA Matters. On October 18, 2010, we received a notice of Paragraph IV Certification from Roxane that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. Roxane's initial notice alleged that all five patents then listed for Xyrem in the FDA's Orange Book on the date of the notice are invalid, unenforceable or not infringed by Roxane's proposed generic product. On November 22, 2010, we filed a lawsuit against Roxane in response to Roxane's initial notice in the U.S. District Court for the District of New Jersey, or the District Court, seeking a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe our patents. In accordance with the Hatch-Waxman Act, as a result of our having filed a timely lawsuit against Roxane, FDA approval of Roxane's ANDA was stayed for 30 months, or until April 2013. That stay has expired. Additional patents covering Xyrem have been issued since

December 2010, and after receiving Paragraph IV Certification notices from Roxane with respect to those patents, we have filed additional lawsuits against Roxane to include these additional patents in the litigation. All of the lawsuits filed against Roxane between 2010 and 2012 have been consolidated by the District Court into a single case, or the first Roxane consolidated case, alleging that 10 of our patents covering Xyrem are or will be infringed by Roxane's ANDA and seeking a permanent injunction to prevent Roxane from launching a generic version of Xyrem that would infringe these patents.

After receiving additional Paragraph IV Certification notices from Roxane, on February 20, 2015 and June 1, 2015, we filed two actions against Roxane in the District Court that have since been consolidated, or the second Roxane consolidated case, alleging that four of our patents covering Xyrem are or will be infringed by Roxane's ANDA and seeking a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe those patents. After receiving an additional Paragraph IV Certification notice from Roxane on December 14, 2015, we filed an action against Roxane on January 27, 2016 alleging that one of our patents covering Xyrem is or will be infringed by Roxane's ANDA and seeking a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe that patent.

In December 2013, the District Court permitted Roxane to amend its answer in the first Roxane consolidated case to allege certain equitable defenses, and the parties were given additional time for discovery on those new defenses. In addition, in March 2014, the District Court granted our motion to bifurcate and stay the portion of the first Roxane consolidated case regarding patents related to the distribution system for Xyrem. Although no trial date has been scheduled, based on the District Court's current schedule, we anticipate that trial on the patents in the first Roxane consolidated case that are not subject to the stay could occur as early as the second quarter of 2016. We do not have any estimate of a possible trial date for trial on the patents in the first Roxane consolidated case that are currently subject to the stay or for any other Roxane cases.

On April 20, 2015, Roxane moved in the second Roxane consolidated case to dismiss claims involving our patent covering a part of the Xyrem label that instructs prescribers on adjusting the dose of Xyrem when it is being co-administered with divalproex sodium (also known as valproate or valproic acid) on the grounds that this patent does not cover patentable subject matter. On October 29, 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of IPR proceedings before the PTAB relating to the patent that was the subject of Roxane's motion.

The actual timing of events in our litigation with Roxane may be significantly earlier or later than we currently anticipate. We cannot predict the specific timing or outcome of events in these matters or the impact of these matters on other ongoing proceedings with any ANDA filer.

On December 10, 2012, we received notice of Paragraph IV Certification from Amneal Pharmaceuticals, LLC, or Amneal, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On January 18, 2013, we filed a lawsuit against Amneal in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Amneal's ANDA and seeking a permanent injunction to prevent Amneal from introducing a generic version of Xyrem that would infringe these patents. On November 21, 2013, we received notice of Paragraph IV Certification from Par Pharmaceutical, Inc., or Par, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On December 27, 2013, we filed a lawsuit against Par in the District Court, alleging that our patents covering Xyrem are infringed or will be infringed by Par's ANDA and seeking a permanent injunction to prevent Par from introducing a generic version of Xyrem that would infringe these patents.

In April 2014, Amneal asked the District Court to consolidate its case with the Par case, stating that both cases would proceed on the schedule for the Par case. The District Court granted this request in May 2014. The order consolidating the cases provides that Amneal's 30-month stay period will be extended to coincide with the date of Par's 30-month stay period. As a result, FDA's approval of both Amneal's and Par's ANDAs is stayed until the earlier of (i) May 20, 2016, or (ii) a District Court decision finding that the identified patents are invalid, unenforceable or not infringed.

Additional patents covering Xyrem have issued since April 2014 and have been listed in the Orange Book for Xyrem. Amneal and Par have given us additional notices of Paragraph IV Certifications regarding such patents, and we have filed additional lawsuits against Amneal and Par in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Amneal's and Par's ANDAs and seeking a permanent injunction to prevent Amneal and Par from introducing a generic version of Xyrem that will infringe these patents.

On June 4, 2014, we received a notice of Paragraph IV Certification from Ranbaxy Laboratories Limited, or Ranbaxy, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On July 15, 2014, we filed a lawsuit against Ranbaxy in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Ranbaxy's ANDA and seeking a permanent injunction to prevent Ranbaxy from introducing a generic version of Xyrem that will infringe these patents. Since June 2014, we have received additional notices of Paragraph IV Certification from Ranbaxy regarding newly issued patents for Xyrem listed in the Orange Book, and we have filed additional lawsuits against Ranbaxy in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Ranbaxy's ANDA and seeking a permanent injunction to prevent Ranbaxy from introducing a generic version of Xyrem that will infringe these patents.

On October 30, 2014, we received a notice of Paragraph IV Certification from Watson Laboratories, Inc., or Watson, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On December 11, 2014, we filed a lawsuit against Watson in the District Court alleging that our patents covering Xyrem are or will be infringed by Watson's ANDA and seeking a permanent injunction to prevent Watson from introducing a generic version of Xyrem that would infringe these patents. On March 23, 2015, Watson moved to dismiss the portion of the case based on our Orange Book-listed patents covering the distribution system for Xyrem on the grounds that these patents do not cover patentable subject matter. On November 4, 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of IPR proceedings before the PTAB relating to the patents that were the subject of Watson's motion. Since March 2015, we have received an additional notice of Paragraph IV Certification from Watson regarding newly issued patents for Xyrem listed in the Orange Book, and we have filed an additional lawsuit against Watson in the District Court alleging that our patents covering Xyrem are or will be infringed by Watson's ANDA and seeking a permanent injunction to prevent Watson from introducing a generic version of Xyrem that would infringe these patents.

In April 2015, the District Court issued an order that consolidated all then-pending lawsuits against Amneal, Par, Ranbaxy and Watson into one case.

On June 8, 2015, we received a Paragraph IV Certification from Wockhardt Bio AG, or Wockhardt, that it has submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On July 17, 2015, we filed a lawsuit in the District Court alleging that our patents covering Xyrem are or will be infringed by Wockhardt's ANDA and seeking a permanent injunction to prevent Wockhardt from introducing a generic version of Xyrem that would infringe our patents. Since July 2015, we have received an additional notice of Paragraph IV Certification from Wockhardt regarding newly issued patents listed in the Orange Book, and we have filed an additional lawsuit against Wockhardt in the District Court alleging that our patents covering Xyrem are or will be infringed by Wockhardt's ANDA and seeking a permanent injunction to prevent Wockhardt from introducing a generic version of Xyrem that would infringe these patents.

On July 23, 2015, we received a Paragraph IV Certification from Lupin Inc., or Lupin, that it has submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On September 2, 2015, we filed a lawsuit in the District Court alleging that our patents covering Xyrem are or will be infringed by Lupin's ANDA and seeking a permanent injunction to prevent Lupin from introducing a generic version of Xyrem that would infringe our patents.

On January 14, 2016, the District Court issued an order consolidating all of the cases then pending against Amneal, Par, Ranbaxy, Watson, Wockhardt and Lupin into a single case for all purposes. We cannot predict the specific timing or outcome of events in this matter or the impact of developments involving any specific parties or patents on other ongoing proceedings with any ANDA filer.

Xyrem Post-Grant Patent Review Matters. In January 2015, certain of the ANDA filers filed petitions for IPR with respect to the validity of six patents covering the distribution system for Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to these petitions, and we expect the PTAB to issue final decisions on the validity of the patents in July 2016. In September 2015, certain of the ANDA filers filed a petition for IPR with respect to the validity of an additional patent covering the distribution system for Xyrem. In October 2015, certain of the ANDA filers filed petitions for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium (also known as valproate or valproic acid). In December 2015, Wockhardt filed a petition for IPR with respect to the validity of one of our patents covering the formulation of Xyrem. In February 2016, Amneal filed a petition for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

Cutler Matter. On October 19, 2011, Dr. Neal Cutler, one of the original owners of FazaClo® (clozapine, USP), filed a complaint against Azur Pharma and one of its subsidiaries, as well as Avanir Pharmaceuticals, Inc., or Avanir, in the California Superior Court in the County of Los Angeles, or the Superior Court. The complaint alleged that Azur Pharma and its subsidiary breached certain contractual obligations that would have required Azur Pharma to pay Cutler approximately $35 million under a contract it assumed when it acquired FazaClo from Avanir in 2007, and further alleged that Cutler was entitled to unspecified punitive damages and attorneys' fees. On December 21, 2015, Cutler filed a First Amended Complaint, and the Superior Court set a trial date for July 2016. Effective February 10, 2016, we entered into a settlement agreement with Cutler resolving all claims in the lawsuit.

From time to time we are involved in legal proceedings arising in the ordinary course of business. We believe there is no other litigation pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our ordinary shares trade on The NASDAQ Global Select Market under the trading symbol "JAZZ." The following table sets forth the high and low intraday sales prices of our ordinary shares on The NASDAQ Global Select Market for the periods indicated.

	High	Low
Calendar Quarter—2014		
First Quarter	$ 176.60	$ 123.55
Second Quarter	$ 156.34	$ 120.38
Third Quarter	$ 176.36	$ 131.69
Fourth Quarter	$ 183.84	$ 137.34
Calendar Quarter—2015		
First Quarter	$ 190.17	$ 155.06
Second Quarter	$ 191.01	$ 165.00
Third Quarter	$ 194.73	$ 121.12
Fourth Quarter	$ 151.28	$ 117.26

On February 17, 2016, the last reported sales price per share of our ordinary shares was $122.79 per share.

Holders of Ordinary Shares

As of February 17, 2016, there were three holders of record of our ordinary shares. Because almost all of our ordinary shares are held by brokers, nominees and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Dividends

In 2015 and 2014, we did not declare or pay cash dividends on our common equity and we do not currently plan to pay cash dividends in 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, the terms of our credit agreement restrict our ability to make certain restricted payments, including dividends and other distributions by us in respect of our ordinary shares, subject to, among other exceptions, (1) a general exception for dividends and restricted payments up to $30 million in the aggregate and (2) an exception that allows for restricted payments, subject to a cap equal the sum of (i) $100 million plus (ii) so long as our total leverage ratio (as defined in our credit agreement) does not exceed 2.5:1 after giving pro forma effect to the restricted payment, a formula-based amount tied to our consolidated net income; provided that such cap applies only if our total leverage ratio (as defined in our credit agreement) exceeds 2:1 after giving pro forma effect to the restricted payment. 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, compliance with the terms of our credit agreement and other factors our board of directors deems relevant.

Unregistered Sales of Equity Securities

Except as previously reported in our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the Securities and Exchange Commission, or SEC, during the year ended December 31, 2015, there were no unregistered sales of equity securities by us during the year ended December 31, 2015.

Irish Law Matters

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 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 European Union, or 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. At present the Financial Transfers Act, 1992 prohibits financial transfers involving the late Slobodan Milosevic and associated persons, 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-Bissau, Afghanistan, Egypt, Eritrea, Libya, Syria, Tunisia, certain known terrorists and terrorist groups, countries that harbor certain terrorist groups and Ukraine without the prior permission of the Central Bank of Ireland.

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 20%), unless an exemption applies.

Dividends on our ordinary shares that are owned by residents of the U.S. 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 U.S.

Dividends on our ordinary shares that are owned by residents of the U.S. 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 U.S. 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 comprised 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% 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.

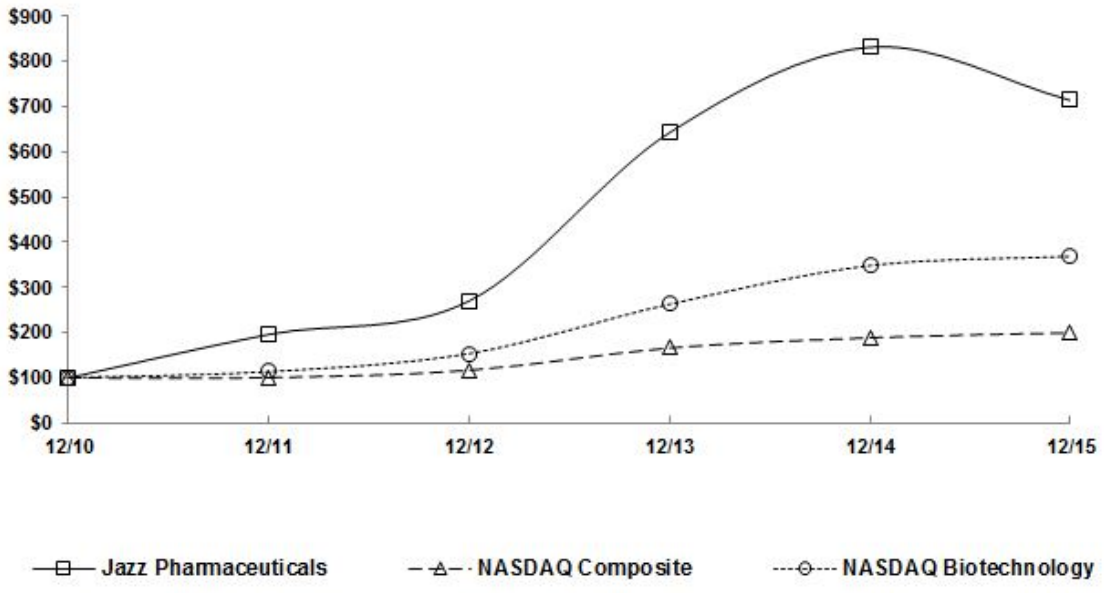
Stamp Duty. Irish stamp duty (if any) may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. A transfer of our ordinary 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 1% 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 being contemplated 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.

Performance Measurement Comparison (1)

The following graph shows the total shareholder return on the last day of each year of an investment of $100 in cash as if made on December 31, 2010 in (i) our ordinary shares; (ii) the NASDAQ Composite Index; and (iii) the NASDAQ Biotechnology Index through December 31, 2015. Information set forth in the graph below represents the performance of the Jazz Pharmaceuticals, Inc. common stock from December 31, 2010 until January 17, 2012, the day before the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company, or Azur Pharma, were combined in a merger transaction, or the Azur Merger, and the performance of our ordinary shares from January 18, 2012 through December 31, 2015. Our ordinary shares trade on the same exchange and under the same trading symbol as the Jazz Pharmaceuticals, Inc. common stock prior to the Azur Merger. The shareholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future shareholder returns.

COMPARISON OF FIVE YEAR CUMULATIVE TOTAL RETURN (2)



(1) This section is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, or Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

(2) Information used in the graph was obtained from Research Data Group, Inc.

Issuer Purchases of Equity Securities

The following table summarizes purchases of our ordinary shares made by or on behalf of us or any of our "affiliated purchasers" as defined in Rule 10b-18(a)(3) under the Exchange Act during each fiscal month during the three-month period ended December 31, 2015:

	Total Number of Shares Purchased (1)	Average Price Paid per Share (2)	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs (3)	Maximum Number (or Approximate Dollar Value) of Shares that May Yet Be Purchased Under the Plans or Programs (4)
October 1 - October 31, 2015	—	$ —	—	$ —
November 1 - November 30, 2015	96,833	$ 139.73	96,833	$ 286,472,388
December 1 - December 31, 2015	189,317	$ 141.15	189,317	$ 259,756,866
Total	286,150	$ 140.67	286,150	

(1) This table does not include ordinary shares that we withheld in order to satisfy minimum tax withholding requirements in connection with the vesting of restricted stock units.
(2) Average price paid per share includes brokerage commissions.
(3) The ordinary shares reported in the table above were purchased pursuant to our publicly announced share repurchase program. In November 2015, we announced that our board of directors authorized the use of up to $300 million to repurchase our ordinary shares. This authorization has no expiration date.
(4) The dollar amount shown represents, as of the end of each period, the approximate dollar value of ordinary shares that may yet be purchased under our publicly announced share repurchase program, exclusive of any brokerage commissions. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under our credit agreement, corporate and regulatory requirements and market conditions, and may be modified, suspended or otherwise discontinued at any time without prior notice.

Item 6. Selected Financial Data

The following selected consolidated financial data should be read together with our consolidated financial statements and accompanying notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section is not intended to replace our consolidated financial statements and the accompanying notes. Our historical results are not necessarily indicative of our future results.

We derived the consolidated statements of income data for the years ended December 31, 2015, 2014 and 2013 and the consolidated balance sheet data as of December 31, 2015 and 2014 from the audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. The consolidated statements of income data for the years ended December 31, 2012 and 2011, and the selected consolidated balance sheet data as of December 31, 2013, 2012 and 2011 are derived from audited consolidated financial statements not included in this Annual Report on Form 10-K. The selected consolidated financial data for periods prior to the year ended December 31, 2012 is that of Jazz Pharmaceuticals, Inc. and its consolidated subsidiaries, while the selected consolidated financial data for periods after and including the year ended December 31, 2012 is that of Jazz Pharmaceuticals plc and its consolidated subsidiaries.

	Year Ended December 31,				
	2015	2014(1)	2013	2012(2)	2011
	(In thousands, except per share amounts)				
Consolidated Statements of Income Data:					
Revenues:					
Product sales, net	$ 1,316,819	$ 1,162,716	$ 865,398	$ 580,527	$ 266,518
Royalties and contract revenues	7,984	10,159	7,025	5,452	5,759
Total revenues	1,324,803	1,172,875	872,423	585,979	272,277
Operating expenses:					
Cost of product sales (excluding amortization and impairment of intangible assets)	102,526	117,418	102,146	78,425	13,942
Selling, general and administrative	449,119	406,114	304,303	223,882	108,936
Research and development	135,253	85,181	41,632	20,477	14,120
Acquired in-process research and development	—	202,626	4,988	—	—
Intangible asset amortization	98,162	126,584	79,042	65,351	7,448
Impairment charges	31,523	39,365	—	—	—
Total operating expenses	816,583	977,288	532,111	388,135	144,446
Income from operations	508,220	195,587	340,312	197,844	127,831
Interest expense, net	(56,917)	(52,713)	(26,916)	(16,869)	(1,600)
Foreign currency gain (loss)	1,445	8,683	(1,697)	(3,620)	—
Loss on extinguishment and modification of debt	(16,815)	—	(3,749)	—	(1,247)
Income from continuing operations before income tax provision (benefit)	435,933	151,557	307,950	177,355	124,984
Income tax provision (benefit)	106,399	94,231	91,638	(83,794)	—
Income from continuing operations	329,534	57,326	216,312	261,149	124,984
Income from discontinued operations, net of taxes	—	—	—	27,437	—
Net income	329,534	57,326	216,312	288,586	124,984
Net loss attributable to noncontrolling interests, net of tax	(1)	(1,061)	—	—	—
Net income attributable to Jazz Pharmaceuticals plc	$ 329,535	$ 58,387	$ 216,312	$ 288,586	$ 124,984
Net income attributable to Jazz Pharmaceuticals plc per ordinary share (3):					
Basic:					
Income from continuing operations	$ 5.38	$ 0.98	$ 3.71	$ 4.61	$ 3.01
Income from discontinued operations	—	—	—	0.48	—
Net income attributable to Jazz Pharmaceuticals plc	$ 5.38	$ 0.98	$ 3.71	$ 5.09	$ 3.01
Diluted:					
Income from continuing operations	$ 5.23	$ 0.93	$ 3.51	$ 4.34	$ 2.67
Income from discontinued operations	—	—	—	0.45	—
Net income attributable to Jazz Pharmaceuticals plc	$ 5.23	$ 0.93	$ 3.51	$ 4.79	$ 2.67
Weighted-average ordinary shares used in per share calculation - basic	61,232	59,746	58,298	56,643	41,499
Weighted-average ordinary shares used in per share calculation - diluted	63,036	62,614	61,569	60,195	46,798

	As of December 31,				
	2015	2014(1)	2013	2012(2)	2011
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 988,785	$ 684,042	$ 636,504	$ 387,196	$ 157,898
Working capital	1,031,025	799,044	660,589	360,034	146,261
Total assets	3,359,663	3,338,955	2,238,221	1,966,493	253,573
Long-term debt, current and non-current	1,204,503	1,342,428	549,976	456,761	—
Retained earnings (accumulated deficit)	302,686	34,704	18,532	(61,296)	(349,882)
Total Jazz Pharmaceuticals plc shareholders' equity	1,598,646	1,371,144	1,295,534	1,121,292	192,788

(1) On January 23, 2014, pursuant to a tender offer, we became the indirect majority shareholder of Gentium S.r.l., or Gentium, acquiring control of Gentium on that date. In February 2014, we completed a subsequent offering period of the tender offer, resulting in total purchases pursuant to the tender offer of approximately 98% of the fully diluted voting securities of Gentium. As of December 31, 2015, we had acquired the remaining 2% interest in Gentium for cash consideration of $17.9 million, resulting in an aggregate acquisition cost to us of $994.1 million, comprising cash payments of $1,011.2 million offset by proceeds from the exercise of Gentium share options of $17.1 million. The results of operations of the acquired Gentium business, along with the estimated fair values of the assets acquired and liabilities assumed in the transaction, have been included in our consolidated financial statements since the completion of the acquisition of Gentium on January 23, 2014, which is referred to as the Gentium Acquisition in this Annual Report on Form 10-K. We recorded noncontrolling interests in our consolidated financial statements that represent the ownership interest of minority shareholders in the equity of Gentium. In future periods, we will no longer record noncontrolling Gentium interests since we had acquired all such remaining noncontrolling interests as of December 31, 2015. In connection with the Gentium Acquisition, on January 23, 2014, we entered into a second amendment to the credit agreement we entered into in June 2012, or the previous credit agreement. We used the proceeds from incremental term loans of $350.0 million and $300.0 million of loans under the revolving credit facility provided for under the previous credit agreement, together with cash on hand, to finance the Gentium Acquisition. In August 2014, we completed a private placement of $575.0 million aggregate principal amount of 1.875% exchangeable senior notes due 2021, or the 2021 Notes, resulting in net proceeds to us, after debt issuance costs, of $558.9 million. We used a portion of the net proceeds from the issuance of the 2021 Notes to repay all then outstanding borrowings under the revolving credit facility provided for under the previous credit agreement.

(2) On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma were combined in the Azur Merger pursuant to which all outstanding shares of Jazz Pharmaceuticals, Inc.'s common stock were canceled and converted into the right to receive, on a one-for-one basis, our ordinary shares. Jazz Pharmaceuticals, Inc. was treated as the acquiring company in the Azur Merger for accounting purposes, and as a result, the historical consolidated financial statements of Jazz Pharmaceuticals, Inc. became our consolidated financial statements. On June 12, 2012, we completed our acquisition of EUSA Pharma Inc., or EUSA Pharma, which we refer to as the EUSA Acquisition. At the closing of the EUSA Acquisition, we paid $678.4 million in cash, and agreed to make an additional contingent payment of $50.0 million in cash if Erwinaze achieved net sales in the U.S. of $124.5 million or more in 2013. In 2013, net sales of Erwinaze in the U.S. exceeded $124.5 million and as a result, we made this payment in 2014. The results of operations of the acquired Azur Pharma and EUSA Pharma businesses, along with the estimated fair values of the assets acquired and liabilities assumed in each transaction, are included in our consolidated financial statements since the effective dates of the Azur Merger and the EUSA Acquisition, respectively. We financed the EUSA Acquisition, in part, by entering into a credit agreement in June 2012, which at the time provided for $475.0 million principal amount of term loans and a $100.0 million revolving credit facility. We used all of the proceeds of those term loans, together with cash on hand, to finance the EUSA Acquisition.

(3) All references to "ordinary shares" refer to Jazz Pharmaceuticals, Inc.'s common stock with respect to periods prior to the year ended December 31, 2012 and to our ordinary shares with respect to periods after and including the year ended December 31, 2012. Our earnings per share in the periods prior to the year ended December 31, 2012 were not impacted by the Azur Merger because each share of Jazz Pharmaceuticals, Inc. common stock issued and outstanding immediately prior to the effective time of the Azur Merger was canceled and converted into the right to receive one ordinary share upon the consummation of the Azur Merger.

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

The following discussion of our financial condition and results of operations should be read in conjunction with the consolidated financial statements and notes to consolidated financial statements included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. When reviewing the discussion below, you should keep in mind the substantial risks and uncertainties that impact our business. In particular, we encourage you to review the risks and uncertainties described in "Risk Factors" in Part I, Item 1A in this Annual Report on Form 10-K. These risks and uncertainties could cause actual results to differ materially from those projected in forward-looking statements contained in this report or implied by past results and trends.

Overview

Jazz Pharmaceuticals plc is an international biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing meaningful products that address unmet medical needs.

We have a diverse portfolio of products and product candidates, with a focus in the areas of sleep and hematology/oncology.

Our lead marketed products are:

- **Xyrem® (sodium oxybate) oral solution**, the only product approved by the U.S. Food and Drug Administration, or FDA, for the treatment of both cataplexy and excessive daytime sleepiness, or EDS, in patients with narcolepsy;
- **Erwinaze® (asparaginase *Erwinia chrysanthemi*)**, a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia, or ALL, who have developed hypersensitivity to *E. coli*-derived asparaginase; and
- **Defitelio® (defibrotide)**, a product approved in Europe for the treatment of severe hepatic veno-occlusive disease, or VOD, in adults and children undergoing hematopoietic stem cell transplantation, or HSCT, therapy.

Our strategy is to create shareholder value by:

- Growing sales of the existing products in our portfolio, including by identifying and investing in growth opportunities such as new treatment indications;
- Acquiring clinically meaningful and differentiated products that are on the market or product candidates that are in late-stage development; and
- Pursuing targeted development of post-discovery differentiated product candidates.

We apply a disciplined approach to allocating our resources between investments in our current commercial and development portfolio and acquisitions or in-licensing of new assets.

Some of the significant developments affecting our business and financial results in 2015 are summarized below.

Increase in Total Net Product Sales

Our total net product sales increased by 13% in 2015 compared to 2014, primarily due to an increase in Xyrem product sales. We expect total net product sales to increase in 2016 over 2015, primarily due to anticipated growth in sales of our lead marketed products.

Emphasis on Research and Development Activities

We have increased our focus on research and development activities, which currently include clinical development of new product candidates, activities related to line extensions and new indications for existing products and the generation of additional clinical data for existing products, all in our sleep and hematology/oncology therapeutic areas.

A summary of our ongoing development activities is provided below:

Project	Disease Area	Status
Sleep		
JZP-110	EDS in narcolepsy	Phase 3 clinical trial initiated in second quarter of 2015; preliminary data expected in fourth quarter of 2016
	EDS in obstructive sleep apnea, or OSA	Two Phase 3 clinical trials initiated in second quarter of 2015; preliminary data expected in fourth quarter of 2016
JZP-386	EDS in narcolepsy	Phase 1 clinical trials completed; further evaluation ongoing
Xyrem	Cataplexy with narcolepsy in children and adolescents	Phase 3 clinical trial ongoing; enrollment completion expected in second half of 2016
Hematology/Oncology		
Defibrotide	VOD with evidence of multi-organ dysfunction following HSCT	New drug application, or NDA, accepted for filing with priority review by the FDA in third quarter of 2015; Prescription Drug User Fee Act, or PDUFA, date of March 31, 2016
Defibrotide	Prevention of VOD in high-risk patients	Preparing to initiate clinical trial

In the sleep area, we have ongoing and planned development programs for Xyrem and certain product candidates.

- *JZP-110.*

  Phase 3 Clinical Trials. JZP-110 is a late-stage investigational compound being developed for potential treatment of EDS in patients with narcolepsy and EDS in patients with OSA. We acquired worldwide development, manufacturing and commercial rights to JZP-110 from Aerial BioPharma LLC, or Aerial, in January 2014, other than in certain jurisdictions in Asia where SK Biopharmaceuticals Co., Ltd, or SK, retains rights. We initiated patient enrollment in our Phase 3 clinical program in the second quarter of 2015. We are conducting one Phase 3 clinical trial in patients with EDS associated with narcolepsy and two Phase 3 clinical trials in patients with EDS associated with OSA. Approximately 880 patients are expected to be enrolled in these three trials in the aggregate. In addition, we expect to enroll up to 450 patients from two of our Phase 3 clinical trials in an open label extension trial evaluating the long-term safety of JZP-110. We expect to receive preliminary data results from these trials in the fourth quarter of 2016.

  Other Activities. We are also exploring additional potential indications for JZP-110.

- *Xyrem.*

  Phase 3 Clinical Trial of Xyrem in Children and Adolescents. While in many patients narcolepsy can begin during childhood and adolescence, there is limited information on the treatment of pediatric narcolepsy patients with Xyrem. We have worked with the FDA and several leading specialists to design a clinical trial to generate additional data on the treatment of pediatric narcolepsy patients with Xyrem. In the fourth quarter of 2014, we initiated a Phase 3 clinical trial to assess the safety and efficacy of Xyrem in children and adolescents aged seven to 17 who have narcolepsy with cataplexy. We expect to complete enrollment in this trial in the second half of 2016.

  Other Activities. We are also pursuing other activities related to the potential development of options for narcolepsy patients that would provide clinically meaningful improvements compared to Xyrem, including once-nightly dosing. Although results from our Phase 1 trial of JZP-386, a deuterium-modified analog of sodium oxybate, which we licensed from Concert Pharmaceuticals, Inc., or Concert, in February 2013, did not support advancing JZP-386 into a later-stage clinical trial, the clinical data demonstrated that JZP-386 provided favorable deuterium-related effects, including higher serum concentrations and correspondingly increased pharmacodynamics effects at clinically relevant time points compared to Xyrem, and a safety profile similar to that observed with Xyrem. We are exploring formulation options designed to leverage the positive effects observed in the studies.

In the hematology and oncology area, we also have ongoing and planned development activities.

- *Defibrotide.*

  Planned Phase 3 Clinical Trial. We are preparing to commence a clinical trial to evaluate the safety and efficacy of defibrotide for the prevention of VOD in high-risk patients. We expect to initiate patient enrollment in the third quarter of 2016.

  Other Activities. We are also exploring additional potential indications for defibrotide and assessing the potential to pursue regulatory approval of defibrotide in additional countries.

- *Erwinaze*. We are pursuing activities related to the potential development of an effective and well-tolerated long-acting recombinant crisantaspase that would offer benefits compared to Erwinaze. We are also assessing the potential to pursue regulatory approval of Erwinaze in additional countries.

We recently terminated certain development activities in the hematology and oncology area. In the fourth quarter of 2015, we discontinued development of Leukotac™ (inolimomab), an anti-CD25 monoclonal antibody for the treatment of steroid-refractory acute graft vs. host disease, or GvHD, based on our analysis of data from a Phase 3 clinical trial that we conducted in Europe. In February 2015, we voluntarily suspended patient enrollment in a pivotal Phase 2 clinical trial of JZP-416 (pegcrisantaspase), a PEGylated recombinant Erwinia chrysanthemi L-asparaginase being developed for the treatment of patients with ALL who are hypersensitive to *E. coli*-derived asparaginase. We terminated this trial in January 2016 based on the occurrence of hypersensitivity-like reactions following the administration of JZP-416 in some treated patients.

For 2016 and beyond, we expect that our research and development expenses will increase from historical levels, particularly as we initiate additional clinical trials and related development work and potentially acquire rights to additional product candidates.

Our Lead Marketed Products

Xyrem. Our financial results remain significantly influenced by sales of Xyrem, which accounted for 73% of our net product sales in 2015 and 67% of our net product sales in 2014. As a result, we continue to place a high priority on seeking to maintain and increase sales of Xyrem in its approved indications, while remaining focused on ensuring the safe and effective use of the product. We are also focusing on the lifecycle management of Xyrem, including seeking to enhance and enforce our intellectual property rights and to develop product, service and safety improvements for patients.

Our ability to maintain or increase Xyrem product sales is subject to risks and uncertainties, including those discussed in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K. In particular, seven companies have sent us notices that they have filed abbreviated new drug applications, or ANDAs, with the FDA seeking approval to market a generic version of Xyrem. We have filed lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and the litigation proceedings are ongoing. We cannot predict the timing or outcome of these proceedings. Although no trial date has been set in any of the ANDA suits, we anticipate that trial on some of the patents in the case against the first ANDA filer, Roxane Laboratories, Inc., or Roxane, could occur as early as the second quarter of 2016. Some of the ANDA filers have also filed petitions for *inter partes* review, or IPR, by the Patent Trial and Appeal Board, or the PTAB, of the U.S. Patent and Trademark Office, or USPTO, with respect to the validity of certain distribution, method of use and formulation patents covering Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to petitions related to certain patents covering the Xyrem distribution system, and we expect the PTAB to issue final decisions on the validity of these patents in July 2016. For a description of these matters, see “Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business. We expect that the approval of an ANDA that results in the launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In late August 2015, we implemented the final Xyrem risk evaluation and mitigation strategy, or REMS, which was approved by the FDA in February 2015. The process under which enrolled patients receive Xyrem is complex and includes multiple mandatory steps taken by the central pharmacy. The transition to the final approved REMS necessitated significant operational changes at the central pharmacy and revised documentation requirements for patients and prescribers. In the third quarter of 2015, Xyrem product sales were adversely impacted by operational disruption and resulting delays in prescription fills and refills. As physicians and patients familiarized themselves with the new REMS process and documentation requirements, the central pharmacy experienced a significantly increased volume of calls from patients and physicians’ offices that the pharmacy was not able to timely address, resulting in a backlog of prescription fills and refills that were delayed. We identified and addressed with the central pharmacy to the extent feasible the processes that led to the operational delays. In the fourth quarter of 2015, we observed an improvement in key operational metrics compared to the third quarter of 2015, and we believe that central pharmacy operations have stabilized. However, we cannot guarantee that we will not experience further disruptions and resulting adverse impacts on Xyrem product sales. Any failure to comply with the REMS obligations could result in enforcement action by the FDA; lead to changes in our Xyrem REMS obligations; continue to negatively affect sales of Xyrem; result in additional costs and expenses for us; and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects. Further, we cannot predict whether the FDA will seek to require or ultimately require modifications to the Xyrem REMS, including with respect to the distribution system, or seek to otherwise impose or ultimately impose additional requirements to the Xyrem REMS, or the potential timing, terms or propriety thereof. Any such modifications or additional requirements could potentially make it more difficult or expensive for us to distribute Xyrem, make it easier for future generic competitors, and/or negatively affect sales of Xyrem.

We may face pressure to develop a single shared REMS with potential generic competitors for Xyrem that is different from the approved Xyrem REMS or to license or share intellectual property pertinent to the Xyrem REMS, or elements of the Xyrem REMS, including proprietary data required for safe distribution of sodium oxybate, with generic competitors. The Xyrem REMS is the subject of multiple issued patents. In January 2014, the FDA held an initial meeting with us and the three then-current sodium oxybate ANDA applicants to facilitate the development of a single shared REMS for sodium oxybate. In October 2015, the FDA held a telephonic meeting with us and the seven current sodium oxybate ANDA applicants to discuss the status of the development of a single shared REMS for sodium oxybate. The parties had regular interactions with respect to developing a single shared REMS prior to this meeting, and we are seeking to continue the interactions with the goal of developing a single shared REMS. However, we are aware that, separate from the discussions with us, the FDA and ANDA applicants have exchanged communications regarding the potential development of a single shared REMS for sodium oxybate. We cannot predict whether, or to what extent, interactions among the parties will continue or whether we will develop a single shared REMS. If we do not develop a single shared REMS or license or share intellectual property pertinent to our Xyrem REMS with generic competitors within a time frame or on terms that the FDA considers acceptable, the FDA may assert that its waiver authority permits it to approve the ANDA of one or more generic competitors with a separate REMS that differs from our approved Xyrem REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the development of a single shared REMS for sodium oxybate, licensing or sharing intellectual property pertinent to our Xyrem REMS, or the FDA's response to a request by one or more ANDA applicants for a waiver of the requirement for a single shared REMS, including in connection with a certification that the applicant had been unable to obtain a license. In addition, the Federal Trade Commission, other governmental authorities or others could claim or determine that we are using the Xyrem REMS in an anticompetitive manner (including in light of the FDA's statement in the Xyrem REMS approval notice that the Xyrem REMS could be used in an anticompetitive manner inconsistent with applicable provisions of the Federal Food, Drug and Cosmetic Act) or have engaged in other anticompetitive practices.

Obtaining and maintaining appropriate reimbursement for Xyrem in the U.S. is increasingly challenging due to, among other things, the attention being paid to healthcare cost containment and prescription drug pricing, pricing pressure from third party payors and increasingly restrictive reimbursement conditions being imposed by third party payors. In this regard, we have experienced and expect to continue to experience increasing pressure from third party payors to agree to discounts, rebates or other pricing terms for Xyrem. Any such restrictive pricing terms or additional reimbursement conditions could have a material adverse effect on our Xyrem revenues. In addition, drug pricing by pharmaceutical companies has recently come under close scrutiny, particularly with respect to companies that have increased the price of products after acquiring those products from other companies. We expect that healthcare policies and reforms intended to curb healthcare costs will continue to be proposed, which could limit the prices that we charge for our products, including Xyrem, limit our commercial opportunity and/or negatively impact revenues from sales of our products. Also, price increases on Xyrem and our other products, and negative publicity regarding pricing and price increases generally, whether with respect to our products or products distributed by other pharmaceutical companies, could negatively affect market acceptance of Xyrem and our other products.

Erwinaze/Erwinase. Sales of our second largest product, Erwinaze/Erwinase (which we refer to in this report as Erwinaze unless otherwise indicated or the context otherwise requires), accounted for 15% of our net product sales in 2015 and 17% of our net product sales in 2014. We seek to maintain and increase sales of Erwinaze, as well as to make Erwinaze more widely available, through ongoing sales and marketing and research and development activities. However, our ability to successfully and sustainably maintain or grow sales of Erwinaze is subject to a number of risks and uncertainties, including the limited population of patients with ALL and the incidence of hypersensitivity reactions to *E. coli*-derived asparaginase within that population, our need to apply for and receive marketing authorizations, through the European Union's mutual recognition procedure or otherwise, in certain additional countries so we can launch promotional efforts in those countries, as well as those other risks and uncertainties discussed in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. In particular, a significant challenge to our ability to maintain current sales levels and to increase sales is our need to avoid supply interruptions of Erwinaze due to capacity constraints, production delays, quality or regulatory challenges or other manufacturing difficulties. Erwinaze is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL. The current manufacturing capacity for Erwinaze is nearly completely absorbed by demand for the product. We are working with PBL to evaluate potential expansion of its production capacity to increase the supply of Erwinaze over the longer term. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build an excess level of product inventory that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues, and we have experienced, and expect to continue to experience, manufacturing and inventory challenges that have resulted in disruptions in our ability to supply certain markets. If capacity constraints continue, whether as a result of continued quality or other manufacturing issues or otherwise, we may be unable to build a desired excess level of product inventory, and our ability to supply the market may continue to be compromised. Additional Erwinaze supply interruptions and/or our inability to expand production capacity could materially adversely affect our sales of and revenues from Erwinaze and our potential future maintenance and growth of the market for this product.

Defitelio/defibrotide. Sales of Defitelio/defibrotide were 5% of our net product sales in 2015. We acquired this product in January 2014 in connection with our acquisition of Gentium S.r.l., or Gentium, which we refer to as the Gentium Acquisition, and secured worldwide rights to the product by acquiring rights to defibrotide in the Americas in August 2014. We launched Defitelio in certain European countries in 2014 and continued to launch in additional European countries on a rolling basis through 2015. We are in the process of making pricing and reimbursement submissions with respect to Defitelio in those European countries where Defitelio is not yet launched, including in countries where pricing and reimbursement approvals are required for launch. Our ability to realize the anticipated benefits from our investment in Defitelio/defibrotide is subject to risks and uncertainties, including those discussed in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. In particular, we may not be able to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval in other countries, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. A key challenge to our success in maintaining or growing sales of Defitelio in Europe is our ability to obtain appropriate pricing and reimbursement approvals in those European countries where Defitelio is not yet launched. If we experience delays or unforeseen difficulties in obtaining favorable pricing and reimbursement approvals, planned launches in the affected countries would be delayed, or, if we are unable to ultimately obtain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country's reimbursed price influences other countries, our growth prospects in Europe could be negatively affected.

In September 2015, the FDA accepted for filing with priority review our NDA for defibrotide for the treatment of VOD with evidence of multi-organ dysfunction following HSCT. Based on timelines established by the PDUFA, we expect FDA review of the NDA to be completed by March 31, 2016. However, the FDA does not always meet the timelines established by PDUFA, and it is possible that the FDA's review of our NDA will not be completed by the PDUFA date, in which case our plans for commercialization of defibrotide in the U.S. may be delayed. In any event, we cannot predict whether our NDA will be approved in a timely manner, if at all. Approval of our NDA is dependent on our and our supplier's ability to obtain FDA certification of current Good Manufacturing Practices in connection with the manufacturing of the defibrotide drug compound and the processing of defibrotide into finished product for the U.S. market and on the outcome of FDA inspections of clinical sites and potentially other entities involved in the development of defibrotide. In 2015, the FDA issued a Form FDA 483 to Patheon Italia S.p.A., or Patheon Italia, that included observations related to the Ferentino, Italy facility that manufactures the defibrotide finished product. Failure by Patheon Italia to timely remediate the observations to the FDA's satisfaction or the discovery of issues that impact the defibrotide finished product could have an adverse impact on the potential approval of our NDA for defibrotide, including the timing thereof.

In the event we are able to obtain U.S. marketing approval, we will also face other challenges that could impact the anticipated value of Defitelio/defibrotide, including the limited size of the population of VOD patients who are indicated for treatment with Defitelio/defibrotide (particularly if the FDA requires more narrow or restricted labeling than we have proposed or if changes in HSCT treatment protocols reduce the incidence of VOD); U.S. market acceptance of defibrotide at its commercial price, particularly in light of past access to defibrotide free of charge through an expanded access treatment protocol; the need to establish U.S. pricing and reimbursement support for defibrotide, including through acceptance by hospital pharmacy and therapeutics committees; the possibility that we may be required to conduct time-consuming and costly clinical trials as a condition of any U.S. marketing approval for the product; the lack of experience of U.S. physicians in diagnosing and treating VOD; and challenges to our ability to develop the product for additional indications. If sales of Defitelio/defibrotide do not reach the levels we expect, our anticipated revenue from the product would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Other Developments

Over the past two years, we have made targeted investments to strengthen our operational capabilities to support our lead marketed products and product candidates in our primary therapeutic areas. During 2014, we reorganized our operations in Europe to focus on our hematology/oncology therapeutic area following the Gentium Acquisition and streamlined our U.S. commercial operations to devote more resources to our lead marketed products. In March 2015, we sold certain products and the related business that we acquired as part of our acquisition of EUSA Pharma Inc., or the EUSA Acquisition, to allow us to focus our European commercial operations on Erwinase and Defitelio. We also completed construction of a manufacturing and development facility in Ireland and expect to begin commercial operations at the facility in 2016.

In June 2015, we terminated our previous credit agreement and entered into a new credit agreement, which we refer to as the June 2015 credit agreement. The June 2015 credit agreement provides for a five-year $750.0 million principal amount term loan, which was drawn in full at closing, and a five-year $750.0 million revolving credit facility, of which $160.0 million was drawn at closing and subsequently repaid. We used the proceeds from borrowings under the June 2015 credit agreement to repay in full the amounts outstanding under the previous credit agreement. The June 2015 credit agreement provides a higher borrowing limit, more favorable interest rates and a longer maturity than our previous credit agreement. For more information, see "Liquidity and Capital Resources" in this Part II, Item 7 of this Annual Report on Form 10-K.

In August 2015, we completed repurchases under a share repurchase program that was initiated in May 2013. In November 2015, our board of directors authorized a new share repurchase program pursuant to which we are authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300 million, exclusive of any brokerage commissions. Under the current share repurchase program, which has no expiration date, we may repurchase our ordinary shares on the open market. The timing and amount of any repurchases will be at management's discretion and will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the June 2015 credit agreement, corporate and regulatory requirements and market conditions. The share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2015, we spent a total of $61.6 million to repurchase an aggregate of 0.4 million of our ordinary shares under the current program and the repurchase program initiated in 2013 at an average total purchase price, including commissions, of $150.24 per share. All ordinary shares repurchased by us were canceled.

Other Challenges and Risks

We anticipate that we will continue to face a number of challenges and risks to our business and our ability to execute our strategy in 2016. Some of these challenges and risks are specific to our business, and others are common to companies in the pharmaceutical industry with development and commercial operations. In addition to risks specifically related to Xyrem, Erwinaze and Defitelio/defibrotide, other key challenges and risks that we face include risks and uncertainties related to:

- the challenges of protecting and enhancing our intellectual property rights;
- the challenges of achieving and maintaining commercial success of our products;
- delays or problems in the supply or manufacture of our products, particularly with respect to certain products as to which we maintain limited inventories, and our dependence on single source suppliers to continue to meet our ongoing commercial demand or our requirements for clinical trial supplies;
- the need to obtain and maintain appropriate pricing and reimbursement for our products in an increasingly challenging environment due to, among other things, the attention being paid to healthcare cost containment and other austerity measures in the U.S. and worldwide, including the need to obtain and maintain reimbursement for Xyrem in the U.S. in an environment in which we are subject to increasingly restrictive conditions for reimbursement required by third party payors;
- our ability to identify and acquire, in-license or develop additional products or product candidates to grow our business;
- the challenges of compliance with the requirements of the FDA, the U.S. Drug Enforcement Administration, or DEA, and non-U.S. regulatory agencies, including with respect to product labeling, requirements for distribution, obtaining sufficient DEA quotas where needed, marketing and promotional activities, adverse event reporting and product recalls or withdrawals;
- the difficulty and uncertainty of pharmaceutical product development, including the timing thereof, and the uncertainty of clinical success, such as the risk that results from preclinical studies and/or early clinical trials may not be predictive of results obtained in later and larger clinical trials planned or anticipated to be conducted for our product candidates;
- the inherent uncertainty associated with the regulatory approval process, especially as we continue to undertake increased activities and make growing investment in our product pipeline development projects;
- the risks associated with business combination or product or product candidate acquisition transactions, such as the challenges inherent in the integration of acquired businesses with our historic business, the increase in geographic dispersion among our centers of operation and the risks that we may acquire unanticipated liabilities along with acquired businesses or otherwise fail to realize the anticipated benefits (commercial or otherwise) from such transactions; and
- possible restrictions on our ability and flexibility to pursue certain future opportunities as a result of our substantial outstanding debt obligations.

All of these risks are discussed in greater detail, along with other risks, in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K.

Results of Operations

The following table presents revenues and expenses for the years ended December 31, 2015, 2014 and 2013 (in thousands except percentages):

	2015	Change	2014 (1)	Change	2013
Product sales, net	$ 1,316,819	13%	$ 1,162,716	34%	$ 865,398
Royalties and contract revenues	7,984	(21)%	10,159	45%	7,025
Cost of product sales (excluding amortization and impairment of intangible assets)	102,526	(13)%	117,418	15%	102,146
Selling, general and administrative	449,119	11%	406,114	33%	304,303
Research and development	135,253	59%	85,181	105%	41,632
Acquired in-process research and development	—	N/A(2)	202,626	N/A(2)	4,988
Intangible asset amortization	98,162	(22)%	126,584	60%	79,042
Impairment charges	31,523	(20)%	39,365	N/A(2)	—
Interest expense, net	56,917	8%	52,713	96%	26,916
Foreign currency (gain) loss	(1,445)	(83)%	(8,683)	N/A(2)	1,697
Loss on extinguishment and modification of debt	16,815	N/A(2)	—	N/A(2)	3,749
Income tax provision	106,399	13%	94,231	3%	91,638
Net loss attributable to noncontrolling interests, net of tax	(1)	N/A(2)	(1,061)	N/A(2)	—

(1) Our financial results include the financial results of the historic Gentium business since the closing of the Gentium Acquisition on January 23, 2014.
(2) Comparison to prior period is not meaningful.

Revenues

The following table presents product sales, royalties and contract revenues, and total revenues for the years ended December 31, 2015, 2014 and 2013 (in thousands except percentages):

	2015	Change	2014	Change	2013
Xyrem	$ 955,187	23%	$ 778,584	37%	$ 569,113
Erwinaze/Erwinase	203,261	2%	199,665	15%	174,251
Defitelio/defibrotide	70,731	—%	70,537	N/A(1)	—
Prialt® (ziconotide) intrathecal infusion	26,440	—%	26,421	(3%)	27,103
Psychiatry	37,135	(9%)	40,879	(17%)	49,226
Other	24,065	(48%)	46,630	2%	45,705
Product sales, net	1,316,819	13%	1,162,716	34%	865,398
Royalties and contract revenues	7,984	(21%)	10,159	45%	7,025
Total revenues	$ 1,324,803	13%	$ 1,172,875	34%	$ 872,423

(1) Comparison to prior period is not meaningful.

Product Sales, Net

Xyrem product sales increased by 23% in 2015 and by 37% in 2014 compared to the immediately preceding years, primarily due to higher average net selling prices in the 2015 and 2014 periods and, to a lesser extent, increases in sales volume. Price increases were instituted in February 2015, August 2014 and February 2014. Xyrem product sales volumes increased by 6% and 10% in 2015 and 2014, respectively, compared to the immediately preceding years. The sales volume increases in both periods were driven by an increase in the average number of patients on Xyrem, which includes new patients, patients who have restarted Xyrem therapy and active patients who remained on Xyrem therapy. In late August 2015, we implemented the final REMS that was approved by the FDA in February 2015. In the third quarter of 2015, Xyrem product sales were adversely impacted by operational disruption and resulting delays in prescription fills and refills. In the fourth quarter of 2015, we observed an improvement in key operational metrics compared to the third quarter of 2015. Erwinaze

product sales increased by 2% in 2015 compared to 2014, primarily due to an increase in sales volume and, to a lesser extent, price increases instituted in January 2015 and July 2015, partially offset primarily by higher chargebacks and rebates resulting from increased utilization under the 340B drug pricing discount and Medicaid programs and, to a lesser extent, the impact of foreign exchange on sales made in euro. Erwinaze product sales increased by 15% in 2014 compared to 2013, primarily due to an increase in sales volume and, to a lesser extent, price increases instituted in January 2014 and July 2014. The Erwinaze sales volume increases in 2015 and 2014 were primarily driven by existing treatment sites identifying additional ALL patients with hypersensitivity to *E. coli*-derived asparaginase and, to a lesser extent, growth in new treatment sites prescribing Erwinaze. Defitelio/defibrotide product sales were consistent in 2015 compared to 2014, beginning from the closing of the Gentium Acquisition on January 23, 2014, and included a sales volume increase of 19% which was partially offset by the impact of foreign exchange on sales made in euro. On a pro forma basis, assuming the Gentium Acquisition had closed on January 1, 2014, Defitelio/defibrotide product sales decreased by 4% in 2015 compared to 2014, primarily due to the impact of foreign exchange on sales made in euro, partially offset by an increase in sales volumes of 13%. On a pro forma basis, Defitelio/defibrotide product sales were $73.4 million in 2014 compared with $44.6 million in 2013. Defitelio/defibrotide product sales increased, on a pro forma basis, in 2014 compared to 2013 primarily due to territory-specific price increases instituted in April 2013, continuing roll-out to new launch territories and commercial pricing in launch territories. Prior to the commercial launch of Defitelio in Europe in March 2014 we provided, and we continue to provide, access to defibrotide to patients where it is not commercially available. Prialt product sales were consistent in 2015 compared to 2014 and decreased by 3% in 2014 compared to 2013. Psychiatry product sales decreased in 2015 and 2014 compared to the immediately preceding years primarily due to the impact of generic competition. Other product sales decreased by 48% in 2015 compared to 2014, primarily due to our disposition, in March 2015, of certain products and the related business that we originally acquired in the EUSA Acquisition. Other product sales in 2014 increased slightly compared to 2013. We expect total product sales will increase in 2016 over 2015, primarily due to anticipated growth in sales of our lead marketed products, partially offset by decreases in sales of certain other products.

Royalties and Contract Revenues

Royalties and contract revenues decreased in 2015 compared to 2014 and increased in 2014 compared to 2013, primarily due to a $2.0 million milestone payment we received in 2014 under an agreement with UCB Pharma Limited, or UCB, under which UCB has the right to market Xyrem for certain indications in various countries outside of the U.S. We expect royalties and contract revenues in 2016 to increase slightly compared to 2015, primarily due to higher royalties on our out-licensed products.

Cost of Product Sales

Cost of product sales decreased in 2015 compared to 2014, primarily due to a decrease in acquisition accounting inventory fair value step-up adjustments of $10.5 million and a change in product mix, partially offset by an increase in sales. Cost of product sales increased in 2014 compared to 2013, primarily due to increased sales and an increase of $6.7 million in acquisition accounting inventory fair value step-up adjustments. Gross margins as a percentage of net product sales were 92.2%, 89.9% and 88.2% in 2015, 2014 and 2013, respectively. The increase in our gross margin percentage in 2015 compared to 2014 was primarily due to a change in product mix and a decrease in acquisition accounting inventory fair value step-up adjustments. The increase in our gross margin percentage in 2014 compared to 2013 was primarily due to higher net product sales partially offset by an increase in acquisition accounting inventory fair value step-up adjustments. We expect that our gross margin in 2016 will be higher compared to 2015, primarily due to increased net product sales.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased in 2015 compared to 2014, primarily due to an increase in compensation-related expenses of $23.6 million driven by higher headcount, an increase in other expenses related to the expansion of our business of $28.9 million and a one-time charge of $18.0 million for settlement of a contract claim originally asserted against Azur Pharma prior to the Azur Merger, partially offset by a decrease in transaction and integration expenses of $27.5 million. Selling, general and administrative expenses increased in 2014 compared to 2013, primarily due to an increase in compensation-related expenses of $48.2 million driven by higher headcount primarily due to our expanded business and the Gentium Acquisition, an increase in other expenses related to the expansion of our business of $46.7 million and an increase in transaction and integration expenses of $22.1 million, partially offset by a $15.2 million change in fair value of contingent consideration in connection with the EUSA Acquisition in 2012 in which we agreed to make a contingent payment of $50.0 million in cash if Erwinaze achieved net sales in the U.S. of $124.5 million or more in 2013. We expect selling, general and administrative expenses in 2016 to increase compared to 2015, primarily due to expenses related to the potential launch of defibrotide in the U.S., an increase in expenses related to REMS and pharmacy services and an increase in compensation-related expenses driven by higher headcount.

Research and Development Expenses

Research and development expenses consist primarily of costs related to clinical studies and outside services, personnel expenses, milestone payments and other research and development costs. Clinical study and outside services costs relate primarily to services performed by clinical research organizations, materials and supplies, and other third party fees. Personnel expenses relate primarily to salaries, benefits and share-based compensation. Other research and development expenses primarily include overhead allocations consisting of various support and facilities-related costs. We do not track fully-burdened research and development expenses on a project-by-project basis. We manage our research and development expenses by identifying the research and development activities that we anticipate will be performed during a given period and then prioritizing efforts based on our assessment of which development activities are important to our business and have a reasonable probability of success, and by dynamically allocating resources accordingly. We also continually review our development pipeline projects and the status of their development and, as necessary, reallocate resources among our development pipeline projects that we believe will best support the future growth of our business.

The following table provides a breakout of our research and development expenses by major categories of expense (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Clinical studies and outside services	$ 63,079	$ 41,769	16,385
Personnel expenses	39,515	38,228	22,019
Milestone	25,000	—	—
Other	7,659	5,184	3,228
Total	$ 135,253	$ 85,181	$ 41,632

Research and development expenses increased by $50.1 million in 2015 compared to 2014, primarily due to a $25.0 million milestone expense that was triggered by the acceptance for filing by the FDA of our NDA for defibrotide for VOD and increased clinical studies and outside services costs driven primarily by initiation of Phase 3 clinical trials relating to JZP-110. Research and development expenses increased by $43.5 million in 2014 compared to 2013, primarily due to increased clinical studies and outside services costs of $25.4 million as a result of higher costs incurred to develop our sleep and hematology/oncology product candidates as well as the addition of costs related to development programs for defibrotide. Personnel expenses in 2015 were in line with 2014. Personnel expenses increased by $16.2 million in 2014 compared to 2013, primarily due to salary and benefit-related expenses (including share-based compensation) in support of our development programs and, to a lesser extent, increased headcount due to the Gentium Acquisition.

For 2016 and beyond, we expect that our research and development expenses will continue to increase from historical levels particularly as we initiate additional clinical trials and related development work and potentially acquire rights to additional product candidates. A discussion of the risks and uncertainties with respect to our research and development activities, including completing the development of our product candidates, and the consequences to our business, financial position and growth prospects can be found in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K.

Acquired In-Process Research and Development

In 2014, we acquired the rights to defibrotide in the Americas from Sigma-Tau Pharmaceuticals, Inc., or Sigma-Tau, for an upfront payment of $75.0 million, and we also acquired the worldwide development, manufacturing and commercial rights to JZP-110, other than in certain jurisdictions in Asia where SK retained rights, for an upfront payment of $125.0 million to Aerial. In 2014, we also paid a $2.0 million milestone to SK, which was triggered on assignment of the JZP-110 rights from Aerial to us. In 2014, we paid $0.6 million in license fees in connection with JZP-416. In 2013, we incurred $4.0 million in upfront license fees in connection with our licensing of JZP-386 and $1.0 million in license fees with respect to JZP-416.

Intangible Asset Amortization

Intangible asset amortization decreased in 2015 compared to 2014, due to the cessation of amortization of intangible assets classified as assets held for sale as of December 31, 2014 and certain other intangible assets that were fully amortized in 2014 and the impact of foreign exchange rates on euro denominated assets. The increase in intangible asset amortization in 2014 compared to 2013 was primarily due to the amortization expense related to the intangible assets acquired in the Gentium Acquisition. Intangible asset amortization is not expected to change materially in 2016 compared to 2015.

Impairment Charges

In the fourth quarter of 2015, we recorded an impairment charge of $31.5 million related to our acquired in-process research and development, or IPR&D, asset as a result of our decision to terminate a pivotal Phase 2 clinical trial of JZP-416. In 2014, we recorded impairment charges of $39.4 million related to certain products acquired as part of the EUSA Acquisition that we sold in March 2015.

Interest Expense, Net

Interest expense, net increased in 2015 compared to 2014, primarily due to the inclusion of a full year of interest expense on the 2021 Notes, partially offset by a reduction in interest rates on borrowings under the June 2015 credit agreement compared to our previous credit agreement. In August 2014, we issued $575.0 million principal amount of the 2021 Notes, which remained outstanding at December 31, 2015. In June 2015, we refinanced our existing term loans and revolving credit facility which reduced the interest rate on our term loan and revolving credit facility borrowings. As of December 31, 2015, $740.6 million principal amount of term loan was outstanding under the June 2015 credit agreement and the interest rate was 2.36%. As of December 31, 2015, there were no borrowings outstanding under our revolving credit facility. Interest expense, net increased in 2014 compared to 2013, primarily due to a larger average debt balance, partially offset by a decrease in interest rates associated with our term loan borrowings. We expect interest expense will be lower in 2016 compared to 2015 due to a decrease in our average debt balance and the reduction in interest rates on borrowings under the June 2015 credit agreement compared to our previous credit agreement.

Foreign Currency (Gain) Loss

The foreign currency gain in 2015 and 2014 primarily related to the translation of euro denominated net monetary liabilities, including intercompany balances, held by subsidiaries with a U.S. dollar functional currency. The foreign currency loss in 2013 related to the translation of foreign currency monetary assets and liabilities, including intercompany balances.

Loss on Extinguishment and Modification of Debt

In 2015, we recorded a loss of $16.8 million in connection with the refinancing of our term loans and revolving credit facility in June 2015, which was comprised of $16.0 million related to the expensing of unamortized deferred financing costs and unamortized original issue discount associated with extinguished debt and $0.8 million related to new third party fees associated with the modification of existing debt. We recorded a loss on extinguishment and modification of debt of $3.7 million in 2013 in connection with the refinancing of the term loans then outstanding.

Income Tax Provision

Our income tax provision was $106.4 million, $94.2 million and $91.6 million in 2015, 2014 and 2013, respectively. The effective tax rates for 2015, 2014 and 2013 were 24.4%, 62.2% and 29.8%, respectively. After adjusting the income before income tax provision for 2014 by excluding a total of $202.0 million in upfront and milestone payments for rights to JZP-110 and to defibrotide in the Americas, which were acquired by our subsidiaries in a non-taxable jurisdiction, the effective tax rate on the resulting income before income tax provision for 2014 was 26.7%. The effective tax rate for 2015 was higher than the Irish statutory rate of 12.5%, primarily due to income taxable at a rate higher than the Irish statutory rate, unrecognized tax benefits, and various expenses not deductible for tax purposes, partially offset by originating tax credits, deductions available in relation to subsidiary equity and reductions in tax rates in certain jurisdictions. The effective tax rates for 2014 and 2013 were higher than the Irish statutory rate of 12.5%, primarily due to income taxable at a rate higher than the Irish statutory rate, unrecognized tax benefits, current year losses in some jurisdictions for which no tax benefit is available and various expenses not deductible for tax purposes, partially offset by changes in U.S. state valuation allowances in 2014 and benefits from certain originating income tax credits. The decrease in the effective tax rate in 2015 compared to 2014 was primarily due to changes in income mix among the various jurisdictions in which we operate, increased originating tax credits, increased deductions available in relation to subsidiary equity and reductions in tax rates in certain jurisdictions, partially offset by the impact of impairments of intangible assets and changes in U.S. state valuation allowances during 2014. The decrease in the effective tax rate, after excluding the upfront and milestone payments, for 2014 compared to 2013 was primarily due to changes in income mix among the various jurisdictions in which we operate, changes in U.S. state valuation allowances and benefits from certain originating income tax credits.

Net Loss Attributable to Noncontrolling Interests, Net of Tax

Net loss attributable to noncontrolling interests, net of tax relates to the portion of the net loss of Gentium not attributable, directly or indirectly, to our ownership interest. During 2015, we acquired the remaining noncontrolling interests in Gentium.

Non-GAAP Financial Measures

To supplement our financial results presented on a U.S. generally accepted accounting principles, or GAAP basis, we use certain non-GAAP, also referred to as adjusted or non-GAAP adjusted, financial measures as shown in the table below. We believe that each of these non-GAAP financial measures is helpful in understanding our past financial performance and potential future results, particularly in light of the effect of various acquisition and divestiture transactions effected by us. They are not meant to be considered in isolation or as a substitute for comparable GAAP measures and should be read in conjunction with our consolidated financial statements prepared in accordance with GAAP. Our management regularly uses these supplemental non-GAAP financial measures internally to understand, manage and evaluate our business and make operating decisions. Compensation of our executives is based in part on the performance of our business based on certain of these non-GAAP financial measures. In addition, we believe that the presentation of these non-GAAP financial measures is useful to investors because it enhances the ability of investors to compare our results from period to period and allows for greater transparency with respect to key financial metrics we use in making operating decisions, and also because our investors and analysts regularly use them to model and track our financial performance. Investors should note that these non-GAAP financial measures are not prepared under any comprehensive set of accounting rules or principles and do not reflect all of the amounts associated with our results of operations as determined in accordance with GAAP. Investors should also note that these non-GAAP financial measures have no standardized meaning prescribed by GAAP and, therefore, have limits in their usefulness to investors. In addition, from time to time there may be other items that we may exclude for purposes of our non-GAAP financial measures, and we have ceased, and may in the future cease, to exclude items that we have historically excluded for purposes of our non-GAAP financial measures. In this regard, in 2015, we no longer included an adjustment for depreciation expense in our non-GAAP financial measures. For purposes of comparability, non-GAAP adjusted financial measures for 2014 and 2013 do not include an adjustment for depreciation expense. In addition, because of the non-standardized definitions of non-GAAP financial measures, the non-GAAP financial measures used in this Annual Report on Form 10-K may be calculated differently from, and therefore may not be directly comparable to, similarly titled measures used by our competitors and other companies.

Reconciliations of GAAP reported net income attributable to Jazz Pharmaceuticals plc to non-GAAP adjusted net income attributable to Jazz Pharmaceuticals plc and the related per share amounts are as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2015	2014 (1)	2013 (1)
GAAP reported net income attributable to Jazz Pharmaceuticals plc	$ 329,535	$ 58,387	$ 216,312
Intangible asset amortization	98,162	126,584	79,042
Share-based compensation expense	91,550	69,638	44,551
Impairment charges	31,523	39,365	—
Upfront and milestone payments	25,000	202,626	4,988
Transaction and integration related costs (2)	18,155	28,840	6,240
Restructuring charges	1,641	1,941	1,457
Acquisition accounting inventory fair value step-up adjustments	—	10,477	3,826
Change in fair value of contingent consideration	—	—	15,200
Non-cash interest expense	22,738	13,725	4,591
Loss on extinguishment and modification of debt	16,815	—	3,749
Income tax adjustments (3)	(35,009)	(29,620)	5,253
Adjustments for amount attributable to noncontrolling interests (4)	(2)	(1,506)	—
Non-GAAP adjusted net income attributable to Jazz Pharmaceuticals plc	$ 600,108	$ 520,457	$ 385,209
GAAP reported net income attributable to Jazz Pharmaceuticals plc per diluted share	$ 5.23	$ 0.93	$ 3.51
Non-GAAP adjusted net income attributable to Jazz Pharmaceuticals plc per diluted share	$ 9.52	$ 8.31	$ 6.26
Weighted-average ordinary shares used in diluted per share calculation	63,036	62,614	61,569

(1) For purposes of comparability with our 2015 presentation, non-GAAP adjusted financial measures for 2014 and 2013 do not include an adjustment for depreciation expense.
(2) In 2014, the adjustment was primarily related to the Gentium Acquisition. In 2015, the adjustment was primarily related to a one-time charge of $18.0 million for settlement of a contract claim that was originally asserted against Azur Pharma prior to the Azur Merger.
(3) Tax adjustments to convert the income tax provision to the estimated amount of taxes payable in cash.
(4) The noncontrolling interests' share of the above adjustments, as applicable.

Liquidity and Capital Resources

As of December 31, 2015, we had cash and cash equivalents of $988.8 million, borrowing availability under our revolving credit facility of $748.9 million and a long-term debt principal amount of $1.3 billion. Our long-term debt included our $740.6 million aggregate principal amount term loan, $575.0 million principal amount of the 2021 Notes and other borrowings of $0.5 million. During 2015, 2014 and 2013, we generated cash flows from operations of $531.9 million, $405.8 million and $288.4 million, respectively, and we expect to continue to generate positive cash flow from operations.

On June 18, 2015, we entered into the June 2015 credit agreement and terminated our previous credit agreement. The June 2015 credit agreement provides for a five-year $750.0 million principal amount term loan, which was drawn in full at closing, and a five-year $750.0 million revolving credit facility, of which $160.0 million was drawn at closing and subsequently repaid. We used the proceeds from initial borrowings under the June 2015 credit agreement to repay in full the $893.1 million principal amount of term loans outstanding under the previous credit agreement and to pay related fees and expenses. We expect to use future loans under the new revolving credit facility, if any, for general corporate purposes, including potential business development activities.

In March 2015, we sold certain products and the related business that we originally acquired as part of the EUSA Acquisition. The purchase price for the products and related business was $34.0 million, subject to pre- and post-closing purchase price adjustments.

We believe that our existing cash balances, cash we expect to generate from operations and funds available under our revolving credit facility will be sufficient to fund our operations and to meet our existing obligations for the foreseeable future, including our obligations under the June 2015 credit agreement. The adequacy of our cash resources depends on many assumptions, including primarily our assumptions with respect to product sales and expenses, as well as the other factors set forth in "Risk Factors" under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales," and "*To continue to grow our business, we will need to commit substantial resources, which could result in future losses or otherwise limit our opportunities or affect our ability to operate our business,*" in Part I, Item 1A of this Annual Report on Form 10-K. Our assumptions may prove to be wrong or other factors may adversely affect our business, and as a result we could exhaust or significantly decrease our available cash resources and we may not be able to generate sufficient cash to service our debt obligations which could, among other things, force us to raise additional funds and/or force us to reduce our expenses, either of which could have a material adverse effect on our business.

To continue to grow our business over the longer term, we plan to commit substantial resources to product acquisition and in-licensing, product development, clinical trials of product candidates and expansion of our commercial, manufacturing and other operations. In this regard, we have evaluated and expect to continue to evaluate a wide array of strategic transactions as part of our strategy to acquire or in-license and develop additional products and product candidates. Acquisition opportunities that we pursue could materially affect our liquidity and capital resources and may require us to incur additional indebtedness, seek equity capital or both. In addition, we may pursue new operations or continue the expansion of our existing operations. Accordingly, we expect to continue to opportunistically seek access to additional capital to license or acquire additional products, product candidates or companies to expand our operations or for general corporate purposes. Raising additional capital could be accomplished through one or more public or private debt or equity financings, collaborations or partnering arrangements. Any equity financing would be dilutive to our shareholders, and the consent of the lenders under the June 2015 credit agreement could be required for certain financings.

In May 2013, our board of directors authorized a share repurchase program pursuant to which we were authorized to repurchase a number of ordinary shares having an aggregate repurchase price of up to $200.0 million, exclusive of any brokerage commissions. As of August 2015, we had completed this share repurchase program. On November 5, 2015, our board of directors authorized a new share repurchase program pursuant to which we are authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300.0 million, exclusive of any brokerage commissions. Under this share repurchase program, which has no expiration date, we may repurchase ordinary shares from time to time on the open market. The timing and amount of repurchases will be at management's discretion and will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the June 2015 credit agreement, corporate and regulatory requirements and market conditions. The share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2015, we spent a total of $61.6 million to repurchase 0.4 million of our ordinary shares under both share repurchase programs at an average total purchase price, including brokerage commissions, of $150.24 per share. All ordinary shares repurchased were canceled. As of December 31, 2015, the remaining amount authorized under the new share repurchase program was $259.8 million.

The following table shows a summary of our cash flows for the periods indicated (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Net cash provided by operating activities	$ 531,943	$ 405,765	$ 288,431
Net cash used in investing activities	(2,255)	(1,067,649)	(16,264)
Net cash provided by (used in) financing activities	(214,323)	712,875	(23,856)
Effect of exchange rates on cash and cash equivalents	(10,622)	(3,453)	997
Net increase in cash and cash equivalents	$ 304,743	$ 47,538	$ 249,308

Net cash provided by operating activities in 2015 related to net income of $329.5 million, adjusted for non-cash items of $208.5 million primarily related to intangible asset amortization, share-based compensation expense, impairment charges, amortization of debt discount and deferred financing costs and loss on extinguishment and modification of debt, which was partially offset by a net cash outflow of $6.1 million due to changes in operating assets and liabilities. Net cash provided by operating activities in 2014 related to net income of $57.3 million, adjusted for upfront and milestone payments totaling $202.6 million primarily in connection with our acquisition of rights to JZP-110 and to defibrotide in the Americas and non-cash items of $212.2 million primarily related to intangible asset amortization, share-based compensation expense, impairment charges, amortization of debt discount and deferred financing costs, acquisition accounting inventory fair value step-up adjustments and deferred income taxes. This was partially offset by $66.3 million of net cash outflow related to changes in operating assets and liabilities which included an increase of $55.0 million in our accounts receivable, primarily due to an increase in sales, and $14.9 million in respect of the payment of the contingent consideration in connection with the EUSA Acquisition. Net cash provided by operating activities in 2013 related to net income of $216.3 million, adjusted for non-cash items of $153.3 million,

primarily related to intangible asset amortization, share-based compensation expense and the change in fair value of contingent consideration. This was partially offset by $81.0 million of net cash outflow related to changes in operating assets and liabilities which included an increase in accounts receivable of $48.8 million, primarily related to a pre-negotiated change in payment terms under a long-term contract with one large customer in connection with the elimination of a prompt pay discount as well as the impact of income tax payments.

Net cash used in investing activities in 2015 related to purchases of property and equipment of $36.0 million primarily related to the construction of a manufacturing and development facility in Ireland, partially offset by net proceeds of $33.7 million from the sale of certain products and the related business that we originally acquired as part of the EUSA Acquisition. Net cash used in investing activities in 2014 primarily related to the funding of the Gentium Acquisition, the acquisition of rights to JZP-110 and to defibrotide in the Americas and, to a lesser extent, expenditures related to property and equipment. Net cash used in investing activities in 2013 primarily related to purchases of property and equipment and acquisition of IPR&D.

Net cash used in financing activities in 2015 primarily related to repayments of long-term debt of $905.8 million primarily for the total principal amount of term loans outstanding under a previous credit agreement, repayment of $160.0 million of borrowings under the revolving credit facility provided for under the June 2015 credit agreement, $61.6 million used to repurchase our ordinary shares under our previous and current share repurchase programs and payment of employee withholding taxes of $26.1 million related to share-based awards, partially offset by proceeds from borrowings totaling $898.6 million under the June 2015 credit agreement and proceeds of $40.5 million from employee equity incentive and purchase plans. Net cash provided by financing activities in 2014 primarily related to net proceeds of $1,194.4 million from long-term debt and proceeds of $58.5 million from employee equity incentive and purchase plans and exercise of warrants, partially offset by repayment of $300.0 million borrowings under the revolving credit facility provided for under a previous credit agreement, $137.0 million for the acquisition of noncontrolling interests in Gentium, $35.1 million in respect of the payment of the contingent consideration in connection with the EUSA Acquisition and $42.2 million used to repurchase our ordinary shares under our previous share repurchase program. Net cash used in financing activities in 2013 primarily related to repayments of long-term debt of $465.9 million, primarily for the full principal amount outstanding under previous term loans, $136.5 million used to repurchase our ordinary shares under our previous share repurchase program and payment of employee withholding taxes of $5.6 million related to share-based awards, partially offset by net proceeds of $553.4 million from previous term loans and proceeds of $30.7 million from employee equity incentive and purchase plans and exercise of warrants.

Credit Agreement

On June 18, 2015, Jazz Pharmaceuticals plc, as guarantor, and certain of its wholly owned subsidiaries, as borrowers, entered into the June 2015 credit agreement, which provides for a $750.0 million principal amount term loan, which was drawn in full at closing, and a $750.0 million revolving credit facility, of which $160.0 million was drawn at closing and subsequently repaid. We used the proceeds from initial borrowings under the June 2015 credit agreement to repay in full the $893.1 million principal amount of term loans outstanding under the previous credit agreement and to pay related fees and expenses. The previous credit agreement was terminated upon repayment of the term loans under this agreement.

Under the June 2015 credit agreement, the term loan matures on June 18, 2020 and the revolving credit facility terminates, and any loans outstanding thereunder become due and payable, on June 18, 2020.

Borrowings under the June 2015 credit agreement bear interest, at our option, at a rate equal to either (a) the LIBOR rate, plus an applicable margin ranging from 1.50% to 2.25% per annum, based upon our secured leverage ratio, or (b) the prime lending rate, plus an applicable margin ranging from 0.50% to 1.25% per annum, based upon our secured leverage ratio. The revolving credit facility has a commitment fee payable on the undrawn amount ranging from 0.25% to 0.35% per annum based upon our secured leverage ratio.

As of December 31, 2015, the interest rate on the term loan was 2.36% and the effective interest rate was 2.38%. As of December 31, 2015, we had undrawn revolving credit facilities totaling $750.0 million of which $1.1 million was committed for an outstanding letter of credit.

Jazz Pharmaceuticals plc and certain of our wholly owned subsidiaries are borrowers under the June 2015 credit agreement. The borrowers' obligations under the credit agreement, and any hedging or cash management obligations entered into with a lender, are guaranteed on a senior secured basis by Jazz Pharmaceuticals plc and certain of its subsidiaries (including the issuer of the 2021 Notes as described below) and are secured by substantially all of Jazz Pharmaceuticals plc's, the borrowers' and the guarantor subsidiaries' assets.

We may make voluntary prepayments of principal at any time without payment of a premium. We are required to make mandatory prepayments of the term loan (without payment of a premium) with (1) net cash proceeds from certain non-ordinary

course asset sales (subject to reinvestment rights and other exceptions), (2) net cash proceeds from issuances of debt (other than certain permitted debt), and (3) casualty proceeds and condemnation awards (subject to reinvestment rights and other exceptions).

Principal repayments of the term loan, which are due quarterly, began in December 2015 and are equal to 5.0% per annum of the original principal amount of $750.0 million during the first two years, 7.5% per annum during the third year, 10.0% per annum during the fourth year and 12.5% per annum during the fifth year, with any remaining balance payable on the maturity date.

The June 2015 credit agreement contains customary representations and warranties and customary affirmative and negative covenants applicable to us and our restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness and dividends and other distributions. The June 2015 credit agreement contains financial covenants that require us not to (a) exceed a maximum secured net leverage ratio or (b) fall below a cash interest coverage ratio. We were, as of December 31, 2015, and are currently in compliance with these financial covenants.

Exchangeable Senior Notes

In August 2014, Jazz Pharmaceuticals plc, through its wholly owned finance subsidiary Jazz Investments I Limited, completed a private placement of $575.0 million principal amount of the 2021 Notes. The 2021 Notes are the senior unsecured obligations of Jazz Investments I Limited and are fully and unconditionally guaranteed on a senior unsecured basis by Jazz Pharmaceuticals plc. Interest on the 2021 Notes is payable semi-annually in cash in arrears on February 15 and August 15 of each year, beginning on February 15, 2015, at a rate of 1.875% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2021 Notes. The 2021 Notes mature on August 15, 2021, unless earlier exchanged, repurchased or redeemed.

The holders of the 2021 Notes have the ability to require us to repurchase all or a portion of their 2021 Notes for cash in the event we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution or the delisting of our ordinary shares from The NASDAQ Global Select Market. Prior to August 15, 2021, we may redeem the 2021 Notes, in whole but not in part, subject to compliance with certain conditions, if we have, or on the next interest payment date would, become obligated to pay to the holder of any 2021 Note additional amounts as a result of certain tax-related events. We also may redeem the 2021 Notes on or after August 20, 2018, in whole or in part, if the last reported sale price per ordinary share 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 we provide the notice of redemption.

The 2021 Notes are exchangeable at an initial exchange rate of 5.0057 ordinary shares per $1,000 principal amount of 2021 Notes, which is equivalent to an initial exchange price of approximately $199.77 per ordinary share. Upon exchange, the 2021 Notes may be settled in cash, ordinary shares or a combination of cash and ordinary shares, at our election. Our intent and policy is to settle the principal amount of the 2021 Notes in cash upon exchange. 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 make-whole fundamental changes occurring prior to the maturity date of the 2021 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2021 Notes who elect to exchange their 2021 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to February 15, 2021, the 2021 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

Contractual Obligations

The table below presents a summary of our contractual obligations as of December 31, 2015 (in thousands):

	Payments due by period				
Contractual Obligations (1)	**Total**	**Less than 1 Year**	**1-3 Years**	**3-5 Years**	**More than 5 years**
Term and other loans - principal	$ 741,138	$ 37,587	$ 103,314	$ 600,209	$ 28
Term and other loans - interest (2)	68,562	17,433	31,784	19,345	—
2021 Notes - principal	575,000	—	—	—	575,000
2021 Notes - interest (3)	64,688	10,781	21,563	21,563	10,781
Revolving credit facility - commitment fee (4)	10,179	2,284	4,556	3,339	—
Purchase obligations (5)	99,022	97,461	400	431	730
Operating and facility lease obligations (6)	113,238	11,757	21,019	13,900	66,562
Total	$ 1,671,827	$ 177,303	$ 182,636	$ 658,787	$ 653,101

(1) This table does not include potential future milestone payment or royalty obligations to third parties under asset purchase, product development, license and other agreements as the timing and likelihood of such milestone payments are not known, and, in the case of royalty obligations, as the amount of such obligations are not estimable. In 2014, we signed a definitive agreement with Aerial under which we acquired worldwide development, manufacturing and commercial rights to JZP-110 (other than in certain jurisdictions in Asia where SK retains rights). Aerial and SK are currently eligible to receive milestone payments up to an aggregate of $270.0 million based on development, regulatory and sales milestones and tiered royalties from high single digits to mid-teens based on potential future sales of JZP-110. In 2014, we entered into a definitive agreement to acquire rights to defibrotide in the U.S. and all other countries in the Americas from Sigma-Tau. In 2015, the FDA accepted for filing with priority review our NDA for defibrotide and, as a result, a milestone payment of $25.0 million was made to Sigma-Tau. Sigma-Tau is eligible to receive up to an additional $150.0 million based on the timing of potential FDA approval of defibrotide for VOD. Potential future milestone payments to other third parties under other agreements could be up to an aggregate of $250.0 million, of which up to $120.0 million will become due and payable to Perrigo Company plc (formerly Elan Pharmaceuticals, Inc.) in tiered contingent payments, with the first such payment becoming due if net sales of Prialt of at least $75.0 million are achieved in a calendar year. The remainder would become due and payable to other third parties upon the achievement of certain developmental, clinical, regulatory and/or commercial milestones, the timing and likelihood of which are not known. We are also obligated under these agreements to pay royalties on net sales of certain products at specified rates, which royalties are dependent on future product sales and are not provided for in the table above as they are not estimable.

(2) Estimated interest was calculated based on the interest rates in effect as of December 31, 2015. The interest rate for our term loan was 2.36% at December 31, 2015.

(3) We used the fixed interest rate of 1.88% to estimate interest owed on the 2021 Notes as of December 31, 2015 until the final maturity date in August 2021.

(4) Our revolving credit facility has a commitment fee payable on the undrawn amount ranging from 0.25% to 0.35% per annum based upon our secured leverage ratio. In the table above, we used a rate of 0.30% and assumed undrawn amounts of $748.9 million as of December 31, 2015 to estimate commitment fees owed. Undrawn borrowing capacity does not include an amount of $1.1 million committed under an outstanding letter of credit.

(5) Consists primarily of non-cancelable commitments to third party manufacturers.

(6) Includes automobile lease payments for our sales force and the minimum lease payments for our office buildings, including a lease agreement we entered into in January 2015 to lease office space located in Palo Alto, California. We expect to occupy this office space by the end of 2017. We are obligated to make lease payments totaling approximately $88 million over the initial term of the lease. Not included in the table above are our estimated costs of approximately $20 million associated with the design, development and construction of tenant improvements under this lease agreement, which estimate does not include a tenant improvement allowance to be provided by the landlord. Operating expenses associated with our leased office buildings are also not included in table above.

No provision for income tax in Ireland has been recognized on undistributed earnings of our foreign subsidiaries because we consider such earnings to be indefinitely reinvested. Cumulative unremitted earnings of our foreign subsidiaries totaled approximately $983.8 million at December 31, 2015. In the event of the distribution of those earnings in the form of dividends or otherwise, we may be liable for income taxes, subject to an adjustment, if any, for foreign tax credits and foreign withholding taxes payable to certain foreign tax authorities. As of December 31, 2015, it is not practicable to determine the amount of the income tax liability related to these undistributed earnings due to a variety of factors.

As of December 31, 2015, our liability for unrecognized tax benefits amounted to $66.4 million (excluding interest and penalties). Due to the nature and timing of the ultimate outcome of these unrecognized tax benefits, we cannot make a reasonably reliable estimate of the amount and period of related future payments, if any. Therefore, our 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.

Critical Accounting Policies and Significant Estimates

A critical accounting policy is one that is both important to the portrayal of our financial condition and results of operations and requires management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. While our significant accounting policies are more fully described in Note 2 of the Notes to the Consolidated Financial Statements included in this Annual Report on Form 10-K, we believe the following accounting estimates and policies to be critical.

Revenue Recognition

Revenues are recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed and determinable and collection is reasonably assured.

Product Sales, Net

Product sales revenue is recognized when title has transferred to the customer and the customer has assumed the risks and rewards of ownership, which is typically on delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer removes product from our consigned inventory location for shipment directly to a patient.

A significant portion of our net product revenues are derived from sales of Xyrem. We sell Xyrem in the U.S. to a single central pharmacy, Express Scripts Specialty Distribution Services and its affiliate CuraScript, Inc., or Express Scripts. In 2015, sales of Xyrem to Express Scripts accounted for 72.4% of our net product sales. We recognize revenues from sales of Xyrem within the U.S. upon transfer of title, which occurs when Express Scripts removes product from our consigned inventory location at its facility for shipment directly to a patient. We accept returns from and provide Express Scripts with a credit for any product returned by patients to Express Scripts with defects that were not reasonably discoverable upon receipt of the consigned product by Express Scripts. Based on our experience over the past eight years, product returns to Express Scripts from patients are rare; during 2015, we issued credits totaling less than $0.1 million to Express Scripts for returned product.

Items Deducted from Gross Product Sales. Revenues from sales of products are recorded net of government rebates and rebates under managed care plans, estimated allowances for sales returns, government chargebacks, prompt payment discounts, patient coupon programs, and specialty distributor and wholesaler fees. Calculating certain of these items involves estimates and judgments based on sales or invoice data, contractual terms, historical utilization rates, new information regarding changes in applicable regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates and channel inventory data. We review the adequacy of our provisions for sales deductions on a quarterly basis. Amounts accrued for sales deductions are adjusted when trends or significant events indicate that adjustment is appropriate and to reflect actual experience. Because we derive a significant portion of our revenues from sales of Xyrem in the U.S. to one specialty pharmacy customer, Express Scripts, we have a much higher level of knowledge about each prescription than if we sold the product through the normal pharmaceutical wholesaler channel as we do with most of our other products. The most significant items deducted from gross product sales where we exercise judgment are rebates, sales returns and chargebacks.

The following table presents the activity and ending balances for our sales-related accruals and allowances (in thousands):

	Rebates Payable	Sales Returns Reserve	Chargebacks	Discounts and Distributor Fees	Total
Balance at December 31, 2012 (1)	$ 25,247	$ 26,385	$ 2,536	$ 3,646	$ 57,814
Provision, net	66,895	2,836	21,777	51,432	142,940
Payments/credits	(60,584)	(8,111)	(19,903)	(49,188)	(137,786)
Balance at December 31, 2013 (1)	31,558	21,110	4,410	5,890	62,968
Provision, net	88,729	3,148	28,722	71,864	192,463
Payments/credits	(75,854)	(10,219)	(28,588)	(71,879)	(186,540)
Balance at December 31, 2014 (1)	44,433	14,039	4,544	5,875	68,891
Provision, net	124,618	(4,444)	39,124	46,533	205,831
Payments/credits	(107,013)	(3,485)	(38,772)	(48,684)	(197,954)
Balance at December 31, 2015	$ 62,038	$ 6,110	$ 4,896	$ 3,724	$ 76,768

(1) Includes both continuing operations and discontinued operations to the date of disposal.

Total items deducted from gross product sales were $205.8 million, $192.5 million and $142.9 million, or 13.5%, 14.2% and 14.2% as a percentage of gross product sales, in 2015, 2014 and 2013, respectively. Included in these amounts are immaterial adjustments related to prior-year sales due to changes in estimates. Such amounts represented less than 1% of net product sales for each of the years ended December 31, 2015, 2014 and 2013.

Rebates

We are subject to rebates on sales made under governmental and managed-care pricing programs in the U.S. The largest of these rebates is associated with sales covered by Medicaid. We participate in state government-managed Medicaid programs as well as certain other qualifying federal and state government programs under the terms of which discounts and rebates are provided to participating government entities. We offer rebates and discounts to managed health care organizations in the U.S. In estimating our provisions for rebates, we consider relevant statutes with respect to governmental pricing programs and contractual sales terms with managed-care providers and group purchasing organizations. We estimate the rebate provision based on historical utilization rates, historical payment experience, new information regarding changes in regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates and channel inventory data obtained from our major U.S. wholesalers in accordance with our inventory management agreements. Estimating these rebates is complex, in part due to the time delay between the date of sale and the actual settlement of the liability. We believe that the methodology we use to estimate rebates on product sales made under governmental and managed-care pricing programs is reasonable and appropriate given current facts and circumstances. However, estimates may vary from actual experience.

Rebates were $124.6 million, $88.7 million and $66.9 million, or 8.2%, 6.5% and 6.6% as a percentage of gross product sales, in 2015, 2014 and 2013, respectively. Rebates as a percentage of gross product sales increased in 2015 compared to 2014 primarily due to increased Medicaid utilization rates and increased Tricare per unit rebate amounts. Rebates as a percentage of gross product sales did not materially change in 2014 compared to 2013. We expect that rebates will continue to significantly impact our reported net sales. However, rebates as a percentage of gross product sales are not expected to change materially in 2016 compared to 2015.

Sales returns

For certain products, we allow customers to return product within a specified period before and after the applicable expiration date and issue credits which may be applied against existing or future invoices. We account for sales returns as a reduction in net revenue at the time a sale is recognized by establishing an accrual in an amount equal to the estimated value of products expected to be returned. The sales return accrual is estimated principally based on historical experience, the level and estimated shelf life of inventory in the distribution channel, our return policy and expected market events including generic competition.

Sales returns represented a credit of $4.4 million in 2015 and a charge of $3.1 million and $2.8 million in 2014 and 2013, respectively, or (0.3%), 0.3% and 0.9% as a percentage of gross product sales, in 2015, 2014 and 2013, respectively. Sales returns as a percentage of gross product sales decreased in 2015 compared to 2014 due to a change in the estimated returns rate for certain products with generic competition based on actual returns experience in addition to the lapse of the product return

period for certain products. Sales returns as a percentage of gross product sales did not materially change in 2014 compared to 2013. Sales returns as a percentage of gross product sales are expected to increase in 2016 compared to 2015 to be generally in line with 2014 and 2013 levels.

Chargebacks

We participate in chargeback programs with a number of entities, principally the U.S. Department of Defense, the U.S. Department of Veterans Affairs and other public parties, under which pricing on products below wholesalers' list prices is provided to participating entities. These entities purchase product through wholesalers at the lower negotiated price and the wholesalers charge back to us the difference between their acquisition cost and the lower negotiated price. We record the difference as allowances against accounts receivable. We determine our estimate of the chargebacks provision primarily based on historical experience on a product and program basis, current contract prices under the chargeback programs and channel inventory data.

Chargebacks were $39.1 million, $28.7 million and $21.8 million, or 2.6%, 2.1% and 2.2%, as a percentage of gross product sales, in 2015, 2014 and 2013, respectively. Chargebacks as a percentage of gross product sales increased in 2015 compared to 2014 primarily due to increased 340B drug pricing discount program utilization and increased chargeback per unit amounts. Chargebacks as a percentage of gross product sales did not change materially in 2014 compared to 2013. As a result of the products we acquired in the EUSA Acquisition, particularly Erwinaze, chargebacks are expected to continue to significantly impact our reported net product sales. Chargebacks as a percentage of gross product sales are expected to increase slightly in 2016 compared to 2015 primarily due to an increase in both Erwinaze chargeback utilization and the Erwinaze chargeback per unit amounts.

Discounts and distributor fees

Discounts and distributor fees comprise prompt payment discounts, patient coupon programs and specialty distributor and wholesaler fees. We offer customers a cash discount on gross product sales as an incentive for prompt payment. We estimate provisions for prompt pay discounts based on contractual sales terms with customers and historical payment experience. To help patients afford our products, we have various programs to assist them, including patient assistance programs, a free product voucher program and co-pay coupon programs for certain products. We estimate provisions for these programs primarily based on expected program utilization, adjusted as necessary to reflect our actual experience on a product and program basis. Specialty distributor and wholesaler fees comprise fees for distribution of our products. We estimate provisions for distributor and wholesaler fees primarily based on sales volumes and contractual terms with our distributors.

Discounts and distributor fees were $46.5 million, $71.9 million and $51.4 million, or 3.1%, 5.3% and 5.1% as a percentage of gross product sales, in 2015, 2014 and 2013, respectively. Discounts and distributor fees as a percentage of gross product sales decreased in 2015 compared to 2014 primarily due to a change in the patient coupon programs threshold and the patient eligibility criteria. Discounts and distributor fees as a percentage of gross product sales increased slightly in 2014 compared to 2013 primarily due to an increase in patient coupon programs. We expect that discounts and distributor fees as a whole will continue to significantly impact our reported net product sales. Discounts and distributor fees as a percentage of gross product sales are not expected to change materially in 2016 compared to 2015.

Goodwill and Intangible Assets

Goodwill

Goodwill represents the excess of the acquisition consideration over the fair value of assets acquired and liabilities assumed. We test goodwill for impairment annually in October and when events or changes in circumstances indicate that the carrying value may not be recoverable. We have determined that we operate in a single segment and have a single reporting unit associated with the development and commercialization of pharmaceutical products. The annual test for goodwill impairment is a two-step process. The first step is a comparison of the fair value of the reporting unit with its carrying amount, including goodwill. If this step indicates impairment, then in the second step, the loss is measured as the excess of recorded goodwill over its implied fair value. Implied fair value is the excess of the fair value of the reporting unit over the fair value of all identified assets and liabilities. We have determined the fair value of our single reporting unit to be equal to our market capitalization, as determined by our traded share price, plus a control premium. The control premium used was based on a review of such premiums identified in recent acquisitions of companies of similar size and in similar industries. We performed our annual goodwill impairment test in October 2015 and concluded that goodwill was not impaired as the fair value of the reporting unit significantly exceeded its carrying amount, including goodwill. As of December 31, 2015, we had $657.1 million of goodwill primarily resulting from the Azur Merger on January 18, 2012, the EUSA Acquisition on June 12, 2012 and the Gentium Acquisition on January 23, 2014.

Intangible Assets

In connection with the Azur Merger, the EUSA Acquisition and the Gentium Acquisition, we acquired a number of intangible assets, including intangible assets related to currently marketed products (developed technology) and intangible assets related to product candidates (IPR&D). When significant identifiable intangible assets are acquired, we engage an independent third party valuation firm to assist in determining the fair values of these assets as of the acquisition date. Discounted cash flow models are typically used in these valuations, which require the use of significant estimates and assumptions, including but not limited to:

- estimating the timing of and expected costs to complete the in-process projects;
- projecting regulatory approvals;
- estimating future cash flows from product sales resulting from completed products and in-process projects; and
- developing appropriate discount rates and probability rates by project.

We believe the fair values that we assign to the intangible assets acquired are based upon reasonable estimates and assumptions given available facts and circumstances as of the acquisition dates. No assurance can be given, however, that the underlying assumptions used to estimate expected cash flows will transpire as estimated. In addition, we are required to estimate the period of time over which to amortize the intangible assets, which requires significant judgment.

Our finite-lived intangible assets are amortized on a straight-line basis over their estimated useful lives, which range from two to 16 years. The estimated useful lives associated with intangible assets are consistent with the estimated lives of the products and may be modified when circumstances warrant. Intangible assets with finite lives are reviewed for impairment whenever events or circumstances indicate that the carrying value of an asset may not be recoverable. Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. Factors that we consider in deciding when to perform an impairment review include significant under-performance of a product in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in our use of the assets. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Estimating future cash flows related to an intangible asset involves estimates and assumptions. If our assumptions are not correct, there could be an impairment loss or, in the case of a change in the estimated useful life of the asset, a change in amortization expense.

IPR&D is not amortized but is tested for impairment annually or when events or circumstances indicate that the fair value may be below the carrying value of the asset. If the carrying value of the assets is not expected to be recovered, the assets are written down to their estimated fair values.

As of December 31, 2015, we had $1.0 billion of finite-lived intangible assets and $182.3 million of IPR&D assets related to the marketed products and the IPR&D projects that we acquired in the Azur Merger, the EUSA Acquisition and the Gentium Acquisition. In 2015, we recorded an impairment charge of $31.5 million to our acquired IPR&D asset as a result of our decision to terminate a pivotal Phase 2 clinical trial of JZP-416. In 2014, we recorded impairment charges of $39.4 million related to certain products acquired as part of the EUSA Acquisition that we sold in March 2015.

We did not recognize an impairment charge related to our intangible assets during 2013. Please refer to the Notes to Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for further information about our intangible assets and the remaining useful lives of our finite-lived intangible assets as of December 31, 2015.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amount and the tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. We provide a valuation allowance when it is more-likely-than-not that deferred tax assets will not be realized.

Our most significant tax jurisdictions are Ireland, the United States, Italy and France. Significant estimates are required in determining our provision for income taxes. Some of these estimates are based on management’s interpretations of jurisdiction-specific tax laws or regulations and the likelihood of settlement related to tax audit issues. Various internal and external factors may have favorable or unfavorable effects on our future effective income tax rate. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years’ items, the impact of accounting for share-based compensation, changes in our international organization, likelihood of settlement, and changes in overall levels of income before taxes.

Realization of our deferred tax assets is dependent upon the generation of future taxable income, the amount and timing of which are uncertain. In evaluating our ability to recover our deferred tax assets, we consider all available positive and

negative evidence, including cumulative income in recent fiscal years, our forecast of future taxable income exclusive of certain reversing temporary differences and significant risks and uncertainties related to our business. In determining future taxable income, we are responsible for assumptions utilized including the amount of state, federal and international pre-tax operating income, the reversal of certain temporary differences and the implementation of feasible and prudent tax planning strategies. These assumptions require significant judgment about the forecasts of future taxable income and are consistent with the plans and estimates that we are using to manage our underlying business.

We maintain a valuation allowance against certain other deferred tax assets where realizability is not certain. We periodically evaluate the likelihood of the realization of deferred tax assets and reduce the carrying amount of these deferred tax assets by a valuation allowance to the extent we believe a portion will not be realized. This determination depends on a variety of factors, some of which are subjective, including our recent cumulative earnings experience by taxing jurisdiction, expectations of future taxable income, carryforward periods available to us for tax reporting purposes, various income tax strategies and other relevant factors. If we determine that the deferred tax assets are not realizable in a future period, we would record material changes to income tax expense in that period.

We have also provided for unrecognized tax benefits that we believe are not more-likely-than-not to be sustained upon examination by tax authorities. The evaluation of unrecognized tax benefits is based on factors that include, but are not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate unrecognized tax benefits on a quarterly basis and adjust the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Our liabilities for unrecognized tax benefits can be relieved only if the contingency becomes legally extinguished through either payment to the taxing authority or the expiration of the statute of limitations, the recognition of the benefits associated with the position meet the more-likely-than-not threshold or the liability becomes effectively settled through the examination process. We consider matters to be effectively settled once the taxing authority has completed all of its required or expected examination procedures, including all appeals and administrative reviews. We also accrue for potential interest and penalties related to unrecognized tax benefits in income tax provision (benefit).

Share-Based Compensation

We have elected to use the Black-Scholes option pricing model to calculate the fair value of share option grants under our equity incentive plans and grants under our employee stock purchase plan, or ESPP, and we are using the straight-line method to allocate compensation cost to reporting periods. The fair value of share options was estimated using the following assumptions:

	Year Ended December 31,		
	2015	2014	2013
Volatility	39%	45%	58%
Expected term (years)	4.2	4.3	4.4
Range of risk-free rates	1.1-1.5%	1.1-1.4%	0.5-1.4%
Expected dividend yield	—%	—%	—%

The two inputs which require the greatest judgment and have a large impact on fair values are volatility and expected term.

We rely only on a blend of the historical and implied volatilities of our own ordinary shares to determine expected volatility for share option grants. In addition, we use a single volatility estimate for each share option grant. The weighted-average volatility is determined by calculating the weighted average of volatilities for all share options granted in a given year.

The expected term of share option grants represents the weighted-average period the awards are expected to remain outstanding. We estimated the weighted-average expected term based on historical exercise data.

Recent Accounting Pronouncements

In November 2015, the Financial Accounting Standards Board, or the FASB, issued Accounting Standards Update, or ASU, No. 2015-17, “Balance Sheet Classification of Deferred Taxes”, or ASU No. 2015-17, which simplifies the presentation of deferred income taxes. ASU No. 2015-17 requires that deferred tax assets and liabilities be classified as non-current in a statement of financial position. We early adopted ASU 2015-17 effective December 31, 2015 on a prospective basis. Adoption of this ASU resulted in a reclassification of our net current deferred tax assets and liabilities to net non-current deferred tax assets and liabilities in our consolidated balance sheet as of December 31, 2015. No prior periods were retrospectively adjusted.

In April 2015, the FASB issued ASU No. 2015-03, “Interest - Imputation of Interest”, or ASU No. 2015-03. ASU No. 2015-03 requires debt issuance costs related to a recognized debt liability to be presented in the balance sheet as a direct deduction from the debt liability instead of as an asset. ASU No. 2015-03 does not affect the recognition and measurement guidance for debt issuance costs. 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 - Amendments to SEC Paragraphs Pursuant to Staff Announcements at the June 2015 EITF Meeting”, or ASU No. 2015-15. ASU No. 2015-15 indicates that the guidance in ASU No. 2015-03 did not address presentation or subsequent measurement of debt issuance costs related to line of credit arrangements. Given the absence of authoritative guidance within ASU No. 2015-03, the SEC staff has indicated that they would not object to an entity deferring and presenting debt issuance costs as an asset and subsequently amortizing the costs ratably over the term of the line of credit arrangement, regardless of whether there are any outstanding borrowings on the line of credit arrangement. This guidance is effective for us beginning January 1, 2016 and requires retrospective application. This guidance is not expected to have a material impact on our consolidated balance sheets or related disclosures.

In April 2015, the FASB issued ASU No. 2015-05, “Intangibles-Goodwill and Other-Internal-Use Software”, or ASU No. 2015-05. ASU No. 2015-05 provides guidance on whether a cloud computing arrangement contains a software license to be accounted for as internal-use software to assist in the evaluation of the accounting for fees paid by a customer in the arrangement. ASU No. 2015-05 will be effective for us beginning January 1, 2016 and may be applied either prospectively to new cloud computing arrangements or retrospectively. This guidance is not expected to have a material impact on our financial position or results of operations.

In May 2014, the FASB issued ASU No. 2014-09, “Revenue from Contracts with Customers”, or ASU No. 2014-09, which states that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To achieve this, an entity will need to identify the contract with a customer; identify the separate performance obligations in the contract; determine the transaction price; allocate the transaction price to the separate performance obligations in the contract; and recognize revenue when (or as) the entity satisfies each performance obligation. In August 2015, the FASB issued ASU No. 2015-14, “Revenue from Contracts with Customers: Deferral of the Effective Date”, which deferred by one year the effective date of ASU No. 2014-09 which will now be effective for us beginning January 1, 2018 and can be adopted on a full retrospective basis or on a modified retrospective basis. We are currently assessing our approach to the adoption of this standard and the potential impact on our results of operations and financial position.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk. The primary objectives of our investment policy, in order of priority, are as follows: safety and preservation of principal and diversification of risk; liquidity of investments sufficient to meet cash flow requirements; and competitive yield. Although our investments are subject to market risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or certain types of investment. Our investment policy allows us to maintain a portfolio of cash equivalents and short-term investments in a variety of securities, including U.S. federal government and federal agency securities, corporate bonds or commercial paper issued by U.S. corporations, money market instruments, certain qualifying money market mutual funds, certain repurchase agreements, and tax-exempt obligations of states, agencies and municipalities in the U.S. Our cash equivalents as of December 31, 2015 consisted of time deposits which are not subject to significant interest rate risk.

We are exposed to risks associated with changes in interest rates in connection with our term loan and borrowings under our revolving credit facility. Based on indebtedness under our term loan of $740.6 million as of December 31, 2015, a 1.0% change in interest rates would increase net interest expense on our term loan for 2016 by $7.5 million. As of December 31, 2015, there were no borrowings outstanding under our revolving credit facility.

In August 2014, we completed a private placement of $575.0 million aggregate principal amount of the 2021 Notes. The 2021 Notes have a fixed annual interest rate of 1.875% and we, therefore, do not have economic interest rate exposure on the 2021 Notes. However, the fair value of the 2021 Notes is exposed to interest rate risk. Generally, the fair value of the 2021 Notes will increase as interest rates fall and decrease as interest rates rise. The fair value of the 2021 Notes is also affected by volatility in our ordinary share price. As of December 31, 2015, the fair value of the 2021 Notes was estimated to be $601 million.

Foreign Exchange Risk. We have significant operations in Europe as well as in the U.S. The functional currency of each foreign subsidiary is generally the local currency. We are exposed to foreign currency exchange risk as the functional currency

financial statements of foreign subsidiaries are translated to U.S. dollars. The assets and liabilities of our foreign subsidiaries having a functional currency other than the U.S. dollar are translated into U.S. dollars at the exchange rate prevailing at the balance sheet date, and at the average exchange rate for the reporting period for revenue and expense accounts. The cumulative foreign currency translation adjustment is recorded as a component of accumulated other comprehensive loss in shareholders' equity. The reported results of our foreign subsidiaries will be influenced by their translation into U.S. dollars by currency movements against the U.S. dollar. Our primary currency translation exposure is related to our subsidiaries that have functional currencies denominated in the euro. A 10% strengthening/(weakening) in the rates used to translate the results of our foreign subsidiaries that have functional currencies denominated in the euro would have increased/(decreased) net income for the year ended December 31, 2015 by approximately $9 million.

Transactional exposure arises where transactions occur in currencies other than the functional currency. Transactions in foreign currencies are recorded at the exchange rate prevailing at the date of the transaction. The resulting monetary assets and liabilities are translated into the appropriate functional currency at exchange rates prevailing at the balance sheet date and the resulting gains and losses are reported in foreign currency gain (loss) in the consolidated statements of income. As of December 31, 2015, our primary exposure to transaction risk related to euro net monetary liabilities held by subsidiaries with a U.S. dollar functional currency. As of December 31, 2015, a 10% strengthening/(weakening) in the euro against the U.S. dollar would have (decreased)/increased net income by approximately $1 million.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements as listed below are included in this Annual Report on Form 10-K as pages F-1 through F-40.

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

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures. We have carried out an evaluation under the supervision and with the participation of management, including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on their evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2015.

Limitations on the Effectiveness of Controls. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met and, as set forth above, our principal executive officer and principal financial officer have concluded, based on their evaluation as of the end of the period covered by this report, that our disclosure controls and procedures were effective to provide reasonable assurance that the objectives of our disclosure control system were met.

Changes in Internal Control over Financial Reporting. During the quarter ended December 31, 2015, there were no changes to our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting. The following report is provided by management in respect of our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act):

1. Our management is responsible for establishing and maintaining adequate internal control over financial reporting.
2. Our management used the Committee of Sponsoring Organizations of the Treadway Commission Internal Control - Integrated Framework (2013), or the COSO framework, to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.
3. Management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2015 and has concluded that such internal control over financial reporting was effective. There were no material weaknesses in internal control over financial reporting identified by management.
4. KPMG, our independent registered public accounting firm, has audited the consolidated financial statements of Jazz Pharmaceuticals plc as of and for the year ended December 31, 2015, included herein, and has issued an audit report on our internal control over financial reporting, which is included below.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders
Jazz Pharmaceuticals plc

We have audited Jazz Pharmaceuticals plc's internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Jazz Pharmaceuticals plc's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

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

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

In our opinion, Jazz Pharmaceuticals plc maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control - Integrated Framework (2013) issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Jazz Pharmaceuticals plc and subsidiaries as of December 31, 2015 and 2014, and the related consolidated statements of income, comprehensive income (loss), shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2015, and the related financial statement schedule, and our report dated February 23, 2016 expressed an unqualified opinion on those consolidated financial statements and the related financial statement schedule.

/s/ KPMG

Dublin, Ireland
February 23, 2016

Item 9B. Other Information

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and incorporated by reference to our definitive proxy statement for our 2016 annual general meeting of shareholders, or our 2016 Proxy Statement, to be filed pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, or Exchange Act. If our 2016 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is to be included in our 2016 Proxy Statement as follows:

- The information relating to our directors and nominees for director is to be included in the section entitled “Proposal 1—Election of Directors;”
- The information relating to our executive officers is to be included in the section entitled “Executive Officers;”
- The information relating to our audit committee, audit committee financial expert and procedures by which shareholders may recommend nominees to our board of directors is to be included in the section entitled “Corporate Governance and Board Matters;” and
- The information regarding compliance with Section 16(a) of the Exchange Act is to be included in the section entitled “Section 16(a) Beneficial Ownership Reporting Compliance.”

Such information is incorporated herein by reference to our 2016 Proxy Statement, provided that if the 2016 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Our Code of Conduct applies to all of our employees, directors and officers, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, and those of our subsidiaries. The Code of Conduct is available on our website at *www.jazzpharmaceuticals.com* under the section entitled “About” under “Corporate Ethics.” We intend to satisfy the disclosure requirements under Item 5.05 of the SEC Form 8-K regarding an amendment to, or waiver from, a provision of our Code of Conduct by posting such information on our website at the website address and location specified above.

Item 11. Executive Compensation

The information required by this item is to be included in our 2016 Proxy Statement under the sections entitled “Executive Compensation,” “Director Compensation,” “Corporate Governance and Board Matters—Compensation Committee Interlocks and Insider Participation” and “Corporate Governance and Board Matters—Compensation Committee Report” and is incorporated herein by reference, provided that if the 2016 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

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

The information required by this item with respect to equity compensation plans is to be included in our 2016 Proxy Statement under the section entitled “Equity Compensation Plan Information” and the information required by this item with respect to security ownership of certain beneficial owners and management is to be included in our 2016 Proxy Statement under the section entitled “Security Ownership of Certain Beneficial Owners and Management” and in each case is incorporated herein by reference, provided that if the 2016 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

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

The information required by this item is to be included in our 2016 Proxy Statement under the sections entitled "Certain Relationships and Related Party Transactions" and "Corporate Governance and Board Matters—Independence of the Board of Directors" and is incorporated herein by reference, provided that if the 2016 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 14. Principal Accountant Fees and Services

The information required by this item is to be included in our 2016 Proxy Statement under the section entitled "Proposal 2—On a Non-Binding Advisory Basis, Ratify Appointment of Independent Auditors and, On a Binding Basis, Authorize the Board of Directors, Acting Through the Audit Committee, to Determine the Independent Auditors' Remuneration" and is incorporated herein by reference, provided that if the 2016 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Index to Financial Statements:

See Index to Consolidated Financial Statements in Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules:

The following financial statement schedule of Jazz Pharmaceuticals plc is filed as part of this Annual Report on Form 10-K on page F-40 and should be read in conjunction with the consolidated financial statements of Jazz Pharmaceuticals plc.

Schedule II: Valuation and Qualifying Accounts

All other schedules are omitted because they are not applicable, not required under the instructions, or the requested information is shown in the consolidated financial statements or related notes thereto.

(b) Exhibits—The following exhibits are included herein or incorporated herein by reference:

Exhibit Number	Description of Document
2.1	Agreement and Plan of Merger and Reorganization, dated as of September 19, 2011, by and among Azur Pharma Limited (now Jazz Pharmaceuticals plc), Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500) filed with the SEC on September 19, 2011).
2.2	Letter Agreement, dated as of January 17, 2012, by and among Jazz Pharmaceuticals plc, Jaguar Merger Sub Inc. Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated by reference to Exhibit 2.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
2.3	Agreement and Plan of Merger, dated as of April 26, 2012, by and among Jazz Pharmaceuticals plc, Jewel Merger Sub Inc., EUSA Pharma Inc., and Essex Woodlands Health Ventures, Inc., Mayflower L.P., and Bryan Morton, in their capacity as the representatives of the equity holders of EUSA Pharma Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on April 27, 2012).
2.4	Assignment, dated as of June 11, 2012, by and among Jazz Pharmaceuticals plc and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 2.1B in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 12, 2012).
2.5	Tender Offer Agreement, dated December 19, 2013, by and among Jazz Pharmaceuticals Public Limited Company, Jazz Pharmaceuticals Italy S.r.l. and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K/A (File No. 001-33500), as filed with the SEC on December 20, 2013).

2.6†	Asset Purchase Agreement, dated January 13, 2014, by and among Jazz Pharmaceuticals International III Limited, Aerial BioPharma, LLC and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 13, 2014).
2.7†	Assignment Agreement, dated July 1, 2014, by and among Jazz Pharmaceuticals International II Limited, Sigma-Tau Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 5, 2014).
2.8	Amended and Restated Agreement for the Acquisition of the Topaz Portfolio Business of Jazz Pharmaceuticals plc, dated March 20, 2015, between Jazz Pharmaceuticals plc and Essex Bidco Limited (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's current report on Form 8-K (File No. 001-33500), as filed with the SEC on March 23, 2015).
3.1	Memorandum and Articles of Association of Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 3.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
4.1	Reference is made to Exhibit 3.1.
4.2A	Investor Rights Agreement, dated July 7, 2009 by and between Jazz Pharmaceuticals, Inc. and the other parties named therein (incorporated herein by reference to Exhibit 10.88 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on July 7, 2009).
4.2B	Assignment, Assumption and Amendment Agreement, dated as of January 18, 2012, by and among Jazz Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and the other parties named therein (incorporated herein by reference to Exhibit 4.7B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
4.2C	Indenture, dated as of August 13, 2014, by and among Jazz Pharmaceuticals plc, Jazz Investments I Limited and U.S. Bank National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 13, 2014).
4.2D	Form of 1.875% Exchangeable Senior Note due 2021 (incorporated herein by reference to Exhibit 4.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 13, 2014).
10.1†	Supply Agreement, dated as of April 1, 2010, by and between Jazz Pharmaceuticals, Inc. and Siegfried (USA) Inc. (incorporated herein by reference to Exhibit 10.54 in Jazz Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2010, as filed with the SEC on May 6, 2010).
10.2†	Master Services Agreement, dated April 15, 2011, by and between Jazz Pharmaceuticals, Inc., CuraScript, Inc. and Express Scripts Specialty Distribution Services, Inc. (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2011, as filed with the SEC on May 9, 2011).
10.3†	Royalty Bearing License Agreement and Supply Agreement Re Erwinia-Derived Asparaginase, dated July 22, 2005, between Public Health England (formerly Health Protection Agency) and EUSA Pharma SAS (formerly OPi, S.A.), as amended on each of December 22, 2009, March 23, 2012 and August 8, 2012 (incorporated herein by reference to Exhibit 10.11 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q/A (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 9, 2012).
10.4	Novation Agreement relating to Royalty Bearing Licence Agreement and Supply Agreement re Erwinia-Derived Asparaginase, dated as of May 13, 2015, by and among EUSA Pharma SAS, the Secretary of State for Health acting through Public Health England and Porton Biopharma Limited (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2015, as filed with the SEC on August 5, 2015).
10.5*	Master Manufacturing Services Agreement, dated as of October 1, 2015, by and between Jazz Pharmaceuticals Ireland Limited and Patheon Pharmaceuticals Inc.
10.6	Credit Agreement, dated as of June 18, 2015, among Jazz Pharmaceuticals plc, Jazz Securities Limited, Jazz Pharmaceuticals, Inc., Jazz Financing I Limited, Jazz Pharmaceuticals Ireland Limited, the lenders party thereto and Bank of America, N.A., as Collateral Agent, Administrative Agent, Swing Line Lender and L/C Issuer (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 0001-33500), as filed with the SEC on June 18, 2015).
10.7A	Commercial Lease, dated as of June 2, 2004, by and between Jazz Pharmaceuticals, Inc. and The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.52 in Jazz Pharmaceuticals, Inc.'s registration statement on Form S-1, as amended (File No. 333-141164), as filed with the SEC on March 27, 2007).

10.7B	First Amendment of Lease, dated June 1, 2009, by and between Jazz Pharmaceuticals, Inc. and Wheatley-Fields, LLC, successor in interest to The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.86 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 4, 2009).
10.7C	Second Amendment of Lease, dated February 28, 2012, by and between Jazz Pharmaceuticals, Inc. and Wheatley-Fields, LLC, successor in interest to The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.31 in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
10.8	Lease, dated May 8, 2012, by and between John Ronan and Castle Cove Property Developments Limited and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.9	Commercial Lease, dated as of January 7, 2015, by and between The Board of Trustees of the Leland Stanford Junior University and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.10+	Form of Indemnification Agreement between Jazz Pharmaceuticals plc and its officers and directors (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
10.11+	Offer Letter from Jazz Pharmaceuticals, Inc. to Suzanne Sawochka Hooper (incorporated herein by reference to Exhibit 10.19 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2012, as filed with the SEC on May 8, 2012).
10.12+	Offer Letter from Jazz Pharmaceuticals, Inc. to Matthew Young (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2014, as filed with the SEC on May 8, 2014).
10.13A+	Employment Agreement by and between EUSA Pharma Inc. and Iain McGill (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2014, as filed with the SEC on November 4, 2014).
10.13B+	Amendment to Employment Agreement by and between Iain McGill and EUSA Pharma (Europe) Limited (incorporated herein by reference to Exhibit 10.15B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.14+	Offer Letter from Jazz Pharmaceuticals, Inc. to Michael Miller (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2014, as filed with the SEC on November 4, 2014).
10.15A+	Employment Agreement by and between Jazz Pharmaceuticals Ireland Limited and Paul Treacy (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2014, as filed with the SEC on November 4, 2014).
10.15B+	Amendment to Employment Agreement by and between Jazz Pharmaceuticals Ireland Limited and Paul Treacy (incorporated herein by reference to Exhibit 10.15A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.16+	Amended and Restated Offer Letter, dated as of July 29, 2015, from Jazz Pharmaceuticals, Inc. to Karen Smith, M.D., Ph.D. ((incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2015, as filed with the SEC on November 9, 2015).
10.17A+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 99.3 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.17B+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan Sub-Plan Governing Awards to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.3B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2012).
10.17C+	Form of Notice of Grant of Stock Options and Form of Option Agreement (U.S.) under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.17D+	Form of Notice of Grant of Stock Options and Form of Option Agreement (Irish) under Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).

10.17E+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.S.) under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27E in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500), as filed with the SEC on February 26, 2013).
10.17F+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (Irish) under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27F in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.17G+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.17H+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18A+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 99.1 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.18B+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan Sub-Plan Governing Awards to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.39B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2012).
10.18C+	Form of Option Grant Notice and Form of Stock Option Agreement (U.S.) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18D+	Form of Stock Option Grant Notice and Form of Option Agreement (Irish) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18E+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.28E in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.18F+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.S.) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18G+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (Irish) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18H+	Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.28H in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.18I+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Option Grant Notice and Form of U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18J+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18K+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).

10.18L+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.19+	Jazz Pharmaceuticals plc Amended and Restated Directors Deferred Compensation Plan (incorporated herein by reference to Exhibit 99.6 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.20A+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 99.4 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.20B+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 10.30B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.20C+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved August 1, 2013) (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.21A+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan, as amended and restated (incorporated herein by reference to Exhibit 10.31A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.21B+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan Sub-Plan Governing Purchase Rights to Participants in the Republic of Ireland (incorporated by reference herein to Exhibit 10.14C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2012, as filed with the SEC on May 8, 2012).
10.22A+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (incorporated herein by reference to Exhibit 10.32B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.22B+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved November 4, 2015).
10.22C+	Jazz Pharmaceuticals Cash Bonus Plan for International Affiliates (2014) (incorporated herein by reference to Exhibit 10.24D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2013, as filed with the SEC on February 25, 2014).
10.22D+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2016).
10.23+	Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (approved February 10, 2016).
10.24+	Jazz Pharmaceuticals plc 2015 Executive Officer Compensation Arrangements (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2015, as filed with the SEC on May 7, 2015).
10.25A+	Jazz Pharmaceuticals plc Non-Employee Director Compensation Policy (approved May 1, 2014) (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's quarterly report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2014, as filed with the SEC on May 8, 2014).
10.25B+	Jazz Pharmaceuticals plc Non-Employee Director Compensation Policy (approved April 30, 2015) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2015, as filed with the SEC on August 5, 2015).
10.26+	Named Officer 2015 Target Bonus Opportunity (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on February 18, 2015).
21.1	Subsidiaries of Jazz Pharmaceuticals plc.
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page hereto).
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1**	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
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 Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

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+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for 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.

** The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed “filed” by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

SIGNATURES

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

Date: February 23, 2016

Jazz Pharmaceuticals public limited company
(Registrant)

/s/ BRUCE C. COZADD

Bruce C. Cozadd
Chairman and Chief Executive Officer and Director
(Principal Executive Officer)

/s/ MATTHEW P. YOUNG

Matthew P. Young
Executive Vice President and Chief Financial Officer (Principal Financial Officer)

/s/ KAREN J. WILSON

Karen J. Wilson
Senior Vice President, Finance
(Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Bruce C. Cozadd, Matthew P. Young, Suzanne Sawochka Hooper and Karen J. Wilson, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with 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 therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ BRUCE C. COZADD **Bruce C. Cozadd**	Chairman, Chief Executive Officer and Director *(Principal Executive Officer)*	February 23, 2016
/s/ MATTHEW P. YOUNG **Matthew P. Young**	Executive Vice President and Chief Financial Officer *(Principal Financial Officer)*	February 23, 2016
/s/ KAREN J. WILSON **Karen J. Wilson**	Senior Vice President, Finance *(Principal Accounting Officer)*	February 23, 2016
/s/ PAUL L. BERNS **Paul L. Berns**	Director	February 23, 2016
/s/ PATRICK G. ENRIGHT **Patrick G. Enright**	Director	February 23, 2016
/s/ PETER GRAY **Peter Gray**	Director	February 23, 2016
/s/ HEATHER ANN MCSHARRY **Heather Ann McSharry**	Director	February 23, 2016
/s/ SEAMUS C. MULLIGAN **Seamus C. Mulligan**	Director	February 23, 2016
/s/ KENNETH W. O'KEEFE **Kenneth W. O'Keefe**	Director	February 23, 2016
/s/ NORBERT G. RIEDEL, PH.D. **Norbert G. Riedel, Ph.D.**	Director	February 23, 2016
/s/ ELMAR SCHNEE **Elmar Schnee**	Director	February 23, 2016
/s/ CATHERINE A. SOHN, PHARM.D. **Catherine A. Sohn, Pharm.D.**	Director	February 23, 2016
/s/ RICK E WINNINGHAM **Rick E Winningham**	Director	February 23, 2016

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders
Jazz Pharmaceuticals plc

We have audited the accompanying consolidated balance sheets of Jazz Pharmaceuticals plc and subsidiaries (the Company) as of December 31, 2015 and 2014, and the related consolidated statements of income, comprehensive income (loss), shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2015. In connection with our audit of the consolidated financial statements, we also have audited the financial statement schedule at Item 15(a)2 for the years ended December 31, 2015, 2014 and 2013. These consolidated financial statements and financial statement schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements and financial statement schedule based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Jazz Pharmaceuticals plc and subsidiaries as of December 31, 2015 and 2014, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule for the years ended December 31, 2015, 2014 and 2013, when considered in relation to the basic consolidated financial statements taken as a whole, presents fairly, in all material respects, the information set forth therein.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated February 23, 2016 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

/s/ KPMG

Dublin, Ireland
February 23, 2016

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED BALANCE SHEETS
(In thousands, except per share amounts)

	December 31,	
	2015	2014
ASSETS		
Current assets:		
Cash and cash equivalents	$ 988,785	$ 684,042
Accounts receivable, net of allowances of $3,693 and $3,483 at December 31, 2015 and 2014, respectively	209,685	186,371
Inventories	19,451	30,037
Prepaid expenses	20,699	12,800
Deferred tax assets, net	—	48,440
Other current assets	19,047	21,322
Assets held for sale	—	32,833
Total current assets	1,257,667	1,015,845
Property and equipment, net	85,572	58,363
Intangible assets, net	1,185,606	1,437,435
Goodwill	657,139	702,713
Deferred tax assets, net, non-current	122,863	75,494
Deferred financing costs	23,268	33,174
Other non-current assets	27,548	15,931
Total assets	$ 3,359,663	$ 3,338,955
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 21,807	$ 25,126
Accrued liabilities	164,070	164,091
Current portion of long-term debt	37,587	9,428
Income taxes payable	1,808	7,588
Deferred tax liability, net	—	9,430
Deferred revenue	1,370	1,138
Total current liabilities	226,642	216,801
Deferred revenue, non-current	3,721	4,499
Long-term debt, less current portion	1,166,916	1,333,000
Deferred tax liability, net, non-current	294,485	375,054
Other non-current liabilities	69,253	38,393
Commitments and contingencies (Note 11)		
Shareholders' equity:		
Ordinary shares, nominal value $0.0001 per share; 300,000 shares authorized; 61,305 and 60,643 shares issued and outstanding at December 31, 2015 and 2014, respectively	6	6
Non-voting euro deferred shares, €0.01 par value per share; 4,000 shares authorized, issued and outstanding at both December 31, 2015 and 2014	55	55
Capital redemption reserve	471	471
Additional paid-in capital	1,562,900	1,458,005
Accumulated other comprehensive loss	(267,472)	(122,097)
Retained earnings	302,686	34,704
Total Jazz Pharmaceuticals plc shareholders' equity	1,598,646	1,371,144
Noncontrolling interests	—	64
Total shareholders' equity	1,598,646	1,371,208
Total liabilities and shareholders' equity	$ 3,359,663	$ 3,338,955

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF INCOME

(In thousands, except per share amounts)

	Year Ended December 31,		
	2015	**2014**	**2013**
Revenues:			
Product sales, net	$ 1,316,819	$ 1,162,716	$ 865,398
Royalties and contract revenues	7,984	10,159	7,025
Total revenues	1,324,803	1,172,875	872,423
Operating expenses:			
Cost of product sales (excluding amortization and impairment of intangible assets)	102,526	117,418	102,146
Selling, general and administrative	449,119	406,114	304,303
Research and development	135,253	85,181	41,632
Acquired in-process research and development	—	202,626	4,988
Intangible asset amortization	98,162	126,584	79,042
Impairment charges	31,523	39,365	—
Total operating expenses	816,583	977,288	532,111
Income from operations	508,220	195,587	340,312
Interest expense, net	(56,917)	(52,713)	(26,916)
Foreign currency gain (loss)	1,445	8,683	(1,697)
Loss on extinguishment and modification of debt	(16,815)	—	(3,749)
Income before income tax provision	435,933	151,557	307,950
Income tax provision	106,399	94,231	91,638
Net income	329,534	57,326	216,312
Net loss attributable to noncontrolling interests, net of tax	(1)	(1,061)	—
Net income attributable to Jazz Pharmaceuticals plc	$ 329,535	$ 58,387	$ 216,312
Net income attributable to Jazz Pharmaceuticals plc per ordinary share:			
Basic	$ 5.38	$ 0.98	$ 3.71
Diluted	$ 5.23	$ 0.93	$ 3.51
Weighted-average ordinary shares used in per share calculation - basic	61,232	59,746	58,298
Weighted-average ordinary shares used in per share calculation - diluted	63,036	62,614	61,569

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(In thousands)

	Year Ended December 31,		
	2015	2014	2013
Net income	$ 329,534	$ 57,326	$ 216,312
Other comprehensive income (loss):			
Foreign currency translation adjustments	(145,375)	(178,264)	25,107
Other comprehensive income (loss)	(145,375)	(178,264)	25,107
Total comprehensive income (loss)	184,159	(120,938)	241,419
Comprehensive loss attributable to noncontrolling interests, net of tax	(1)	(1,075)	—
Comprehensive income (loss) attributable to Jazz Pharmaceuticals plc	$ 184,160	$ (119,863)	$ 241,419

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY

(In thousands)

	Ordinary Shares		Non-voting Euro Deferred								
	Shares	Amount	Shares	Amount	Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings (Accumulated Deficit)	Total Jazz Pharmaceuticals plc Shareholders' Equity	Non-controlling interest	Total Equity
Balance at December 31, 2012	58,014	$ 6	4,000	$ 55	$ 471	$ 1,151,010	$ 31,046	$ (61,296)	$ 1,121,292	$ —	$ 1,121,292
Issuance of ordinary shares in conjunction with exercise of share options	904	—	—	—	—	20,895	—	—	20,895	—	20,895
Issuance of ordinary shares under employee stock purchase plan	147	—	—	—	—	5,410	—	—	5,410	—	5,410
Issuance of ordinary shares in conjunction with vesting of restricted stock units	146	—	—	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(5,590)	—	—	(5,590)	—	(5,590)
Issuance of ordinary shares in conjunction with exercise of warrants	471	—	—	—	—	4,398	—	—	4,398	—	4,398
Share-based compensation	—	—	—	—	—	44,367	—	—	44,367	—	44,367
Excess tax benefits from employee share options	—	—	—	—	—	(173)	—	—	(173)	—	(173)
Shares repurchased	(1,828)	—	—	—	—	—	—	(136,484)	(136,484)	—	(136,484)
Other comprehensive income	—	—	—	—	—	—	25,107	—	25,107	—	25,107
Net income	—	—	—	—	—	—	—	216,312	216,312	—	216,312
Balance at December 31, 2013	57,854	$ 6	4,000	$ 55	$ 471	$ 1,220,317	$ 56,153	$ 18,532	$ 1,295,534	$ —	$ 1,295,534

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY—(Continued)
(In thousands)

	Ordinary Shares		Non-voting Euro Deferred								
	Shares	Amount	Shares	Amount	Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Jazz Pharmaceuticals plc Shareholders' Equity	Non-controlling interest	Total Equity
Balance at December 31, 2013	57,854	$ 6	4,000	$ 55	$ 471	$ 1,220,317	$ 56,153	$ 18,532	$ 1,295,534	$ —	$ 1,295,534
Noncontrolling interest on Gentium Acquisition	—	—	—	—	—	—	—	—	—	136,578	136,578
Acquisition of noncontrolling interest	—	—	—	—	—	(1,530)	—	—	(1,530)	(135,439)	(136,969)
Issuance of exchangeable senior notes	—	—	—	—	—	126,863	—	—	126,863	—	126,863
Issuance of ordinary shares in conjunction with exercise of share options	1,185	—	—	—	—	43,043	—	—	43,043	—	43,043
Issuance of ordinary shares under employee stock purchase plan	117	—	—	—	—	7,197	—	—	7,197	—	7,197
Issuance of ordinary shares in conjunction with vesting of restricted stock units	222	—	—	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(18,030)	—	—	(18,030)	—	(18,030)
Issuance of ordinary shares in conjunction with exercise of warrants	1,552	—	—	—	—	8,247	—	—	8,247	—	8,247
Shares issued under directors deferred compensation plan	17	—	—	—	—	—	—	—	—	—	—
Share-based compensation	—	—	—	—	—	70,057	—	—	70,057	—	70,057
Excess tax benefits from employee share options	—	—	—	—	—	1,841	—	—	1,841	—	1,841
Shares repurchased	(304)	—	—	—	—	—	—	(42,215)	(42,215)	—	(42,215)
Other comprehensive loss	—	—	—	—	—	—	(178,250)	—	(178,250)	(14)	(178,264)
Net income	—	—	—	—	—	—	—	58,387	58,387	(1,061)	57,326
Balance at December 31, 2014	60,643	$ 6	4,000	$ 55	$ 471	$ 1,458,005	$ (122,097)	$ 34,704	$ 1,371,144	$ 64	$ 1,371,208

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY—(Continued)
(In thousands)

	Ordinary Shares		Non-voting Euro Deferred								
	Shares	Amount	Shares	Amount	Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Jazz Pharmaceuticals plc Shareholders' Equity	Non-controlling interest	Total Equity
Balance at December 31, 2014	60,643	$ 6	4,000	$ 55	$ 471	$ 1,458,005	$ (122,097)	$ 34,704	$ 1,371,144	$ 64	$ 1,371,208
Acquisition of noncontrolling interest	—	—	—	—	—	(10)	—	—	(10)	(63)	(73)
Issuance of ordinary shares in conjunction with exercise of share options	732	—	—	—	—	32,982	—	—	32,982	—	32,982
Issuance of ordinary shares under employee stock purchase plan	75	—	—	—	—	7,541	—	—	7,541	—	7,541
Issuance of ordinary shares in conjunction with vesting of restricted stock units	265	—	—	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(26,102)	—	—	(26,102)	—	(26,102)
Share-based compensation	—	—	—	—	—	91,795	—	—	91,795	—	91,795
Excess tax benefits from employee share options	—	—	—	—	—	(1,311)	—	—	(1,311)	—	(1,311)
Shares repurchased	(410)	—	—	—	—	—	—	(61,553)	(61,553)	—	(61,553)
Other comprehensive loss	—	—	—	—	—	—	(145,375)	—	(145,375)	—	(145,375)
Net income	—	—	—	—	—	—	—	329,535	329,535	(1)	329,534
Balance at December 31, 2015	61,305	$ 6	4,000	$ 55	$ 471	$ 1,562,900	$ (267,472)	$ 302,686	$ 1,598,646	$ —	$ 1,598,646

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2015	**2014**	**2013**
Operating activities			
Net income	$ 329,534	$ 57,326	$ 216,312
Adjustments to reconcile net income to net cash provided by operating activities:			
Intangible asset amortization	98,162	126,584	79,042
Share-based compensation	91,550	69,638	44,551
Impairment charges	31,523	39,365	—
Depreciation	9,894	7,097	3,048
Acquired in-process research and development	—	202,626	4,988
Loss on disposal of property and equipment	172	24	46
Excess tax benefit from share-based compensation	—	(1,841)	—
Acquisition accounting inventory fair value step-up adjustments	—	10,477	3,826
Change in fair value of contingent consideration	—	—	15,200
Deferred income taxes	(61,209)	(43,423)	(10,097)
Provision for losses on accounts receivable and inventory	4,062	2,493	2,446
Loss on extinguishment and modification of debt	16,815	—	3,749
Amortization of debt discount and deferred financing costs	22,738	13,725	4,591
Other non-cash transactions	(5,187)	(11,986)	1,687
Changes in assets and liabilities:			
Accounts receivable	(24,841)	(55,041)	(48,846)
Inventories	6,271	(7,630)	(8,516)
Prepaid expenses and other current assets	3,720	11,936	(13,871)
Other long-term assets	(11,722)	(8,891)	(4,306)
Accounts payable	(2,280)	(37,966)	5,089
Accrued liabilities	2,986	20,997	14,717
Income taxes payable	(6,271)	8,634	(38,984)
Deferred revenue	(536)	(1,203)	(1,061)
Contingent consideration	—	(14,900)	—
Other non-current liabilities	26,562	17,724	14,820
Net cash provided by operating activities	531,943	405,765	288,431
Investing activities			
Acquisitions, net of cash acquired	—	(828,676)	—
Acquisition of in-process research and development	—	(202,626)	(4,988)
Purchases of property and equipment	(35,958)	(36,347)	(9,976)
Net proceeds from sale of business	33,703	—	—
Acquisition of intangible assets	—	—	(1,300)
Net cash used in investing activities	(2,255)	(1,067,649)	(16,264)
Financing activities			
Net proceeds from issuance of debt	898,642	1,194,385	553,425
Proceeds from employee equity incentive and purchase plans and exercise of warrants	40,523	58,487	30,703
Share repurchases	(61,553)	(42,215)	(136,484)
Acquisition of noncontrolling interests	(73)	(136,969)	—
Payment of contingent consideration	—	(35,100)	—
Payment of employee withholding taxes related to share-based awards	(26,102)	(18,030)	(5,590)
Excess tax benefit from share-based compensation	—	1,841	—
Repayments of long-term debt	(905,760)	(9,524)	(465,910)
Repayments under revolving credit facility	(160,000)	(300,000)	—
Net cash provided by (used in) financing activities	(214,323)	712,875	(23,856)
Effect of exchange rates on cash and cash equivalents	(10,622)	(3,453)	997
Net increase in cash and cash equivalents	304,743	47,538	249,308
Cash and cash equivalents, at beginning of period	684,042	636,504	387,196
Cash and cash equivalents, at end of period	$ 988,785	$ 684,042	$ 636,504

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS—(Continued)
(In thousands)

	Year Ended December 31,		
	2015	2014	2013
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 40,099	$ 31,978	$ 18,278
Cash paid for income taxes	145,597	108,189	137,616
Non-cash investing activities:			
Construction-in-progress related to facility lease obligation	4,351	—	—

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

Jazz Pharmaceuticals plc is an international biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing meaningful products that address unmet medical needs.

We have a diverse portfolio of products and product candidates, with a focus in the areas of sleep and hematology/oncology.

Our lead marketed products are:

- **Xyrem® (sodium oxybate) oral solution**, the only product approved by the U.S. Food and Drug Administration, or FDA, for the treatment of both cataplexy and excessive daytime sleepiness, or EDS, in patients with narcolepsy;
- **Erwinaze® (asparaginase *Erwinia chrysanthemi*)**, a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia, or ALL, who have developed hypersensitivity to *E. coli*-derived asparaginase; and
- **Defitelio® (defibrotide)**, a product approved in Europe for the treatment of severe hepatic veno-occlusive disease, or VOD, in adults and children undergoing hematopoietic stem cell transplantation, or HSCT, therapy.

Our strategy is to create shareholder value by:

- Growing sales of the existing products in our portfolio, including by identifying and investing in growth opportunities such as new treatment indications;
- Acquiring clinically meaningful and differentiated products that are on the market or product candidates that are in late-stage development; and
- Pursuing targeted development of post-discovery differentiated product candidates.

We apply a disciplined approach to allocating our resources between investments in our current commercial and development portfolio and acquisitions or in-licensing of new assets.

Throughout this report, unless otherwise indicated or the context otherwise requires, all references to "Jazz Pharmaceuticals," "the registrant," "we," "us," and "our" refer to Jazz Pharmaceuticals plc and its consolidated subsidiaries. Throughout this report, all references to "ordinary shares" refer to Jazz Pharmaceuticals plc's ordinary shares.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP, and include the accounts of Jazz Pharmaceuticals plc and our subsidiaries and intercompany transactions and balances have been eliminated. Our consolidated financial statements include the results of operations of businesses we have acquired from the date of each acquisition for the applicable reporting periods.

Significant Risks and Uncertainties

Our financial results remain significantly influenced by sales of Xyrem. In 2015, net product sales of Xyrem were $955.2 million, which represented 73% of total net product sales. Our ability to maintain or increase sales of Xyrem in its approved indications is subject to a number of risks and uncertainties, including the potential introduction of generic competition or an alternative sodium oxybate product that competes with Xyrem; changed or increased regulatory restrictions or regulatory actions by the FDA; our suppliers' ability to obtain sufficient quotas from the U.S. Drug Enforcement Administration, or DEA; any supply, manufacturing or distribution problems arising with any of our suppliers or distributors, all of whom are sole source providers for us; any increase in pricing pressure from or restrictive conditions for reimbursement required by, and the availability of reimbursement from, third party payors; changes in healthcare laws and policy; continued acceptance of Xyrem by physicians and patients; changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell Xyrem; and operational disruptions at the central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA.

Seven companies have sent us notices that they have filed abbreviated new drug applications, or ANDAs, with the FDA seeking approval to market a generic version of Xyrem. We have filed lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and the litigation proceedings are

ongoing. We cannot predict the timing or outcome of these proceedings. Although no trial date has been set in any of the ANDA suits, we anticipate that trial on some of the patents in the case against the first ANDA filer, Roxane Laboratories, Inc., or Roxane, could occur as early as the second quarter of 2016. Some of the ANDA filers have also filed petitions for *inter partes* review, or IPR, by the Patent Trial and Appeal Board, or the PTAB, of the U.S. Patent and Trademark Office, or USPTO, with respect to the validity of certain distribution, method of use and formulation patents covering Xyrem. In July 2015, the PTAB issued decisions instituting IPR trials with respect to petitions related to certain patents covering the Xyrem distribution system, and we expect the PTAB to issue final decisions on the validity of these patents in July 2016. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business. We expect that the approval of an ANDA that results in the launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In late August 2015, we implemented the final REMS that was approved by the FDA in February 2015. The process under which enrolled patients receive Xyrem is complex and includes multiple mandatory steps taken by the central pharmacy. The transition to the final approved REMS necessitated significant operational changes at the central pharmacy and revised documentation requirements for patients and prescribers. In the third quarter of 2015, Xyrem product sales were adversely impacted by operational disruption and resulting delays in prescription fills and refills. As physicians and patients familiarized themselves with the new REMS process and documentation requirements, the central pharmacy experienced a significantly increased volume of calls from patients and physicians' offices that the pharmacy was not able to timely address, resulting in a backlog of prescription fills and refills that were delayed. We identified and addressed with the central pharmacy to the extent feasible the processes that led to the operational delays. In the fourth quarter of 2015, we observed an improvement in key operational metrics compared to the third quarter of 2015, and we believe that central pharmacy operations have stabilized. However, we cannot guarantee that we will not experience further disruptions and resulting adverse impacts on Xyrem product sales. Any failure to comply with the REMS obligations could result in enforcement action by the FDA; lead to changes in our Xyrem REMS obligations; continue to negatively affect sales of Xyrem; result in additional costs and expenses for us; and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects. Further, we cannot predict whether the FDA will seek to require or ultimately require modifications to the Xyrem REMS, including with respect to the distribution system, or seek to otherwise impose or ultimately impose additional requirements to the Xyrem REMS, or the potential timing, terms or propriety thereof. Any such modifications or additional requirements could potentially make it more difficult or expensive for us to distribute Xyrem, make it easier for future generic competitors, and/or negatively affect sales of Xyrem.

We may face pressure to develop a single shared REMS with potential generic competitors for Xyrem that is different from the approved Xyrem REMS or to license or share intellectual property pertinent to the Xyrem REMS, or elements of the Xyrem REMS, including proprietary data required for safe distribution of sodium oxybate, with generic competitors. The Xyrem REMS is the subject of multiple issued patents. In January 2014, the FDA held an initial meeting with us and the three then-current sodium oxybate ANDA applicants to facilitate the development of a single shared REMS for sodium oxybate. In October 2015, the FDA held a telephonic meeting with us and the seven current sodium oxybate ANDA applicants to discuss the status of the development of a single shared REMS for sodium oxybate. The parties had regular interactions with respect to developing a single shared REMS prior to this meeting, and we are seeking to continue the interactions with the goal of developing a single shared REMS. However, we are aware that, separate from the discussions with us, the FDA and ANDA applicants have exchanged communications regarding the potential development of a single shared REMS for sodium oxybate. We cannot predict whether, or to what extent, interactions among the parties will continue or whether we will develop a single shared REMS. If we do not develop a single shared REMS or license or share intellectual property pertinent to our Xyrem REMS with generic competitors within a time frame or on terms that the FDA considers acceptable, the FDA may assert that its waiver authority permits it to approve the ANDA of one or more generic competitors with a separate REMS that differs from our approved Xyrem REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the development of a single shared REMS for sodium oxybate, licensing or sharing intellectual property pertinent to our Xyrem REMS, or the FDA's response to a request by one or more ANDA applicants for a waiver of the requirement for a single shared REMS, including in connection with a certification that the applicant had been unable to obtain a license. In addition, the Federal Trade Commission, other governmental authorities or others could claim or determine that we are using the Xyrem REMS in an anticompetitive manner (including in light of the FDA's statement in the Xyrem REMS approval notice that the Xyrem REMS could be used in an anticompetitive manner inconsistent with applicable provisions of the Federal Food, Drug and Cosmetic Act) or have engaged in other anticompetitive practices.

Obtaining and maintaining appropriate reimbursement for Xyrem in the U.S. is increasingly challenging due to, among other things, the attention being paid to healthcare cost containment and prescription drug pricing, pricing pressure from third party payors and increasingly restrictive reimbursement conditions being imposed by third party payors. In this regard, we have experienced and expect to continue to experience increasing pressure from third party payors to agree to discounts, rebates or other pricing terms for Xyrem. Any such restrictive pricing terms or additional reimbursement conditions could have a material adverse effect on our Xyrem revenues. In addition, drug pricing by pharmaceutical companies has recently come under close scrutiny, particularly with respect to companies that have increased the price of products after acquiring those products from other companies. We expect that healthcare policies and reforms intended to curb healthcare costs will continue to be proposed, which could limit the prices that we charge for our products, including Xyrem, limit our commercial opportunity and/or negatively impact revenues from sales of our products. Also, price increases on Xyrem and our other products, and negative publicity regarding pricing and price increases generally, whether with respect to our products or products distributed by other pharmaceutical companies, could negatively affect market acceptance of Xyrem and our other products.

In 2015, sales of our second largest product, Erwinaze/Erwinase (which we refer to in this report as Erwinaze unless otherwise indicated or the context otherwise requires) were $203.3 million, which represented 15% of total net product sales. We seek to maintain and increase sales of Erwinaze, as well as to make Erwinaze more widely available, through ongoing sales and marketing and research and development activities. However, our ability to successfully and sustainably maintain or grow sales of Erwinaze is subject to a number of risks and uncertainties, including the limited population of patients with ALL and the incidence of hypersensitivity reactions to *E. coli*-derived asparaginase within that population, our need to apply for and receive marketing authorizations, through the European Union's mutual recognition procedure or otherwise, in certain additional countries so we can launch promotional efforts in those countries, as well as those other risks and uncertainties discussed in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. In particular, a significant challenge to our ability to maintain current sales levels and to increase sales is our need to avoid supply interruptions of Erwinaze due to capacity constraints, production delays, quality or regulatory challenges or other manufacturing difficulties. Erwinaze is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL. The current manufacturing capacity for Erwinaze is nearly completely absorbed by demand for the product. We are working with PBL to evaluate potential expansion of its production capacity to increase the supply of Erwinaze over the longer term. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build an excess level of product inventory that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues, and we have experienced, and expect to continue to experience, manufacturing and inventory challenges that have resulted in disruptions in our ability to supply certain markets. If capacity constraints continue, whether as a result of continued quality or other manufacturing issues or otherwise, we may be unable to build a desired excess level of product inventory, and our ability to supply the market may continue to be compromised. Additional Erwinaze supply interruptions and/or our inability to expand production capacity could materially adversely affect our sales of and revenues from Erwinaze and our potential future maintenance and growth of the market for this product.

Sales of Defitelio/defibrotide were 5% of our net product sales in 2015. We acquired this product in January 2014 in connection with our acquisition of Gentium S.r.l., or Gentium, which we refer to as the Gentium Acquisition, and secured worldwide rights to the product by acquiring rights to defibrotide in the Americas in August 2014. We launched Defitelio in certain European countries in 2014 and continued to launch in additional European countries on a rolling basis through 2015. We are in the process of making pricing and reimbursement submissions with respect to Defitelio in those European countries where Defitelio is not yet launched, including in countries where pricing and reimbursement approvals are required for launch. Our ability to realize the anticipated benefits from our investment in Defitelio/defibrotide is subject to risks and uncertainties, including those discussed in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. In particular, we may not be able to successfully maintain or grow sales of Defitelio in Europe, or obtain marketing approval in other countries, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. A key challenge to our success in maintaining or growing sales of Defitelio in Europe is our ability to obtain appropriate pricing and reimbursement approvals in those European countries where Defitelio is not yet launched. If we experience delays or unforeseen difficulties in obtaining favorable pricing and reimbursement approvals, planned launches in the affected countries would be delayed, or, if we are unable to ultimately obtain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country's reimbursed price influences other countries, our growth prospects in Europe could be negatively affected.

In September 2015, the FDA accepted for filing with priority review our NDA for defibrotide for the treatment of VOD with evidence of multi-organ dysfunction following HSCT. Based on timelines established by the Prescription Drug User Fee Act, or PDUFA, we expect FDA review of the NDA to be completed by March 31, 2016. However, the FDA does not always meet the timelines established by PDUFA, and it is possible that the FDA's review of our NDA will not be completed by the

PDUFA date, in which case our plans for commercialization of defibrotide in the U.S. may be delayed. In any event, we cannot predict whether our NDA will be approved in a timely manner, if at all. Approval of our NDA is dependent on our and our supplier's ability to obtain FDA certification of current Good Manufacturing Practices in connection with the manufacturing of the defibrotide drug compound and the processing of defibrotide into finished product for the U.S. market and on the outcome of FDA inspections of clinical sites and potentially other entities involved in the development of defibrotide. In 2015, the FDA issued a Form FDA 483 to Patheon Italia S.p.A., or Patheon Italia, that included observations related to the Ferentino, Italy facility that manufactures the defibrotide finished product. Failure by Patheon Italia to timely remediate the observations to the FDA's satisfaction or the discovery of issues that impact the defibrotide finished product could have an adverse impact on the potential approval of our NDA for defibrotide, including the timing thereof.

In the event we are able to obtain U.S. marketing approval, we will also face other challenges that could impact the anticipated value of Defitelio/defibrotide, including the limited size of the population of VOD patients who are indicated for treatment with Defitelio/defibrotide (particularly if the FDA requires more narrow or restricted labeling than we have proposed or if changes in HSCT treatment protocols reduce the incidence of VOD); U.S. market acceptance of defibrotide at its commercial price, particularly in light of past access to defibrotide free of charge through an expanded access treatment protocol; the need to establish U.S. pricing and reimbursement support for defibrotide, including through acceptance by hospital pharmacy and therapeutics committees; the possibility that we may be required to conduct time-consuming and costly clinical trials as a condition of any U.S. marketing approval for the product; the lack of experience of U.S. physicians in diagnosing and treating VOD; and challenges to our ability to develop the product for additional indications. If sales of Defitelio/defibrotide do not reach the levels we expect, our anticipated revenue from the product would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition to risks specifically related to Xyrem, Erwinaze and Defitelio/defibrotide, we are subject to other challenges and risks specific to our business and our ability to execute on our strategy, as well as risks and uncertainties common to companies in the pharmaceutical industry with development and commercial operations. These risks and uncertainties include:

- the challenges of protecting and enhancing our intellectual property rights;
- the challenges of achieving and maintaining commercial success of our products;
- delays or problems in the supply or manufacture of our products, particularly with respect to certain products as to which we maintain limited inventories, and our dependence on single source suppliers to continue to meet our ongoing commercial demand or our requirements for clinical trial supplies;
- the need to obtain and maintain appropriate pricing and reimbursement for our products in an increasingly challenging environment due to, among other things, the attention being paid to healthcare cost containment and other austerity measures in the United States and worldwide, including the need to obtain and maintain reimbursement for Xyrem in the United States in an environment in which we are subject to increasingly restrictive conditions for reimbursement required by third party payors;
- our ability to identify and acquire, in-license or develop additional products or product candidates to grow our business;
- the challenges of compliance with the requirements of the FDA, the DEA, and non-U.S. regulatory agencies, including with respect to product labeling, requirements for distribution, obtaining sufficient DEA quotas where needed, marketing and promotional activities, adverse event reporting and product recalls or withdrawals;
- the difficulty and uncertainty of pharmaceutical product development, including the timing thereof, and the uncertainty of clinical success, such as the risk that results from preclinical studies and/or early clinical trials may not be predictive of results obtained in later and larger clinical trials planned or anticipated to be conducted for our product candidates;
- the inherent uncertainty associated with the regulatory approval process, especially as we continue to undertake increased activities and make growing investment in our product pipeline development projects;
- the risks associated with business combination or product or product candidate acquisition transactions, such as the challenges inherent in the integration of acquired businesses with our historic business, the increase in geographic dispersion among our centers of operation and the risks that we may acquire unanticipated liabilities along with acquired businesses or otherwise fail to realize the anticipated benefits (commercial or otherwise) from such transactions; and

- possible restrictions on our ability and flexibility to pursue certain future opportunities as a result of our substantial outstanding debt obligations.

Business Acquisitions

Our consolidated financial statements include the results of operations of an acquired business from the date of acquisition. We account for acquired businesses using the acquisition method of accounting. The acquisition method of accounting for acquired businesses requires, among other things, that assets acquired, liabilities assumed and any noncontrolling interests in the acquired business be recognized at their estimated fair values as of the acquisition date, with limited exceptions, and that the fair value of acquired in-process research and development, or IPR&D, be recorded on the balance sheet. Also, transaction costs are expensed as incurred. Any excess of the acquisition consideration over the assigned values of the net assets acquired is recorded as goodwill. Contingent consideration is included within the acquisition cost and is recognized at its fair value on the acquisition date. A liability resulting from contingent consideration is remeasured to fair value at each reporting date until the contingency is resolved and changes in fair value are recognized in earnings.

Concentrations of Risk

Financial instruments that potentially subject us to concentrations of credit risk consist of cash, cash equivalents and marketable securities. Our investment policy permits investments in U.S. federal government and federal agency securities, corporate bonds or commercial paper issued by U.S. corporations, money market instruments, certain qualifying money market mutual funds, certain repurchase agreements, and tax-exempt obligations of U.S. states, agencies and municipalities and places restrictions on credit ratings, maturities, and concentration by type and issuer. We are exposed to credit risk in the event of a default by the financial institutions holding our cash, cash equivalents and marketable securities and issuers of investments to the extent recorded on the balance sheet.

We are also subject to credit risk from our accounts receivable related to our product sales. We monitor our exposure within accounts receivable and record a reserve against uncollectible accounts receivable as necessary. We extend credit to pharmaceutical wholesale distributors and specialty pharmaceutical distribution companies, primarily in the United States, and to other international distributors and hospitals. Customer creditworthiness is monitored and collateral is not required. We monitor deteriorating economic conditions in certain European countries which may result in variability of the timing of cash receipts and an increase in the average length of time that it takes to collect accounts receivable outstanding. Historically, we have not experienced significant credit losses on our accounts receivable and we do not expect to have write-offs or adjustments to accounts receivable which would have a material adverse effect on our financial position, liquidity or results of operations. As of December 31, 2015, five customers accounted for 90% of gross accounts receivable including Express Scripts Specialty Distribution Services, Inc. and its affiliate CuraScript, Inc., or Express Scripts, which accounted for 69% of gross accounts receivable, and IDIS Limited, which accounted for 11% of gross accounts receivable. As of December 31, 2014, five customers accounted for 86% of gross accounts receivable including Express Scripts, which accounted for 66% of gross accounts receivable, and IDIS Limited, which accounted for 11% of gross accounts receivable.

We depend on single source suppliers for each of our products, product candidates and their active pharmaceutical ingredients.

Cash Equivalents and Marketable Securities

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.

Marketable securities are investments in debt securities with maturities of less than one year from the balance sheet date, or securities with maturities of greater than one year that are specifically identified to fund current operations. Collectively, cash equivalents and marketable securities are considered available-for-sale and are recorded at fair value. Unrealized gains and losses, net of tax, are recorded in accumulated other comprehensive loss in shareholders' equity. We use the specific-identification method for calculating realized gains and losses on securities sold. Realized gains and losses and declines in value judged to be other than temporary on marketable securities are included in interest expense, net in the consolidated statements of income.

Inventories

Inventories are valued at the lower of cost or market. Cost is determined using the first-in, first-out method for all inventories. Our policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective

and primarily dependent on our estimates of future demand for a particular product. If our estimate of future demand changes, we consider the impact on the reserve for excess inventory and adjust the reserve as required. Increases in the reserve are recorded as charges in cost of product sales. For product candidates that have not been approved by the FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expense. For products that have been approved by the FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the clinical trial. Prior to receiving FDA approval, costs related to purchases of the active pharmaceutical ingredient and the manufacturing of the product candidate are recorded as research and development expense. All direct manufacturing costs incurred after approval are capitalized into inventory.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which range from three to 10 years. Leasehold improvements are amortized over the shorter of the noncancelable term of our operating leases or their economic useful lives. Maintenance and repairs are expensed as incurred.

Goodwill

Goodwill represents the excess of the acquisition consideration over the fair value of assets acquired and liabilities assumed. We have determined that we operate in a single segment and have a single reporting unit associated with the development and commercialization of pharmaceutical products. The annual test for goodwill impairment is a two-step process. The first step is a comparison of the fair value of the reporting unit with its carrying amount, including goodwill. If this step indicates impairment, then, in the second step, the loss is measured as the excess of recorded goodwill over its implied fair value. Implied fair value is the excess of the fair value of the reporting unit over the fair value of all identified assets and liabilities. We test goodwill for impairment annually in October and when events or changes in circumstances indicate that the carrying value may not be recoverable.

Acquired In-Process Research and Development

The initial costs of rights to IPR&D projects acquired in an asset acquisition are expensed as IPR&D unless the project has an alternative future use. The fair value of IPR&D projects acquired in a business combination are capitalized and accounted for as indefinite-lived intangible assets until the underlying project receives regulatory approval, at which point the intangible asset will be accounted for as a finite-lived intangible asset, or discontinued, at which point the intangible asset will be written off. Development costs incurred after an acquisition are expensed as incurred.

Intangible Assets

Intangible assets with finite useful lives consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives, which range from two to 16 years. The estimated useful lives associated with finite-lived intangible assets are consistent with the estimated lives of the associated products and may be modified when circumstances warrant. Such assets are reviewed for impairment when events or circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset and its eventual disposition are less than its carrying amount. The amount of any impairment is measured as the difference between the carrying amount and the fair value of the impaired asset.

Revenue Recognition

Revenues are recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed and determinable and collection is reasonably assured.

Product Sales, Net

Product sales revenue is recognized when title has transferred to the customer and the customer has assumed the risks and rewards of ownership, which is typically on delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer removes product from our consigned inventory location for shipment directly to a patient.

Revenue from sales transactions where the buyer has the right to return the product is recognized at the time of sale only if (i) the seller’s price to the buyer is substantially fixed or determinable at the date of sale, (ii) the buyer has paid the seller, or the buyer is obligated to pay the seller and the obligation is not contingent on resale of the product, (iii) the buyer’s obligation to the seller would not be changed in the event of theft or physical destruction or damage of the product, (iv) the buyer

acquiring the product for resale has economic substance apart from that provided by the seller, (v) the seller does not have significant obligations for future performance to directly bring about resale of the product by the buyer, and (vi) the amount of future returns can be reasonably estimated.

Revenues from sales of products are recorded net of estimated allowances for returns, specialty distributor fees, wholesaler fees, prompt payment discounts, government rebates, government chargebacks, coupon programs and rebates under managed care plans. Provisions for returns, specialty distributor fees, wholesaler fees, government rebates, coupon programs and rebates under managed care plans are included within current liabilities in our consolidated balance sheets. Provisions for government chargebacks and prompt payment discounts are generally shown as a reduction in accounts receivable. Calculating certain of these items involves estimates and judgments based on sales or invoice data, contractual terms, historical utilization rates, new information regarding changes in these programs' regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates for these programs and channel inventory data. Adjustments to estimates for these allowances have not been material.

Royalties and Contract Revenues

We receive royalties from third parties based on sales of our products under licensing and distribution arrangements. For those arrangements where royalties are reasonably estimable, we recognize revenues based on estimates of royalties earned during the applicable period, and adjust for differences between the estimated and actual royalties in the following quarter. Historically, these adjustments have not been significant.

Our contract revenues consist of fees and milestone payments. Non-refundable fees where we have no continuing performance obligations are recognized as revenues when there is persuasive evidence of an arrangement and collection is reasonably assured. In situations where we have continuing performance obligations, non-refundable fees are deferred and are recognized ratably over our projected performance period. We recognize at-risk milestone payments, which are typically related to regulatory, commercial or other achievements by us or our licensees and distributors, as revenues when the milestone is accomplished and collection is reasonably assured. Sales-based milestone payments are typically payments made to us that are triggered when aggregate net sales of a product by a collaborator for a specified period (for example, an annual period) reach an agreed upon threshold amount. We recognize sales-based milestone payments from a collaborator when the event which triggers the obligation of payment has occurred, there is no further obligation on our part in connection with the payment, and collection is reasonably assured. Refundable fees are deferred and recognized as revenues upon the later of when they become nonrefundable or when our performance obligations are completed.

Cost of Product Sales

Cost of product sales includes manufacturing and distribution costs, the cost of drug substance, royalties due to third parties on product sales, product liability and cargo insurance, FDA user fees, freight, shipping, handling and storage costs and salaries and related costs of employees involved with production. Cost of product sales included $10.5 million and $3.8 million of inventory costs associated with the fair value step-up in acquired inventory in 2014 and 2013, respectively. Excluded from cost of product sales shown on the consolidated statements of income is amortization of acquired developed technology of $93.0 million, $122.6 million and $78.8 million in 2015, 2014 and 2013, respectively.

Research and Development

Research and development expenses consist primarily of costs related to clinical studies and outside services, personnel expenses and other research and development costs, including milestone payments incurred prior to regulatory approval of products. Clinical study and outside services costs relate primarily to services performed by clinical research organizations, clinical studies performed at clinical sites, materials and supplies, and other third party fees. Personnel expenses relate primarily to salaries, benefits and share-based compensation. Other research and development expenses primarily include overhead allocations consisting of various support and facilities-related costs. Research and development costs are expensed as incurred. For product candidates that have not been approved by the FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expense. For products that have been approved by the FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the trial.

Advertising Expenses

We expense the costs of advertising, including promotional expenses, as incurred. Advertising expenses were $4.2 million, $1.0 million and $1.0 million in 2015, 2014 and 2013, respectively.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amount and the tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more-likely-than-not that some portion or all of a deferred tax asset will not be realized. We account for unrecognized tax benefits using a "more-likely-than-not" threshold for recognizing and resolving unrecognized tax benefits. A recognized tax benefit is then measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon settlement. Interest and penalties related to unrecognized tax benefits are included in the income tax provision and classified with the related liability on the consolidated balance sheets.

Foreign Currency

Our functional and reporting currency is the U.S. dollar. The assets and liabilities of our subsidiaries that have a functional currency other than the U.S. dollar are translated into U.S. dollars at the exchange rate prevailing at the balance sheet date with the results of operations of subsidiaries translated at the average exchange rate for the reporting period. The cumulative foreign currency translation adjustment is recorded as a component of accumulated other comprehensive income (loss) in shareholders' equity.

Transactions in foreign currencies are translated into the functional currency of the relevant subsidiary at the rate of exchange prevailing at the date of the transaction. Any monetary assets and liabilities arising from these transactions are translated into the relevant functional currency at exchange rates prevailing at the balance sheet date or on settlement. Resulting gains and losses are recorded in foreign currency gain (loss) in our consolidated statements of income.

Financing Costs

Deferred financing costs are reported at cost, less accumulated amortization and the related amortization expense is included in interest expense, net in our consolidated statements of income. The carrying amount of debt includes any related unamortized original issue discount.

Contingencies

From time to time, we may become involved in claims and other legal matters arising in the ordinary course of business. We record accruals for loss contingencies to the extent that we conclude 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.

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles, or GAAP, requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures in the condensed consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates.

Net Income per Ordinary Share

Basic net income per ordinary share attributable to Jazz Pharmaceuticals plc is based on the weighted-average number of ordinary shares outstanding. Diluted net income per ordinary share attributable to Jazz Pharmaceuticals plc is based on the weighted-average number of ordinary shares outstanding and potentially dilutive ordinary shares outstanding.

Basic and diluted net income per ordinary share attributable to Jazz Pharmaceuticals plc were computed as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2015	2014	2013
Numerator:			
Net income attributable to Jazz Pharmaceuticals plc	$ 329,535	$ 58,387	$ 216,312
Denominator:			
Weighted-average ordinary shares used in per share calculation - basic	61,232	59,746	58,298
Dilutive effect of employee equity incentive and purchase plans	1,804	2,402	1,772
Dilutive effect of warrants	—	466	1,499
Weighted-average ordinary shares used in per share calculation - diluted	63,036	62,614	61,569
Net income attributable to Jazz Pharmaceuticals plc per ordinary share :			
Basic	$ 5.38	$ 0.98	$ 3.71
Diluted	$ 5.23	$ 0.93	$ 3.51

Potentially dilutive ordinary shares from our employee equity incentive and purchase plans, warrants and our 1.875% exchangeable senior notes due 2021, or the 2021 Notes, are determined by applying the treasury stock method to the assumed exercise of share options and warrants, the assumed vesting of outstanding restricted stock units, or RSUs, the assumed issuance of ordinary shares under our employee stock purchase plan, or ESPP, and the assumed issuance of ordinary shares upon exchange of the 2021 Notes. The approximately 2.9 million ordinary shares issuable upon exchange of the 2021 Notes had no effect on diluted net income attributable to Jazz Pharmaceuticals plc per ordinary share because the average price of our ordinary shares for the year ended December 31, 2015 did not exceed the effective exchange price of $199.77 per ordinary share under the 2021 Notes.

The following table represents the weighted-average ordinary shares that were excluded from the computation of diluted net income attributable to Jazz Pharmaceuticals plc per ordinary share for the periods presented because including them would have an anti-dilutive effect (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Options to purchase ordinary shares and RSUs	1,609	819	1,584
1.875% exchangeable senior notes due 2021	2,878	1,112	—

Share-Based Compensation

We account for compensation cost for all share-based awards at fair value on the date of grant. The fair value is recognized as expense over the service period, net of estimated forfeitures, using the straight-line method. The estimation of share-based awards that will ultimately vest requires judgment, and, to the extent actual results or updated estimates differ from current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. We primarily consider historical experience when estimating expected forfeitures.

Recent Accounting Pronouncements

In November 2015, the Financial Accounting Standards Board, or the FASB, issued Accounting Standards Update, or ASU, No. 2015-17, “Balance Sheet Classification of Deferred Taxes”, or ASU No. 2015-17, which simplifies the presentation of deferred income taxes. ASU No. 2015-17 requires that deferred tax assets and liabilities be classified as non-current in a statement of financial position. We early adopted ASU 2015-17 effective December 31, 2015 on a prospective basis. Adoption of this ASU resulted in a reclassification of our net current deferred tax assets and liabilities to net non-current deferred tax assets and liabilities in our consolidated balance sheet as of December 31, 2015. No prior periods were retrospectively adjusted.

In April 2015, the FASB issued ASU No. 2015-03, “Interest - Imputation of Interest”, or ASU No. 2015-03. ASU No. 2015-03 requires debt issuance costs related to a recognized debt liability to be presented in the balance sheet as a direct

deduction from the debt liability instead of as an asset. ASU No. 2015-03 does not affect the recognition and measurement guidance for debt issuance costs. 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 - Amendments to SEC Paragraphs Pursuant to Staff Announcements at the June 2015 EITF Meeting", or ASU No. 2015-15. ASU No. 2015-15 indicates that the guidance in ASU No. 2015-03 did not address presentation or subsequent measurement of debt issuance costs related to line of credit arrangements. Given the absence of authoritative guidance within ASU No. 2015-03, the SEC staff has indicated that they would not object to an entity deferring and presenting debt issuance costs as an asset and subsequently amortizing the costs ratably over the term of the line of credit arrangement, regardless of whether there are any outstanding borrowings on the line of credit arrangement. This guidance is effective for us beginning January 1, 2016 and requires retrospective application. This guidance is not expected to have a material impact on our consolidated balance sheets or related disclosures.

In April 2015, the FASB issued ASU No. 2015-05, "Intangibles-Goodwill and Other-Internal-Use Software", or ASU No. 2015-05. ASU No. 2015-05 provides guidance on whether a cloud computing arrangement contains a software license to be accounted for as internal-use software to assist in the evaluation of the accounting for fees paid by a customer in the arrangement. ASU No. 2015-05 will be effective for us beginning January 1, 2016 and may be applied either prospectively to new cloud computing arrangements or retrospectively. This guidance is not expected to have a material impact on our financial position or results of operations.

In May 2014, the FASB issued ASU No. 2014-09, "Revenue from Contracts with Customers", or ASU No. 2014-09, which states that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To achieve this, an entity will need to identify the contract with a customer; identify the separate performance obligations in the contract; determine the transaction price; allocate the transaction price to the separate performance obligations in the contract; and recognize revenue when (or as) the entity satisfies each performance obligation. In August 2015, the FASB issued ASU No. 2015-14, "Revenue from Contracts with Customers: Deferral of the Effective Date", which deferred by one year the effective date of ASU No. 2014-09 which will now be effective for us beginning January 1, 2018 and can be adopted on a full retrospective basis or on a modified retrospective basis. We are currently assessing our approach to the adoption of this standard and the potential impact on our results of operations and financial position.

3. Disposition

In March 2015, we sold certain products and the related business that we originally acquired as part of our June 2012 acquisition of EUSA Pharma Inc., or the EUSA Acquisition. The purchase price for the products and related business was $34.0 million, subject to pre- and post-closing purchase price adjustments. We recognized a loss on disposal of $0.2 million within selling, general and administrative expenses in our consolidated statements of income.

The related assets met the assets held for sale criteria and were reclassified to assets held for sale as of December 31, 2014. Goodwill was allocated to these assets using the relative fair value method. We have determined that the disposition of these assets did not qualify for reporting as a discontinued operation, because the sale did not represent a strategic shift that had or will have a major effect on our operations and financial results.

4. Fair Value Measurement

Cash and cash equivalents consisted of the following (in thousands):

	December 31, 2015				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents
Cash	$ 274,945	$ —	$ —	$ 274,945	$ 274,945
Time deposits	713,840	—	—	713,840	713,840
Totals	$ 988,785	$ —	$ —	$ 988,785	$ 988,785

	December 31, 2014				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents
Cash	$ 338,262	$ —	$ —	$ 338,262	$ 338,262
Time deposits	345,780	—	—	345,780	345,780
Totals	$ 684,042	$ —	$ —	$ 684,042	$ 684,042

Cash equivalents are considered available-for-sale securities. We use the specific-identification method for calculating realized gains and losses on securities sold and include them in interest expense, net in the consolidated statements of income.

The following table summarizes, by major security type, our available-for-sale securities that were measured at fair value on a recurring basis and were categorized using the fair value hierarchy (in thousands):

	December 31, 2015		December 31, 2014	
	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value
Time deposits	$ 713,840	$ 713,840	$ 345,780	$ 345,780

As of December 31, 2015, our available-for-sale securities included 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.

There were no transfers between the different levels of the fair value hierarchy in 2015 or in 2014.

As of December 31, 2015, the estimated fair value of our 2021 Notes, which had a carrying value of $466.0 million, was approximately $601 million. The fair value of the 2021 Notes was estimated using quoted market prices obtained from brokers (Level 2). The estimated fair value of our borrowings under our term loan and other borrowings were approximately equal to their respective book values based on the borrowing rates currently available for variable rate loans (Level 2).

5. Inventories

Inventories consisted of the following (in thousands):

	December 31,	
	2015	2014
Raw materials	$ 2,608	$ 3,570
Work in process	11,836	9,870
Finished goods	5,007	16,597
Total inventories	$ 19,451	$ 30,037

6. Property and Equipment

Property and equipment consisted of the following (in thousands):

	December 31,	
	2015	2014
Construction-in-progress	$ 63,008	$ 37,145
Computer software	15,797	10,634
Leasehold improvements	9,301	7,931
Computer equipment	10,963	7,670
Machinery and equipment	5,828	6,408
Furniture and fixtures	2,580	2,220
Land and buildings	1,775	1,547
Subtotal	109,252	73,555
Less accumulated depreciation and amortization	(23,680)	(15,192)
Property and equipment, net	$ 85,572	$ 58,363

7. Goodwill and Intangible Assets

The gross carrying amount of goodwill was as follows (in thousands):

Balance at December 31, 2014	$ 702,713
Foreign exchange	(45,574)
Balance at December 31, 2015	$ 657,139

The gross carrying amounts and net book values of our intangible assets were as follows (in thousands):

		December 31, 2015			December 31, 2014		
	Remaining Weighted-Average Useful Life (In years)	Gross Carrying Amount	Accumulated Amortization	Net Book Value	Gross Carrying Amount	Accumulated Amortization	Net Book Value
Acquired developed technologies	12.0	$ 1,321,324	$ (324,044)	$ 997,280	$ 1,450,606	$ (259,889)	$ 1,190,717
Manufacturing contracts	2.1	11,697	(5,676)	6,021	13,012	(3,060)	9,952
Trademarks	—	2,882	(2,882)	—	2,914	(2,896)	18
Total finite-lived intangible assets		1,335,903	(332,602)	1,003,301	1,466,532	(265,845)	1,200,687
Acquired IPR&D assets		182,305	—	182,305	236,748	—	236,748
Total intangible assets		$ 1,518,208	$ (332,602)	$ 1,185,606	$ 1,703,280	$ (265,845)	$ 1,437,435

The decrease in the gross carrying amount of intangible assets as of December 31, 2015 compared to December 31, 2014 is primarily due to the negative impact of foreign currency translation adjustments due to the strengthening of the U.S. dollar against the euro.

The assumptions and estimates used to determine future cash flows and remaining useful lives of our intangible and other long-lived assets are complex and subjective. They can be affected by various factors, including external factors, such as industry and economic trends, and internal factors such as changes in our business strategy and our forecasts for specific product lines.

As a result of our decision to terminate a pivotal Phase 2 clinical trial of JZP-416, we recognized an impairment charge of $31.5 million to our acquired IPR&D asset in the fourth quarter of 2015.

Based on finite-lived intangible assets recorded as of December 31, 2015, and assuming the underlying assets will not be impaired and that we will not change the expected lives of the assets, future amortization expenses were estimated as follows (in thousands):

Year Ending December 31,	Estimated Amortization Expense
2016	$ 90,442
2017	90,442
2018	87,636
2019	87,419
2020	86,249
Thereafter	561,113
Total	$ 1,003,301

8. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2015	2014
Rebates and other sales deductions	$ 67,454	$ 51,899
Employee compensation and benefits	35,595	46,143
Contract claim settlement	18,000	—
Sales returns reserve	6,110	14,039
Royalties	4,211	7,964
Accrued interest	4,043	10,327
Professional fees	3,038	3,295
Accrued construction-in-progress	1,637	4,931
Other	23,982	25,493
Total accrued liabilities	$ 164,070	$ 164,091

9. Debt

The following table summarizes the carrying amount of our indebtedness (in thousands):

	December 31,	
	2015	2014
1.875% exchangeable senior notes due 2021	$ 575,000	$ 575,000
Unamortized discount on 1.875% exchangeable senior notes due 2021	(109,048)	(124,735)
1.875% exchangeable senior notes due 2021, net	465,952	450,265
Term loans	738,038	890,479
Other borrowings	513	1,684
Total debt	1,204,503	1,342,428
Less current portion	37,587	9,428
Total long-term debt	$ 1,166,916	$ 1,333,000

Credit Agreement

On June 18, 2015, Jazz Pharmaceuticals plc, as guarantor, and certain of its wholly owned subsidiaries, as borrowers, entered into a credit agreement, which we refer to as the June 2015 credit agreement, that provides for a $750.0 million principal amount term loan, which was drawn in full at closing, and a $750.0 million revolving credit facility, of which

$160.0 million was drawn at closing and subsequently repaid. We used the proceeds from initial borrowings under the June 2015 credit agreement to repay in full the $893.1 million principal amount of term loans outstanding under the credit agreement that we entered into in June 2012, as subsequently amended, which we refer to as the previous credit agreement, and to pay related fees and expenses. The previous credit agreement was terminated upon repayment of the term loans outstanding thereunder.

Under the June 2015 credit agreement, the term loan matures on June 18, 2020 and the revolving credit facility terminates, and any loans outstanding thereunder become due and payable, on June 18, 2020.

Borrowings under the June 2015 credit agreement bear interest, at our option, at a rate equal to either (a) the LIBOR rate, plus an applicable margin ranging from 1.50% to 2.25% per annum, based upon our secured leverage ratio, or (b) the prime lending rate, plus an applicable margin ranging from 0.50% to 1.25% per annum, based upon our secured leverage ratio. The revolving credit facility has a commitment fee payable on the undrawn amount ranging from 0.25% to 0.35% per annum based upon our secured leverage ratio.

As of December 31, 2015, the interest rate on the term loan was 2.36% and the effective interest rate was 2.38%. As of December 31, 2015, we had undrawn revolving credit facilities totaling $750.0 million of which $1.1 million was committed for an outstanding letter of credit.

Jazz Pharmaceuticals plc and certain of our wholly owned subsidiaries are borrowers under the June 2015 credit agreement. The borrowers' obligations under the June 2015 credit agreement, and any hedging or cash management obligations entered into with a lender, are guaranteed on a senior secured basis by Jazz Pharmaceuticals plc and certain of its subsidiaries (including the issuer of the 2021 Notes as described below) and are secured by substantially all of Jazz Pharmaceuticals plc's, the borrowers' and the guarantor subsidiaries' assets.

We may make voluntary prepayments of principal at any time without payment of a premium. We are required to make mandatory prepayments of the term loan (without payment of a premium) with (1) net cash proceeds from certain non-ordinary course asset sales (subject to reinvestment rights and other exceptions), (2) net cash proceeds from issuances of debt (other than certain permitted debt), and (3) casualty proceeds and condemnation awards (subject to reinvestment rights and other exceptions).

Principal repayments of the term loan, which are due quarterly, began in December 2015 and are equal to 5.0% per annum of the original principal amount of $750.0 million during the first two years, 7.5% per annum during the third year, 10.0% per annum during the fourth year and 12.5% per annum during the fifth year, with any remaining balance payable on the maturity date.

The June 2015 credit agreement contains financial covenants that require Jazz Pharmaceuticals plc and its restricted subsidiaries to not (a) exceed a maximum secured net leverage ratio or (b) fall below a cash interest coverage ratio. We were, as of December 31, 2015, and are currently, in compliance with these financial covenants.

In connection with our entry into the June 2015 credit agreement and termination of the previous credit agreement, we recorded a loss on extinguishment and modification of debt of $16.8 million, which was comprised of $16.0 million related to the expensing of unamortized deferred financing costs and unamortized original issue discount associated with extinguished debt and $0.8 million related to new third party fees associated with modified debt.

Exchangeable Senior Notes

In August 2014, we completed a private placement of the 2021 Notes. Interest on the 2021 Notes is payable semi-annually in cash in arrears on February 15 and August 15 of each year, beginning on February 15, 2015, at a rate of 1.875% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2021 Notes. The 2021 Notes mature on August 15, 2021, unless earlier exchanged, repurchased or redeemed.

The holders of the 2021 Notes have the ability to require us to repurchase all or a portion of their 2021 Notes for cash in the event Jazz Pharmaceuticals plc undergoes certain fundamental changes. Prior to August 15, 2021, we may redeem the 2021 Notes, in whole but not in part, subject to compliance with certain conditions, if we have, or on the next interest payment date would, become obligated to pay to the holder of any 2021 Note additional amounts as a result of certain tax-related events. We also may redeem the 2021 Notes on or after August 20, 2018, in whole or in part, if the last reported sale price per ordinary share 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 we provide the notice of redemption.

The 2021 Notes are exchangeable at an initial exchange rate of 5.0057 ordinary shares per $1,000 principal amount of 2021 Notes, which is equivalent to an initial exchange price of approximately $199.77 per ordinary share. Upon exchange, the 2021 Notes may be settled in cash, ordinary shares or a combination of cash and ordinary shares, at our election. Our intent and policy is to settle the principal amount of the 2021 Notes in cash upon exchange. 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 make-whole fundamental changes occurring prior to the maturity date of the 2021 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2021 Notes who elect to exchange their 2021 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to February 15, 2021, the 2021 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

The 2021 Notes were issued by Jazz Investments I Limited, or the Issuer, a 100%-owned finance subsidiary of Jazz Pharmaceuticals plc. The Issuer's obligations under the 2021 Notes are fully and unconditionally guaranteed on a senior unsecured basis by Jazz Pharmaceuticals plc. No subsidiary of Jazz Pharmaceuticals plc guaranteed the 2021 Notes. Subject to certain local law restrictions on payment of dividends, among other things, and potential negative tax consequences, we are not aware of any significant restrictions on the ability of Jazz Pharmaceuticals plc to obtain funds from the Issuer or Jazz Pharmaceuticals plc's other subsidiaries by dividend or loan, or any legal or economic restrictions on the ability of the Issuer or Jazz Pharmaceuticals plc's other subsidiaries to transfer funds to Jazz Pharmaceuticals plc in the form of cash dividends, loans or advances. There is no assurance that in the future such restrictions will not be adopted.

In accounting for the issuance of the 2021 Notes, we separated the 2021 Notes into liability and equity components. The carrying amount of the liability component was calculated by measuring the estimated fair value of a similar liability that does not have an associated exchange feature. The carrying amount of the equity component representing the exchange option was determined by deducting the fair value of the liability component from the face value of the 2021 Notes as a whole. The excess of the principal amount of the liability component over its carrying amount will be amortized to interest expense over the expected life of the 2021 Notes using the effective interest method with an effective interest rate of 6.4% per annum. We have determined the expected life of the 2021 Notes to be equal to the original seven-year term. The equity component is not remeasured as long as it continues to meet the conditions for equity classification. As of December 31, 2015, the "if-converted value" did not exceed the principal amount of the 2021 Notes.

We allocated the total issuance costs incurred of $16.1 million to the liability and equity components based on their relative values. Issuance costs attributable to the liability component will be amortized to expense over the term of the 2021 Notes, and issuance costs attributable to the equity component were included with the equity component in our shareholders' equity.

For the years ended December 31, 2015 and 2014, we recognized $26.5 million and $9.9 million, respectively, in interest expense, net related to the contractual coupon rate and amortization of the debt discount on the 2021 Notes.

As of December 31, 2015, the carrying value of the equity component of the 2021 Notes, net of equity issuance costs, was $126.9 million.

Scheduled maturities with respect to our long-term debt are as follows (in thousands):

Year Ending December 31,	Scheduled Long-Term Debt Maturities
2016	$ 37,587
2017	42,280
2018	61,034
2019	79,789
2020	520,420
Thereafter	575,028
Total	$ 1,316,138

10. Deferred Revenue

The deferred revenue balance primarily relates to an agreement we have with UCB Pharma Limited, or UCB, under which UCB has the right to market Xyrem for certain indications in various countries outside of the U.S. We recognized contract revenues of $1.1 million during each of 2015, 2014 and 2013 relating to two upfront payments received from UCB in 2006 totaling $15.0 million. The deferred revenue balance related to this agreement is being recognized ratably through 2019.

11. Commitments and Contingencies

Indemnification

In the normal course of business, we enter into agreements that contain a variety of representations and warranties and provide for general indemnification, including indemnification associated with product liability or infringement of intellectual property rights. Our exposure under these agreements is unknown because it involves future claims that may be made but have not yet been made against us. To date, we have not paid any claims or been required to defend any action related to these indemnification obligations.

We have agreed to indemnify our officers, directors and certain other employees for losses and costs incurred in connection with certain events or occurrences, including advancing money to cover certain costs, subject to certain limitations. The maximum potential amount of future payments we could be required to make under the indemnification obligations is unlimited; however, we maintain insurance policies that may limit our exposure and may enable us to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits and other policy provisions, we believe the fair value of these indemnification obligations is not significant. Accordingly, we have not recognized any liabilities relating to these obligations as of December 31, 2015 and December 31, 2014. No assurances can be given that the covering insurers will not attempt to dispute the validity, applicability, or amount of coverage without expensive litigation against these insurers, in which case we may incur substantial liabilities as a result of these indemnification obligations.

Lease and Other Commitments

We have noncancelable operating leases for our office buildings and we are obligated to make payments under noncancelable operating leases for automobiles used by our sales force.

Lease expense under our operating leases was as follows (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Lease expense	$ 10,479	$ 10,678	$ 9,114

Future minimum lease payments under our noncancelable operating and facility leases at December 31, 2015, were as follows (in thousands):

Year ending December 31,	Lease Payments
2016	$ 11,757
2017	12,709
2018	8,310
2019	7,165
2020	6,735
Thereafter	66,562
Total	$ 113,238

In January 2015, we entered into an agreement to lease office space located in Palo Alto, California in a building to be constructed by the landlord. We expect to occupy this office space by the end of 2017. The lease has a term of 12 years from the commencement date as defined in the lease agreement and we have an option to extend the term of the lease twice for a period of five years each. We are obligated to make lease payments totaling approximately $88 million over the initial term of the lease. In connection with this lease, the landlord is providing a tenant improvement allowance for the costs associated with the design, development and construction of tenant improvements for the leased facility. We are obligated to fund all costs incurred in excess of the tenant improvement allowance. The scope of the planned tenant improvements do not qualify as “normal tenant improvements” under the lease accounting guidance. Accordingly, for accounting purposes, we have concluded

we are the deemed owner of the building during the construction period. As of December 31, 2015, we recorded project construction costs of $4.4 million incurred by the landlord as construction-in-progress in property and equipment, net and a corresponding financing obligation in other non-current liabilities in our consolidated balance sheets. We will increase the asset and financing obligation as additional building costs are incurred by the landlord during the construction period. In the year ended December 31, 2015, we recorded rent expense associated with the ground lease of $1.8 million in our consolidated statements of income.

As of December 31, 2015, we had $97.5 million of noncancelable purchase commitments due within one year, primarily related to agreements with third party manufacturers.

Legal Proceedings

We are involved in legal proceedings, including the following matters:

Xyrem ANDA Matters. On October 18, 2010, we received a notice of Paragraph IV Certification from Roxane that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. Roxane's initial notice alleged that all five patents then listed for Xyrem in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or Orange Book, on the date of the notice are invalid, unenforceable or not infringed by Roxane's proposed generic product. On November 22, 2010, we filed a lawsuit against Roxane in response to Roxane's initial notice in the U.S. District Court for the District of New Jersey, or the District Court, seeking a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe our patents. In accordance with the Hatch-Waxman Act, as a result of our having filed a timely lawsuit against Roxane, FDA approval of Roxane's ANDA was stayed for 30 months, or until April 2013. That stay has expired. Additional patents covering Xyrem have been issued since December 2010, and after receiving Paragraph IV Certification notices from Roxane with respect to those patents, we have filed additional lawsuits against Roxane to include these additional patents in the litigation. All of the lawsuits filed against Roxane between 2010 and 2012 have been consolidated by the District Court into a single case, or the first Roxane consolidated case, alleging that 10 of our patents covering Xyrem are or will be infringed by Roxane's ANDA and seeking a permanent injunction to prevent Roxane from launching a generic version of Xyrem that would infringe these patents. After receiving additional Paragraph IV Certification notices from Roxane, on February 20, 2015 and June 1, 2015, we filed two actions against Roxane in the District Court that have since been consolidated, or the second Roxane consolidated case, alleging that four of our patents covering Xyrem are or will be infringed by Roxane's ANDA and seeking a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe those patents. After receiving an additional Paragraph IV Certification notice from Roxane on December 14, 2015, we filed an action against Roxane on January 27, 2016 alleging that one of our patents covering Xyrem is or will be infringed by Roxane's ANDA and seeking a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe that patent.

In December 2013, the District Court permitted Roxane to amend its answer in the first Roxane consolidated case to allege certain equitable defenses, and the parties were given additional time for discovery on those new defenses. In addition, in March 2014, the District Court granted our motion to bifurcate and stay the portion of the first Roxane consolidated case regarding patents related to the distribution system for Xyrem. Although no trial date has been scheduled, based on the District Court's current schedule, we anticipate that trial on the patents in the first Roxane consolidated case that are not subject to the stay could occur as early as the second quarter of 2016. We do not have any estimate of a possible trial date for trial on the patents in the first Roxane consolidated case that are currently subject to the stay or for any other Roxane cases.

On April 20, 2015, Roxane moved in the second Roxane consolidated case to dismiss claims involving our patent covering a part of the Xyrem label that instructs prescribers on adjusting the dose of Xyrem when it is being co-administered with divalproex sodium (also known as valproate or valproic acid) on the grounds that this patent does not cover patentable subject matter. On October 29, 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of IPR proceedings before the PTAB, relating to the patent that was the subject of Roxane's motion. The actual timing of events in our litigation with Roxane may be significantly earlier or later than we currently anticipate. We cannot predict the specific timing or outcome of events in these matters or the impact of these matters on any of the Roxane cases or other ongoing proceedings with any ANDA filer.

On December 10, 2012, we received notice of Paragraph IV Certification from Amneal Pharmaceuticals, LLC, or Amneal, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On January 18, 2013, we filed a lawsuit against Amneal in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Amneal's ANDA and seeking a permanent injunction to prevent Amneal from introducing a generic version of Xyrem that would infringe these patents. On November 21, 2013, we received notice of Paragraph IV Certification from Par Pharmaceutical, Inc., or Par, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On December 27, 2013, we filed a lawsuit against Par in the District Court, alleging that our patents covering Xyrem

are infringed or will be infringed by Par's ANDA and seeking a permanent injunction to prevent Par from introducing a generic version of Xyrem that would infringe these patents.

In April 2014, Amneal asked the District Court to consolidate its case with the Par case, stating that both cases would proceed on the schedule for the Par case. The District Court granted this request in May 2014. The order consolidating the cases provides that Amneal's 30-month stay period will be extended to coincide with the date of Par's 30-month stay period. As a result, FDA's approval of both Amneal's and Par's ANDAs is stayed until the earlier of (i) May 20, 2016, or (ii) a District Court decision finding that the identified patents are invalid, unenforceable or not infringed.

Additional patents covering Xyrem have issued since April 2014 and have been listed in the Orange Book for Xyrem. Amneal and Par have given us additional notices of Paragraph IV Certifications regarding such patents, and we have filed additional lawsuits against Amneal and Par in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Amneal's and Par's ANDAs and seeking a permanent injunction to prevent Amneal and Par from introducing a generic version of Xyrem that would infringe these patents.

On June 4, 2014, we received a notice of Paragraph IV Certification from Ranbaxy Laboratories Limited, or Ranbaxy, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On July 15, 2014, we filed a lawsuit against Ranbaxy in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Ranbaxy's ANDA and seeking a permanent injunction to prevent Ranbaxy from introducing a generic version of Xyrem that will infringe these patents. Since June 2014, we have received additional notices of Paragraph IV Certification from Ranbaxy regarding newly issued patents for Xyrem listed in the Orange Book, and we have filed additional lawsuits against Ranbaxy in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Ranbaxy's ANDA and seeking a permanent injunction to prevent Ranbaxy from introducing a generic version of Xyrem that would infringe these patents.

On October 30, 2014, we received a notice of Paragraph IV Certification from Watson Laboratories, Inc., or Watson, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On December 11, 2014, we filed a lawsuit against Watson in the District Court alleging that our patents covering Xyrem are or will be infringed by Watson's ANDA and seeking a permanent injunction to prevent Watson from introducing a generic version of Xyrem that would infringe these patents. On March 23, 2015, Watson moved to dismiss the portion of the case based on our Orange Book-listed patents covering the distribution system for Xyrem on the grounds that these patents do not cover patentable subject matter. On November 4, 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of IPR proceedings before the PTAB relating to the patents that were the subject of Watson's motion. Since March 2015, we have received an additional notice of Paragraph IV Certification from Watson regarding newly issued patents for Xyrem listed in the Orange Book, and we have filed an additional lawsuit against Watson in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Watson's ANDA and seeking a permanent injunction to prevent Watson from introducing a generic version of Xyrem that would infringe these patents.

In April 2015, the District Court issued an order that consolidated all then-pending lawsuits against Amneal, Par, Ranbaxy and Watson into one case.

On June 8, 2015, we received a Paragraph IV Certification from Wockhardt Bio AG, or Wockhardt, that it has submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On July 17, 2015, we filed a lawsuit in the District Court alleging that our patents covering Xyrem are or will be infringed by Wockhardt's ANDA and seeking a permanent injunction to prevent Wockhardt from introducing a generic version of Xyrem that would infringe our patents. Since July 2015, we have received an additional notice of Paragraph IV Certification from Wockhardt regarding newly issued patents listed in the Orange Book, and we have filed an additional lawsuit against Wockhardt in the District Court alleging that our patents covering Xyrem are infringed or will be infringed by Watson's ANDA and seeking a permanent injunction to prevent Watson from introducing a generic version of Xyrem that would infringe these patents.

On July 23, 2015, we received a Paragraph IV Certification from Lupin Inc., or Lupin, that it has submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. On September 2, 2015, we filed a lawsuit in the District Court alleging that our patents covering Xyrem are or will be infringed by Lupin's ANDA and seeking a permanent injunction to prevent Lupin from introducing a generic version of Xyrem that would infringe our patents.

On January 14, 2016, the District Court issued an order consolidating all of the cases then pending against Amneal, Par, Ranbaxy, Watson, Wockhardt and Lupin into a single case for all purposes. We cannot predict the timing or outcome of events in this matter or the impact of developments involving any specific parties or patents on other ongoing proceedings with any ANDA filer.

Xyrem Post-Grant Patent Review Matters. In January 2015, certain of the ANDA filers filed petitions for IPR with respect to the validity of six patents covering the distribution system for Xyrem. In July 2015, the PTAB issued decisions

instituting IPR trials with respect to these petitions, and we expect the PTAB to issue final decisions on the validity of the patents in July 2016. In September 2015, certain of the ANDA filers filed a petition for IPR with respect to the validity of an additional patent covering the distribution system for Xyrem. In October 2015, certain of the ANDA filers filed petitions for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium (also known as valproate or valproic acid). In December 2015, Wockhardt filed a petition for IPR with respect to the validity of one of our patents covering the formulation of Xyrem. In February 2016, Amneal filed a petition for IPR with respect to the validity of one of our patents covering a method for prescribing Xyrem when it is being co-administered with divalproex sodium. We cannot predict whether additional post-grant patent review challenges will be filed by any of the ANDA filers or any other entity, the outcome of any IPR or other proceeding, whether the PTAB will institute any petitioned IPR proceeding that has not yet been instituted, or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

Cutler Matter. On October 19, 2011, Dr. Neal Cutler, one of the original owners of FazaClo, filed a complaint against Azur Pharma Public Limited Company, or Azur Pharma, and one of its subsidiaries, as well as Avanir Pharmaceuticals, Inc., or Avanir, in the California Superior Court in the County of Los Angeles, or the Superior Court. The complaint alleged that Azur Pharma and its subsidiary breached certain contractual obligations that would have required Azur Pharma to pay Cutler approximately $35 million under a contract it assumed when it acquired FazaClo from Avanir in 2007, and further alleged that Cutler was entitled to unspecified punitive damages and attorneys' fees. On December 21, 2015, Cutler filed a First Amended Complaint, and the Superior Court set a trial date for July 2016. Effective February 10, 2016, we entered into a settlement agreement with Cutler resolving all claims in the lawsuit. The settlement amount was included within accrued liabilities in our consolidated balance sheet as of December 31, 2015.

From time to time we are involved in legal proceedings arising in the ordinary course of business. We believe there is no other litigation pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.

Other Contingencies

We have not previously submitted pricing data for two radiopharmaceutical products, Quadramet® (samarium sm 153 lexidronam injection) and ProstaScint® (capromab pendetide), for Medicaid and the Public Health Service's 340B drug pricing discount program. We engaged in interactions with the Centers for Medicare and Medicaid Services, or CMS, and a trade group, the Council on Radionuclides and Radiopharmaceuticals, or CORAR, regarding the reporting of Medicaid pricing data and paying Medicaid rebates for radiopharmaceutical products. In addition to the discussions with CMS as part of CORAR, we have had separate discussions with CMS directly regarding Quadramet. We sold Quadramet to a third party in December 2013, but we retained any liabilities related to sales of the product during prior periods. Similarly, we sold ProstaScint to a third party in May 2015, but we retained any liabilities related to sales of the product during prior periods. We are currently unable to predict whether price reporting and rebates will be required for Quadramet and ProstaScint and, if so, for what period they will be required. The initiation of any reporting of Medicaid pricing data for Quadramet or ProstaScint could result in retroactive 340B ceiling price liability for these two products. We are currently unable to reasonably estimate an amount or range of a potential contingent loss. Any material liability resulting from radiopharmaceutical price reporting would negatively impact our financial results.

12. Shareholders' Equity

Share Repurchase Program

In May 2013, our board of directors authorized a share repurchase program pursuant to which we were authorized to repurchase a number of ordinary shares having an aggregate repurchase price of up to $200.0 million, exclusive of any brokerage commissions. In August 2015, we completed repurchases under the May 2013 share repurchase program. On November 5, 2015, our board of directors authorized a new share repurchase program pursuant to which we are authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300.0 million, exclusive of any brokerage commissions. Under this share repurchase program, which has no expiration date, we may repurchase ordinary shares from time to time on the open market. The timing and amount of repurchases will be at management's discretion and will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the June 2015 credit agreement, corporate and regulatory requirements and market conditions. The share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2015, under both repurchase programs, we spent a total of $61.6 million to repurchase 0.4 million of our ordinary shares at an average total purchase price, including brokerage

commissions, of $150.24 per share. All ordinary shares repurchased were canceled. As of December 31, 2015, the remaining amount authorized under the November 2015 share repurchase program was $259.8 million.

Authorized But Unissued Ordinary Shares

We had reserved the following shares of authorized but unissued ordinary shares (in thousands):

	December 31, 2015
2011 Equity Incentive Plan	11,900
2007 Equity Incentive Plan	937
2007 Employee Stock Purchase Plan	512
Amended and Restated 2007 Non-Employee Directors Stock Option Plan	451
Amended and Restated Directors Deferred Compensation Plan	178
Total	13,978

13. Comprehensive Income (Loss)

Comprehensive income (loss) includes net income and all changes in shareholders' equity during a period, except for those changes resulting from investments by shareholders or distributions to shareholders.

Accumulated Other Comprehensive Loss

The components of accumulated other comprehensive loss attributable to Jazz Pharmaceuticals plc at December 31, 2015 and December 31, 2014 were as follows (in thousands):

	Foreign Currency Translation Adjustments	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2014	$ (122,097)	$ (122,097)
Other comprehensive loss	(145,375)	(145,375)
Balance at December 31, 2015	$ (267,472)	$ (267,472)

In 2015, other comprehensive loss reflects foreign currency translation adjustments, primarily due to the strengthening of the U.S. dollar against the euro, resulting in a reduction in the dollar value of certain non-current euro denominated assets.

14. Segment and Other Information

Our operating segment is reported in a manner consistent with the internal reporting provided to the chief operating decision maker or, CODM. Our CODM has been identified as our chief executive officer. We have determined that we operate in one business segment, which is the development and commercialization of meaningful products that address unmet medical needs. The following table presents a summary of total revenues (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Xyrem	$ 955,187	$ 778,584	$ 569,113
Erwinaze/Erwinase	203,261	199,665	174,251
Defitelio/defibrotide	70,731	70,537	—
Prialt® (ziconotide) intrathecal infusion	26,440	26,421	27,103
Psychiatry	37,135	40,879	49,226
Other	24,065	46,630	45,705
Product sales, net	1,316,819	1,162,716	865,398
Royalties and contract revenues	7,984	10,159	7,025
Total revenues	$ 1,324,803	$ 1,172,875	$ 872,423

The following table presents a summary of total revenues attributed to geographic sources (in thousands):

	Year Ended December 31,		
	2015	2014	2013
United States	$ 1,192,879	$ 1,007,396	$ 792,518
Europe	103,614	126,715	61,843
All other	28,310	38,764	18,062
Total revenues	$ 1,324,803	$ 1,172,875	$ 872,423

The following table presents a summary of the percentage of total revenues from customers that represented more than 10% of our total revenues:

	Year Ended December 31,		
	2015	2014	2013
Express Scripts	72%	66%	65%
Accredo Health Group, Inc.	6%	14%	16%

The following table presents total long-lived assets by location (in thousands):

	December 31,	
	2015	2014
Ireland	$ 62,795	$ 37,775
United States	12,794	9,795
Italy	7,928	8,462
Other	2,055	2,331
Total long-lived assets (1)	$ 85,572	$ 58,363

(1) Long-lived assets consist of property and equipment.

15. Share-Based Compensation

2011 Equity Incentive Plan

On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma were combined in a merger transaction, or the Azur Merger. In connection with the Azur Merger, Jazz Pharmaceuticals, Inc.'s board of directors adopted the 2011 Equity Incentive Plan, or the 2011 Plan, in October 2011 and its stockholders approved the 2011 Plan at the special meeting of the stockholders held in December 2011 in connection with the Azur Merger. The 2011 Plan became effective immediately before the consummation of the Azur Merger and was assumed and adopted by us upon the consummation of the Azur Merger. The terms of the 2011 Plan provide for the grant of stock options, stock appreciation rights, restricted stock awards, RSUs, other stock awards, and performance awards that may be settled in cash, shares, or other property. All outstanding grants under the 2011 Plan were granted to employees and vest ratably over service periods of four years and expire no more than 10 years after the date of grant. As of December 31, 2015, a total of 16,278,263 of our ordinary shares had been authorized for issuance under the 2011 Plan. In addition, the share reserve under the 2011 Plan will automatically increase on January 1 of each year through January 1, 2022, by the least of (a) 4.5% of the total number of ordinary shares outstanding on December 31 of the preceding calendar year, (b) 5,000,000 shares, or (c) such lesser number of ordinary shares as determined by our board of directors. On January 1, 2016, the share reserve under the 2011 Plan automatically increased by 2,758,722 ordinary shares pursuant to this provision.

2007 Equity Incentive Plan

The 2007 Equity Incentive Plan, or the 2007 Plan, which was initially adopted by the Jazz Pharmaceuticals, Inc. board of directors and approved by the Jazz Pharmaceuticals, Inc. stockholders in connection with its initial public offering, was continued and assumed by us upon consummation of the Azur Merger. The 2007 Plan provided for the grant of stock options, restricted stock awards, RSUs, stock appreciation rights, performance stock awards and other forms of equity compensation to employees, including officers, non-employee directors and consultants. Prior to the consummation of the Azur Merger, all of the grants under the 2007 Plan were granted to employees and vest ratably over service periods of three to five years and expire

no more than 10 years after the date of grant. Effective as of the closing of the Azur Merger on January 18, 2012, the number of shares reserved for issuance under the 2007 Plan was set to 1,000,000 ordinary shares. The share reserve under the 2007 Plan will not automatically increase. Since the Azur Merger, all of the new grants under the 2007 Plan were granted to non-employee directors, vest ratably over service periods of one to three years and expire no more than 10 years after the date of grant.

2007 Employee Stock Purchase Plan

In 2007, Jazz Pharmaceuticals, Inc.'s employees became eligible to participate in the Employee Stock Purchase Plan, or ESPP. The ESPP was amended and restated by Jazz Pharmaceuticals, Inc.'s board of directors in October 2011 and approved by its stockholders in December 2011. The amended and restated ESPP became effective immediately prior to the effective time of the Azur Merger and was assumed by us upon the consummation of the Azur Merger. The amended and restated ESPP allows our eligible employee participants (including employees of any of a parent or subsidiary company if our board of directors designates such company as eligible to participate) to purchase our ordinary shares at a discount of 15% through payroll deductions. The ESPP consists of a fixed offering period of 24 months with four purchase periods within each offering period. The number of shares available for issuance under our ESPP during any six-month purchase period is 175,000 shares. As of December 31, 2015, a total of 2,660,000 of our ordinary shares had been authorized for issuance under the ESPP. The share reserve under the ESPP will automatically increase on January 1 of each year through January 1, 2022, by the least of (a) 1.5% of the total number of ordinary shares outstanding on December 31 of the preceding calendar year, (b) 1,000,000 shares, or (c) such lesser number of ordinary shares as determined by our board of directors or a duly-authorized committee thereof. Our compensation committee determined not to automatically increase the share reserve under the ESPP on January 1, 2016.

Amended and Restated 2007 Non-Employee Directors Stock Option Plan

The Amended and Restated 2007 Non-Employee Directors Stock Option Plan, or the 2007 Directors Option Plan, which was initially adopted by the Jazz Pharmaceuticals, Inc. board of directors and approved by the Jazz Pharmaceuticals, Inc. stockholders in connection with its initial public offering, was continued and assumed by us upon the consummation of the Azur Merger. Until October 2011, the 2007 Directors Option Plan provided for the automatic grant of stock options to purchase shares of Jazz Pharmaceuticals, Inc.'s common stock to its non-employee directors initially at the time any individual first became a non-employee director, which vest over three years, and then annually over their period of service on its board of directors, which vest over one year. On October 24, 2011, Jazz Pharmaceuticals, Inc.'s board of directors amended the 2007 Directors Option Plan to eliminate all future initial and annual automatic grants so that future automatic grants would not be made that would be subject to the excise tax imposed by Section 4985 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, in connection with the Azur Merger. Accordingly, all future stock option grants under the 2007 Directors Option Plan will be at the discretion of our board of directors. Since the Azur Merger, all of the new grants under the 2007 Directors Option Plan were granted to non-employee directors and vest ratably over service periods of one to three years and expire no more than 10 years after the date of grant. In addition, the 2007 Directors Option Plan provides the source of shares to fund distributions made prior to August 15, 2010 under the Directors Deferred Compensation Plan described below. As of December 31, 2015, a total of 869,768 of our ordinary shares had been authorized for issuance under the 2007 Directors Option Plan. The number of shares reserved for issuance under the 2007 Directors Plan automatically increases on each January 1, from January 1, 2008 through (and including) January 1, 2017, by the excess of (a) the number of shares subject to options granted, over (b) the number of shares added back to the share reserve, in each case, during the preceding calendar year under the 2007 Directors Plan; provided, that, for any year, the automatic increase may not exceed 200,000 shares and the board of directors may approve a lesser, or no, automatic increase. On January 1, 2016, the share reserve under the 2007 Directors Option Plan automatically increased by 34,150 ordinary shares pursuant to this provision.

Amended and Restated Directors Deferred Compensation Plan

In May 2007, the Jazz Pharmaceuticals, Inc. board of directors adopted the Directors Deferred Compensation Plan, or the Directors Deferred Plan, which was amended in December 2008 and was then amended and restated in August 2010, and which was continued and assumed by us upon consummation of the Azur Merger. The Directors Deferred Plan allows each non-employee director to elect to defer receipt of all or a portion of his or her annual retainer fees to a future date or dates. Amounts deferred under the Directors Deferred Plan are credited as shares of Jazz Pharmaceuticals, Inc.'s common stock (or our ordinary shares following the Azur Merger) to a phantom stock account, the number of which are based on the amount of the retainer fees deferred divided by the market value of Jazz Pharmaceuticals, Inc.'s common stock (or our ordinary shares following the Azur Merger) on the first trading day of the first open window period following the date the retainer fees are deemed earned. On the 10th business day following the day of separation from the board of directors or the occurrence of a change in control,

or as soon thereafter as practical once the non-employee director has provided the necessary information for electronic deposit of the deferred shares, each non-employee director will receive (or commence receiving, depending upon whether the director has elected to receive distributions from his or her phantom stock account in a lump sum or in installments over time) a distribution of his or her phantom stock account, in our ordinary shares (i) reserved under the 2007 Directors Option Plan prior to August 15, 2010 and (ii) from a new reserve of 200,000 shares set up under the Directors Deferred Plan on August 15, 2010. Although we continue to maintain the Directors Deferred Plan, since the consummation of the Azur Merger we have not permitted and will not permit non-employee directors to defer any annual retainer fees under the Directors Deferred Plan. We recorded no expense in 2015, 2014 and 2013 related to retainer fees earned and deferred. As of December 31, 2015, 14,499 of our ordinary shares that were unissued related to retainer fees that were deferred under the Directors Deferred Plan.

Share-Based Compensation

The table below shows, for all share option grants, the weighted-average assumptions used in the Black-Scholes option pricing model and the resulting weighted-average grant date fair value of share options granted in each of the past three years:

	Year Ended December 31,		
	2015	2014	2013
Grant date fair value	$ 57.19	$ 60.29	$ 29.09
Volatility	39%	45%	58%
Expected term (years)	4.2	4.3	4.4
Range of risk-free rates	1.1-1.5%	1.1-1.4%	0.5-1.4%
Expected dividend yield	—%	—%	—%

We rely on a blend of the historical and implied volatilities of our own ordinary shares to determine expected volatility for share option grants. In addition, we use a single volatility estimate for each share option grant. The weighted-average volatility is determined by calculating the weighted average of volatilities for all share options granted in a given year.

The expected term of share option grants represents the weighted-average period the awards are expected to remain outstanding and our estimates were based on historical exercise data. The risk-free interest rate assumption was based on zero coupon U.S. Treasury instruments whose term was consistent with the expected term of our share option grants. The expected dividend yield assumption was based on our history and expectation of dividend payouts.

Share-based compensation expense related to share options, RSUs and grants under our ESPP was as follows (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Selling, general and administrative	$ 74,653	$ 55,083	$ 35,674
Research and development	13,356	12,179	6,673
Cost of product sales	3,541	2,376	2,204
Total share-based compensation expense, pre-tax	91,550	69,638	44,551
Tax benefit from share-based compensation expense	(26,608)	(20,795)	(13,822)
Total share-based compensation expense, net of tax	$ 64,942	$ 48,843	$ 30,729

We realized tax benefits related to share option exercises of $15.4 million, $11.8 million and $6.7 million in 2015, 2014 and 2013, respectively.

Share Options

The following table summarizes information as of December 31, 2015 and activity during 2015 related to our share option plans:

	Shares Subject to Outstanding Options (In thousands)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2015	3,870	$ 72.77		
Options granted	1,118	173.30		
Options exercised	(732)	45.04		
Options forfeited	(319)	118.05		
Options expired	—	—		
Outstanding at December 31, 2015	3,937	102.81	7.4	$ 198,666
Vested and expected to vest at December 31, 2015	3,731	99.87	7.3	196,654
Exercisable at December 31, 2015	1,992	64.48	6.3	159,156

Aggregate intrinsic value shown in the table above is equal to the difference between the exercise price of the underlying share options and the fair value of our ordinary shares for share options that were in the money. The aggregate intrinsic value changes based on the fair market value of our ordinary shares. The aggregate intrinsic value of share options exercised was $93.3 million, $138.2 million and $46.0 million during 2015, 2014 and 2013, respectively. We issued new ordinary shares upon exercise of share options.

As of December 31, 2015, total compensation cost not yet recognized related to unvested share options was $75.2 million, which is expected to be recognized over a weighted-average period of 2.4 years.

As of December 31, 2015, total compensation cost not yet recognized related to grants under the ESPP was $4.0 million, which is expected to be recognized over a weighted-average period of less than one year.

Restricted Stock Units

In 2015, we granted RSUs covering an equal number of our ordinary shares to employees with a weighted-average grant date fair value of $173.25. The fair value of RSUs is determined on the date of grant based on the market price of our ordinary shares as of that date. The fair value of the RSUs is recognized as expense ratably over the vesting period of four years. In 2015, 414,000 RSUs were released with 265,000 ordinary shares issued and 149,000 ordinary shares withheld for tax purposes. The total fair value of shares vested was $72.2 million, $50.9 million and $16.1 million during 2015, 2014 and 2013, respectively.

As of December 31, 2015, total compensation cost not yet recognized related to unvested RSUs was $84.9 million, which is expected to be recognized over a weighted-average period of 2.1 years.

The following table summarizes information as of December 31, 2015 and activity during 2015 related to our RSUs:

	Number of RSUs (in thousands)	Weighted-Average Grant-Date Fair Value	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2015	1,188	$ 96.41		
RSUs granted	430	173.25		
RSUs released	(414)	86.03		
RSUs forfeited	(150)	113.44		
RSUs expired	—	—		
Outstanding at December 31, 2015	1,054	129.40	1.2	$ 148,172

16. Employee Benefit Plans

We operate a number of defined contribution retirement plans. The costs of these plans are charged to the consolidated statements of income in the period they are incurred. We recorded expense related to our defined contribution plans of $2.2 million, $2.0 million and $1.1 million in 2015, 2014 and 2013, respectively. In Ireland, we operate a defined contribution plan in which we contribute up to 8% of an employee's eligible earnings. We recorded expense of $0.6 million, $0.5 million and $0.3 million in 2015, 2014 and 2013, respectively, in connection with the contributions we made under the Irish defined contribution plan. In the United States, we provide a qualified 401(k) savings plan for our U.S.-based employees. All U.S.-based employees are eligible to participate, provided they meet the requirements of the plan. In 2013, we elected to match certain employee contributions under the 401(k) savings plan and recorded expense of $1.1 million, $1.0 million and $0.4 million in 2015, 2014 and 2013, respectively. In the United Kingdom, we operate a defined contribution plan in which we contribute up to 12% of an employee's eligible earnings. We recorded expense of $0.4 million, $0.5 million and $0.4 million in 2015, 2014 and 2013, respectively, in connection with contributions we made under the U.K. defined contribution plan. In France, we accrue for a potential liability which is payable if an employee retires. The accrued liability for France was $0.2 million, $0.4 million and $0.3 million as of December 31, 2015, 2014 and 2013, respectively. In Italy, we accrue for a potential liability which is payable if an employee leaves employment. The accrued liability for Italy was $0.3 million and $0.4 million as of December 31, 2015 and 2014, respectively.

17. Restructuring

In the fourth quarter of 2015, we recorded severance costs of $1.1 million for terminated employees in connection with the reorganization of our operations in France. These one-time termination benefits were recorded over the remaining service period where employees were required to stay through their termination date to receive the benefits and included within cost of product sales and selling, general and administrative expenses in our consolidated statements of income. We expect to incur additional one-time termination benefit costs of $0.6 million in 2016.

In 2014, we recorded severance costs for terminated employees in connection with our decision to discontinue sales representative-led promotion of our psychiatry products starting in 2015. In addition, we initiated a restructuring plan related to the consolidation of our U.K. office locations and recorded severance costs for terminated employees and facility closure costs in connection with this plan. The one-time termination benefits were recorded over the remaining service period where employees were required to stay through their termination date to receive the benefits. We recorded costs related to these one-time termination benefits of $0.4 million and $1.8 million in 2015 and 2014, respectively, within selling, general and administrative expenses in our consolidated statements of income. Facility closure costs of $0.2 million and $0.1 million were incurred in 2015 and 2014, respectively, and recorded within selling, general and administrative expenses in our consolidated statements of income.

In June 2012, we initiated a restructuring plan to re-align certain support functions across the company following the Azur Merger and the EUSA Acquisition. In connection with this restructuring plan, we incurred restructuring costs of $1.5 million in the year ended December 31, 2013, which were recorded within selling, general and administrative expenses in our consolidated statements of income.

The following table summarizes the amounts related to restructuring through December 31, 2015 (in thousands):

	Termination Benefits	Facility Closure Costs	Total
Balance at December 31, 2012	$ 1,227	$ —	$ 1,227
Expense	1,045	412	1,457
Payments	(2,272)	(160)	(2,432)
Balance at December 31, 2013	—	252	252
Expense	1,823	118	1,941
Payments	—	(252)	(252)
Balance at December 31, 2014	1,823	118	1,941
Expense	1,469	172	1,641
Payments	(2,187)	(290)	(2,477)
Balance at December 31, 2015	$ 1,105	$ —	$ 1,105

The balances as of December 31, 2015, 2014 and 2013 were included within accrued liabilities in our consolidated balance sheets.

18. Income Taxes

The components of income before the income tax provision were as follows (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Ireland	$ 233,785	$ 238,351	$ 186,903
United States	285,420	222,328	132,855
Other	(83,272)	(309,122)	(11,808)
Total	$ 435,933	$ 151,557	$ 307,950

The following table sets forth the details of the income tax provision (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Current			
Ireland	$ 22,599	$ 23,506	$ 17,089
United States	116,301	97,679	71,964
Other	28,708	16,469	12,682
Total current income tax	167,608	137,654	101,735
Deferred, exclusive of other components below			
Ireland	494	2,323	8,353
United States	332	(15,003)	(3,513)
Other	(40,532)	(30,743)	(14,937)
Total deferred, exclusive of other components	(39,706)	(43,423)	(10,097)
Deferred, change in tax rates			
United States	294	—	—
Other	(21,797)	—	—
Total deferred, change in tax rates	(21,503)	—	—
Total deferred income tax benefit	(61,209)	(43,423)	(10,097)
Total income tax provision	$ 106,399	$ 94,231	$ 91,638

Our income tax provision was $106.4 million, $94.2 million and $91.6 million in 2015, 2014 and 2013, respectively, related to tax arising on income in Ireland, the United States and certain other foreign jurisdictions, certain unrecognized tax benefits and various expenses not deductible for tax purposes.

The effective tax rates for 2015, 2014 and 2013 were 24.4%, 62.2% and 29.8%, respectively. After adjusting the income before income tax provision for the year ended December 31, 2014 by excluding a total of $202.0 million in upfront and milestone payments for rights to JZP-110 and to defibrotide in the Americas, which were acquired by our subsidiaries in a non-taxable jurisdiction, the effective tax rate on the resulting income before income tax provision for 2014 was 26.7%. The effective tax rate for 2015 was higher than the Irish statutory rate of 12.5%, primarily due to income taxable at a rate higher than the Irish statutory rate, unrecognized tax benefits, and various expenses not deductible for tax purposes, partially offset by originating tax credits, deductions available in relation to subsidiary equity and reductions in tax rates in certain jurisdictions. The effective tax rates for 2014 and 2013 were higher than the Irish statutory rate of 12.5%, primarily due to income taxable at a rate higher than the Irish statutory rate, unrecognized tax benefits, current year losses in some jurisdictions for which no tax benefit is available and various expenses not deductible for tax purposes, partially offset by changes in U.S. state valuation allowances in 2014 and benefits from certain originating income tax credits. The decrease in the effective tax rate in 2015 compared to 2014 was primarily due to changes in income mix among the various jurisdictions in which we operate, increased originating tax credits, increased deductions available in relation to subsidiary equity and reductions in tax rates in certain jurisdictions, partially offset by the impact of impairments of intangible assets and changes in U.S. state valuation allowances during 2014. The decrease in the effective tax rate, after excluding the upfront and milestone payments, for 2014 compared to

2013 was primarily due to changes in income mix among the various jurisdictions in which we operate, changes in U.S. state valuation allowances and benefits from certain originating income tax credits. We are currently paying taxes in Ireland, the United States and certain other foreign jurisdictions where we have operations and either all net operating losses, or NOLs, have been utilized, or are restricted as a result of the Azur Merger.

The reconciliation between the statutory income tax rate applied to income before income tax provision and our effective income tax rate was as follows:

	Year Ended December 31,		
	2015	2014	2013
Statutory income tax rate	12.5 %	12.5 %	12.5 %
Foreign income tax rate differential	19.1 %	50.0 %	10.3 %
Change in tax rate	(4.5)%	— %	— %
Research and other tax credits	(3.8)%	(9.4)%	(1.9)%
Change in unrecognized tax benefits	3.6 %	6.2 %	2.8 %
Deduction on subsidiary equity	(2.7)%	(7.5)%	— %
Change in estimates	(1.0)%	(3.0)%	1.1 %
Non-deductible compensation	1.9 %	4.6 %	1.3 %
Change in valuation allowance	(0.6)%	5.7 %	1.1 %
Financing costs	(0.4)%	0.7 %	— %
Acquisition-related costs	— %	3.1 %	1.7 %
Other	0.3 %	(0.7)%	0.9 %
Effective income tax rate	24.4 %	62.2 %	29.8 %

Deferred income taxes reflect the tax effects of NOLs and tax credit carryforwards and the net temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes using currently enacted tax rates and regulations that are expected to be in effect when the differences are expected to be recovered or settled.

Significant components of our net deferred tax assets/(liabilities) were as follows (in thousands):

	December 31,	
	2015	2014
Deferred tax assets:		
Net operating loss carryforwards	$ 57,091	$ 74,057
Tax credit carryforwards	36,797	23,946
Intangible assets	25,384	19,507
Share-based compensation	20,050	14,033
Accruals	32,355	36,157
Other	31,144	36,222
Total deferred tax assets	202,821	203,922
Valuation allowance	(33,949)	(29,697)
Net deferred tax assets	168,872	174,225
Deferred tax liabilities:		
Acquired intangible assets	(307,356)	(395,651)
Other	(33,138)	(39,124)
Total deferred tax liabilities	(340,494)	(434,775)
Net deferred tax liabilities	$ (171,622)	$ (260,550)

The net change in valuation allowance was $4.3 million, $9.0 million and $3.2 million in 2015, 2014 and 2013, respectively.

The following table presents the breakdown between current and non-current deferred tax assets/(liabilities) (in thousands):

	Year Ended December 31,	
	2015	2014
Current deferred tax assets	$ —	$ 48,440
Current deferred tax liabilities	—	(9,430)
Non-current deferred tax assets	122,863	75,494
Non-current deferred tax liabilities	(294,485)	(375,054)
Net deferred tax liabilities	$ (171,622)	$ (260,550)

During November 2015, the FASB issued ASU 2015-17 which simplifies the presentation of deferred income taxes. This ASU requires that deferred tax assets and liabilities be classified as non-current in a statement of financial position. We early adopted ASU 2015-17 effective December 31, 2015 on a prospective basis. Adoption of this ASU resulted in a reclassification of our net current deferred tax assets and liabilities to net non-current deferred tax assets and liabilities in our consolidated balance sheet as of December 31, 2015. No prior periods were retrospectively adjusted.

As of December 31, 2015, we had NOL carryforwards and tax credit carryforwards for U.S. federal income tax purposes of approximately $227.7 million and $60.5 million, respectively, available to reduce future income subject to income taxes. The NOL carryforwards are inclusive of $97.1 million from the EUSA Acquisition in 2012. The federal NOL carryforwards will expire, if not utilized, in the tax years 2016 to 2034, and the federal tax credits will expire, if not utilized, in the tax years 2016 to 2035, with the exception of alternative minimum tax credits, which have no expiration date. In addition, we had approximately $234.7 million of NOL carryforwards and $7.0 million of tax credit carryforwards as of December 31, 2015 available to reduce future taxable income for state income tax purposes. The state NOL carryforwards will expire, if not utilized, in the tax years 2016 to 2034. The state tax credits have no expiration date. In addition, as of December 31, 2015, there were NOL carryforwards for income tax purposes of approximately $64.8 million and $65.3 million available to reduce future income subject to income taxes in the United Kingdom and Italy, respectively. The NOLs generated in the United Kingdom and Italy have no expiration period. We also had excess foreign tax credits, as of December 31, 2015, of $4.2 million, which may only be utilized against certain sources of income. The excess foreign tax credits have no expiration period.

Utilization of certain of our NOL and tax credit carryforwards in the United States is subject to annual limitation due to the ownership change limitations provided by Sections 382 and 383 of the Internal Revenue Code and similar state provisions. Such an annual limitation may result in the expiration of certain NOLs and tax credits before future utilization. We currently estimate that we have an annual limitation on the utilization of certain acquired federal NOLs and credits of $23.5 million, before tax effect, for 2016 and a combined total of $27.5 million, before tax effect, for 2017 to 2026. In addition, as a result of the Azur Merger, until 2022 we are subject to certain limitations under the Internal Revenue Code in relation to the utilization of U.S. NOLs to offset U.S. taxable income resulting from certain transactions.

Approximately $170.4 million of both the U.S. federal and state NOL carryforwards as of December 31, 2015 included above resulted from exercises of employee share options and certain sales by employees of shares issued under other employee equity compensation plans. We have not recorded the tax benefit of the deduction related to these exercises and sales as deferred tax assets on our balance sheet. When we realize the tax benefit as a reduction to taxable income in our tax returns, we will account for the tax benefit as a credit to shareholders' equity rather than as a reduction of our income tax provision in our financial statements.

Valuation allowances require an assessment of both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. Such assessment is required on a jurisdiction-by-jurisdiction basis. Our valuation allowance was $33.9 million and $29.7 million as of December 31, 2015 and 2014, respectively, for certain U.S. state and foreign deferred tax assets which we maintain until sufficient positive evidence exists to support reversal. During 2015, as part of the overall change in valuation allowance, we recognized a net income tax expense of $2.4 million relating to the creation of a valuation allowance against certain deferred tax assets primarily associated with NOLs arising during the year, partially offset by a release of a valuation allowance due to the impact of the reduction of tax rates in certain jurisdictions on certain deferred tax assets primarily associated with NOLs. During 2014, as part of the overall change in valuation allowance, we recognized a net income tax benefit of $7.7 million relating to the net reversal of a valuation allowance against certain deferred tax assets associated with NOLs and tax credit carryforwards. During 2013, as part of the overall change in valuation allowance, we recognized an income tax expense of $2.3 million relating to the creation of a valuation allowance against certain U.S. state deferred tax assets associated with tax credit carryforwards. We periodically evaluate the likelihood of the realization

of deferred tax assets and will adjust such amounts in light of changing facts and circumstances including, but not limited to, future projections of taxable income, tax legislation, rulings by relevant tax authorities, the progress of tax audits and the regulatory approval of products currently under development. Realization of substantially all the deferred tax assets is dependent on future book income.

Temporary differences related to investments in foreign subsidiaries totaled approximately $983.8 million and $736.9 million as of December 31, 2015 and 2014, respectively. In the event of the distribution of those earnings in the form of dividends, a sale of the subsidiaries, or certain other transactions, we may be liable for income taxes, subject to an adjustment, if any, for foreign tax credits and foreign withholding taxes payable to certain foreign tax authorities. As of December 31, 2015, it was not practicable to determine the amount of the income tax liability related to these investments.

We are 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. As a result, we have established a liability for certain tax benefits which we judge may not be sustained upon examination. A reconciliation of our gross unrecognized tax benefits follows (in thousands):

	December 31,		
	2015	2014	2013
Balance at the beginning of the year	$ 40,802	$ 21,637	$ 7,288
Increases related to current year tax positions	23,664	19,837	14,308
Increases related to prior year tax positions	2,833	—	183
Decreases related to prior year tax positions	(646)	(672)	(142)
Lapse of the applicable statute of limitations	(268)	—	—
Balance at the end of the year	$ 66,385	$ 40,802	$ 21,637

The unrecognized tax benefits were included in other non-current liabilities and deferred tax assets, net, non-current in our consolidated balance sheets. Interest related to our unrecognized tax benefits is recorded in income tax provision in our consolidated statements of income. As of December 31, 2015 and 2014, our accrued interest and penalties related to unrecognized tax benefits were not significant. Included in the balance of unrecognized tax benefits were potential benefits of $48.1 million and $29.7 million at December 31, 2015 and 2014, respectively, that, if recognized, would affect the effective tax rate on income.

Our most significant tax jurisdictions are Ireland, the United States (both at the federal level and in various state jurisdictions), Italy and France. Because of our NOL carryforwards and tax credit carryforwards, substantially all of our tax years remain open to federal, state, and foreign tax examination. Certain of our subsidiaries are currently under examination by the French tax authorities for fiscal years 2012 and 2013 and by the Italian tax authorities for fiscal year 2012. These examinations may lead to ordinary course adjustments or proposed adjustments to our taxes. In December 2015, we received proposed tax assessment notices from the French tax authorities for 2012 and 2013 relating to certain transfer pricing adjustments. The notices propose additional French tax of approximately $41.8 million, including interest and penalties, based on the foreign exchange rate at December 31, 2015 through the date of the assessment. We disagree with the proposed assessment and intend to contest it vigorously.

19. Quarterly Financial Data (Unaudited)

The following interim financial information presents our 2015 and 2014 results of operations on a quarterly basis (in thousands, except per share amounts):

	2015			
	March 31	June 30	September 30	December 31
Revenues	$ 309,303	$ 333,747	$ 340,872	$ 340,881
Gross margin (1)	278,737	310,293	310,369	314,894
Net income attributable to Jazz Pharmaceuticals plc	70,700	88,114	87,960	82,761
Net income attributable to Jazz Pharmaceuticals plc per ordinary share, basic	1.16	1.44	1.43	1.35
Net income attributable to Jazz Pharmaceuticals plc per ordinary share, diluted	1.12	1.40	1.39	1.32

	2014			
	March 31	June 30	September 30	December 31
Revenues	$ 246,919	$ 291,230	$ 306,584	$ 328,142
Gross margin (1)	214,062	258,408	277,413	295,415
Net income (loss) attributable to Jazz Pharmaceuticals plc	(92,650)	43,659	25,766	81,612
Net income (loss) attributable to Jazz Pharmaceuticals plc per ordinary share, basic	(1.58)	0.73	0.43	1.35
Net income (loss) attributable to Jazz Pharmaceuticals plc per ordinary share, diluted	(1.58)	0.70	0.41	1.30

(1) Gross margin is computed by subtracting cost of product sales (excluding amortization and impairment of intangible assets) from product sales, net.

The tables above include the following items:

- Impairment charges of $31.5 million in the fourth quarter of 2015 and $32.8 million and $6.6 million in the second and fourth quarters of 2014, respectively. The 2015 charge resulted from our decision to terminate a pivotal Phase 2 clinical trial of JZP-416. The 2014 charges related to certain products acquired as part of the EUSA Acquisition that we sold in March 2015;
- Upfront and milestone payments of $25.0 million in the third quarter of 2015 and $127.0 million, $75.0 million and $0.6 million in the first, third and fourth quarters of 2014, respectively;
- A one-time charge of $18.0 million in the fourth quarter of 2015 for settlement of a contract claim that was originally asserted against Azur Pharma prior to the Azur Merger;
- A loss on extinguishment and modification of debt of $16.8 million in the second quarter of 2015;
- Acquisition accounting inventory value step-up adjustments $8.0 million and $2.5 million in the first and second quarters of 2014, respectively; and
- Transaction costs of $17.1 million, $4.4 million, $0.7 million and $5.2 million in the first, second, third and fourth quarters of 2014, respectively.

Schedule II

Valuation and Qualifying Accounts
(In thousands)

		Balance at beginning of period	Additions charged to costs and expenses	Other Additions	Deductions	Balance at end of period
For the year ended December 31, 2015						
Allowance for doubtful accounts	(1)	$ 530	$ —	$ —	$ (41)	$ 489
Allowance for sales discounts	(1)	238	2,900	—	(2,957)	181
Allowance for chargebacks	(1)	2,715	39,079	—	(38,771)	3,023
Deferred tax asset valuation allowance	(2)(3)(4)	29,697	5,044	1,888	(2,680)	33,949
For the year ended December 31, 2014						
Allowance for doubtful accounts	(1)	$ 594	$ —	$ —	$ (64)	$ 530
Allowance for sales discounts	(1)	378	3,794	—	(3,934)	238
Allowance for chargebacks	(1)	2,708	28,614	—	(28,607)	2,715
Deferred tax asset valuation allowance	(2)(3)	20,691	18,971	—	(9,965)	29,697
For the year ended December 31, 2013						
Allowance for doubtful accounts	(1)	$ 715	$ (4)	$ —	$ (117)	$ 594
Allowance for sales discounts	(1)	528	5,267	—	(5,417)	378
Allowance for chargebacks	(1)	2,536	21,047	—	(20,875)	2,708
Deferred tax asset valuation allowance	(2)	17,471	3,220	—	—	20,691

(1) Shown as a reduction of accounts receivable. Charges related to sales discounts and chargebacks are reflected as a reduction of revenue.

(2) Additions to the deferred tax asset valuation allowance relate to movements on certain U.S. state and other foreign deferred tax assets where we continue to maintain a valuation allowance until sufficient positive evidence exists to support reversal.

(3) Deductions to the deferred tax asset valuation allowance include movements relating to utilization of NOLs and tax credit carryforwards, release in valuation allowance and other movements including adjustments following finalization of tax returns.

(4) Other additions to the deferred tax asset valuation allowance relate to currency translation adjustments recorded directly in equity.

EXHIBIT INDEX

Exhibit Number	Description of Document
2.1	Agreement and Plan of Merger and Reorganization, dated as of September 19, 2011, by and among Azur Pharma Limited (now Jazz Pharmaceuticals plc), Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500) filed with the SEC on September 19, 2011).
2.2	Letter Agreement, dated as of January 17, 2012, by and among Jazz Pharmaceuticals plc, Jaguar Merger Sub Inc. Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated by reference to Exhibit 2.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
2.3	Agreement and Plan of Merger, dated as of April 26, 2012, by and among Jazz Pharmaceuticals plc, Jewel Merger Sub Inc., EUSA Pharma Inc., and Essex Woodlands Health Ventures, Inc., Mayflower L.P., and Bryan Morton, in their capacity as the representatives of the equity holders of EUSA Pharma Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on April 27, 2012).
2.4	Assignment, dated as of June 11, 2012, by and among Jazz Pharmaceuticals plc and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 2.1B in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 12, 2012).
2.5	Tender Offer Agreement, dated December 19, 2013, by and among Jazz Pharmaceuticals Public Limited Company, Jazz Pharmaceuticals Italy S.r.l. and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K/A (File No. 001-33500), as filed with the SEC on December 20, 2013).
2.6†	Asset Purchase Agreement, dated January 13, 2014, by and among Jazz Pharmaceuticals International III Limited, Aerial BioPharma, LLC and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 13, 2014).
2.7†	Assignment Agreement, dated July 1, 2014, by and among Jazz Pharmaceuticals International II Limited, Sigma-Tau Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 5, 2014).
2.8	Amended and Restated Agreement for the Acquisition of the Topaz Portfolio Business of Jazz Pharmaceuticals plc, dated March 20, 2015, between Jazz Pharmaceuticals plc and Essex Bidco Limited (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's current report on Form 8-K (File No. 001-33500), as filed with the SEC on March 23, 2015).
3.1	Memorandum and Articles of Association of Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 3.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
4.1	Reference is made to Exhibit 3.1.
4.2A	Investor Rights Agreement, dated July 7, 2009 by and between Jazz Pharmaceuticals, Inc. and the other parties named therein (incorporated herein by reference to Exhibit 10.88 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on July 7, 2009).
4.2B	Assignment, Assumption and Amendment Agreement, dated as of January 18, 2012, by and among Jazz Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and the other parties named therein (incorporated herein by reference to Exhibit 4.7B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
4.2C	Indenture, dated as of August 13, 2014, by and among Jazz Pharmaceuticals plc, Jazz Investments I Limited and U.S. Bank National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 13, 2014).
4.2D	Form of 1.875% Exchangeable Senior Note due 2021 (incorporated herein by reference to Exhibit 4.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 13, 2014).
10.1†	Supply Agreement, dated as of April 1, 2010, by and between Jazz Pharmaceuticals, Inc. and Siegfried (USA) Inc. (incorporated herein by reference to Exhibit 10.54 in Jazz Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2010, as filed with the SEC on May 6, 2010).

10.2†	Master Services Agreement, dated April 15, 2011, by and between Jazz Pharmaceuticals, Inc., CuraScript, Inc. and Express Scripts Specialty Distribution Services, Inc. (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2011, as filed with the SEC on May 9, 2011).
10.3†	Royalty Bearing License Agreement and Supply Agreement Re Erwinia-Derived Asparaginase, dated July 22, 2005, between Public Health England (formerly Health Protection Agency) and EUSA Pharma SAS (formerly OPi, S.A.), as amended on each of December 22, 2009, March 23, 2012 and August 8, 2012 (incorporated herein by reference to Exhibit 10.11 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q/A (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 9, 2012).
10.4	Novation Agreement relating to Royalty Bearing Licence Agreement and Supply Agreement re Erwinia-Derived Asparaginase, dated as of May 13, 2015, by and among EUSA Pharma SAS, the Secretary of State for Health acting through Public Health England and Porton Biopharma Limited (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2015, as filed with the SEC on August 5, 2015).
10.5*	Master Manufacturing Services Agreement, dated as of October 1, 2015, by and between Jazz Pharmaceuticals Ireland Limited and Patheon Pharmaceuticals Inc.
10.6	Credit Agreement, dated as of June 18, 2015, among Jazz Pharmaceuticals plc, Jazz Securities Limited, Jazz Pharmaceuticals, Inc., Jazz Financing I Limited, Jazz Pharmaceuticals Ireland Limited, the lenders party thereto and Bank of America, N.A., as Collateral Agent, Administrative Agent, Swing Line Lender and L/C Issuer (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 0001-33500), as filed with the SEC on June 18, 2015).
10.7A	Commercial Lease, dated as of June 2, 2004, by and between Jazz Pharmaceuticals, Inc. and The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.52 in Jazz Pharmaceuticals, Inc.'s registration statement on Form S-1, as amended (File No. 333-141164), as filed with the SEC on March 27, 2007).
10.7B	First Amendment of Lease, dated June 1, 2009, by and between Jazz Pharmaceuticals, Inc. and Wheatley-Fields, LLC, successor in interest to The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.86 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 4, 2009).
10.7C	Second Amendment of Lease, dated February 28, 2012, by and between Jazz Pharmaceuticals, Inc. and Wheatley-Fields, LLC, successor in interest to The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.31 in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
10.8	Lease, dated May 8, 2012, by and between John Ronan and Castle Cove Property Developments Limited and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.9	Commercial Lease, dated as of January 7, 2015, by and between The Board of Trustees of the Leland Stanford Junior University and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.10+	Form of Indemnification Agreement between Jazz Pharmaceuticals plc and its officers and directors (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
10.11+	Offer Letter from Jazz Pharmaceuticals, Inc. to Suzanne Sawochka Hooper (incorporated herein by reference to Exhibit 10.19 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2012, as filed with the SEC on May 8, 2012).
10.12+	Offer Letter from Jazz Pharmaceuticals, Inc. to Matthew Young (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2014, as filed with the SEC on May 8, 2014).
10.13A+	Employment Agreement by and between EUSA Pharma Inc. and Iain McGill (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2014, as filed with the SEC on November 4, 2014).
10.13B+	Amendment to Employment Agreement by and between Iain McGill and EUSA Pharma (Europe) Limited (incorporated herein by reference to Exhibit 10.15B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.14+	Offer Letter from Jazz Pharmaceuticals, Inc. to Michael Miller (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2014, as filed with the SEC on November 4, 2014).

10.15A+	Employment Agreement by and between Jazz Pharmaceuticals Ireland Limited and Paul Treacy (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2014, as filed with the SEC on November 4, 2014).
10.15B+	Amendment to Employment Agreement by and between Jazz Pharmaceuticals Ireland Limited and Paul Treacy (incorporated herein by reference to Exhibit 10.15A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.16+	Amended and Restated Offer Letter, dated as of July 29, 2015, from Jazz Pharmaceuticals, Inc. to Karen Smith, M.D., Ph.D. ((incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2015, as filed with the SEC on November 9, 2015).
10.17A+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 99.3 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.17B+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan Sub-Plan Governing Awards to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.3B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2012).
10.17C+	Form of Notice of Grant of Stock Options and Form of Option Agreement (U.S.) under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.17D+	Form of Notice of Grant of Stock Options and Form of Option Agreement (Irish) under Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.17E+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.S.) under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27E in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500), as filed with the SEC on February 26, 2013).
10.17F+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (Irish) under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.27F in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.17G+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.17H+	Jazz Pharmaceuticals plc 2007 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18A+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 99.1 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.18B+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan Sub-Plan Governing Awards to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.39B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2012).
10.18C+	Form of Option Grant Notice and Form of Stock Option Agreement (U.S.) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18D+	Form of Stock Option Grant Notice and Form of Option Agreement (Irish) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18E+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.28E in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).

10.18F+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.S.) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18G+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (Irish) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.18H+	Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.28H in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.18I+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Option Grant Notice and Form of U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18J+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18K+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18L+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.19+	Jazz Pharmaceuticals plc Amended and Restated Directors Deferred Compensation Plan (incorporated herein by reference to Exhibit 99.6 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.20A+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 99.4 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.20B+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 10.30B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.20C+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved August 1, 2013) (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.21A+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan, as amended and restated (incorporated herein by reference to Exhibit 10.31A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.21B+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan Sub-Plan Governing Purchase Rights to Participants in the Republic of Ireland (incorporated by reference herein to Exhibit 10.14C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2012, as filed with the SEC on May 8, 2012).
10.22A+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (incorporated herein by reference to Exhibit 10.32B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.22B+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved November 4, 2015).
10.22C+	Jazz Pharmaceuticals Cash Bonus Plan for International Affiliates (2014) (incorporated herein by reference to Exhibit 10.24D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2013, as filed with the SEC on February 25, 2014).
10.22D+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2016).
10.23+	Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (approved February 10, 2016).

10.24+	Jazz Pharmaceuticals plc 2015 Executive Officer Compensation Arrangements (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2015, as filed with the SEC on May 7, 2015).
10.25A+	Jazz Pharmaceuticals plc Non-Employee Director Compensation Policy (approved May 1, 2014) (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's quarterly report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2014, as filed with the SEC on May 8, 2014).
10.25B+	Jazz Pharmaceuticals plc Non-Employee Director Compensation Policy (approved April 30, 2015) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2015, as filed with the SEC on August 5, 2015).
10.26+	Named Officer 2015 Target Bonus Opportunity (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on February 18, 2015).
21.1	Subsidiaries of Jazz Pharmaceuticals plc.
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page hereto).
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1**	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
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 Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

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+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for 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.

** The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 10.5

Master Manufacturing Services Agreement

October 1, 2015

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[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

MASTER MANUFACTURING SERVICES AGREEMENT

THIS MASTER MANUFACTURING SERVICES AGREEMENT (the "Agreement") is made as of October 1, 2015 (the "**Effective Date**")

B E T W E E N:

PATHEON PHARMACEUTICALS INC.,
a corporation existing under the laws of the State of Delaware

("**Patheon**"),

- and -

JAZZ PHARMACEUTICALS IRELAND LIMITED,
a corporation existing under the laws of Ireland

("**Client**").

In consideration of the rights conferred and the obligations assumed herein, and for other good and valuable consideration (the receipt and sufficiency of which are acknowledged by each party), and intending to be legally bound the parties agree as follows:

ARTICLE I

STRUCTURE OF AGREEMENT AND INTERPRETATION

1.1 Master Agreement.

This Agreement establishes the general terms and conditions under which Patheon or any Affiliate of Patheon may perform Manufacturing Services for Client or any Affiliate of Client, at the manufacturing site where the Affiliate of Patheon resides. This "master" form of agreement is intended to allow the parties, or any of their Affiliates, to contract for the manufacture of multiple Products through Patheon's global network of manufacturing sites through the issuance of site specific Product Agreements without having to re-negotiate the basic terms and conditions contained herein.

1.2 Product Agreements.

This Agreement is structured so that a Product Agreement may be entered into by the parties or their respective Affiliates for Manufacturing Services for a particular Product or multiple Products at a Patheon Manufacturing Site. Each Product Agreement will be governed by the terms and conditions of this Agreement unless the parties to the Product Agreement expressly reference the applicable section of this Agreement and modify its terms in the Product Agreement. Unless otherwise agreed by the parties, each Product Agreement will be in the general form and contain the information set forth in Appendix 1 hereto.

The parties intend that, after the parties enter into a Product Agreement with respect to the Client's Xyrem® Product(s), this Agreement and such Product Agreement issued hereunder related to Client's

Xyrem® Product(s) will supersede the Manufacturing Services and Supply Agreement between Patheon and Client (as successor in interest to Jazz Pharmaceuticals, Inc.) dated March 13, 2007 as amended.

1.3 Definitions.

The following terms will, unless the context otherwise requires, have the respective meanings set out below and grammatical variations of these terms will have corresponding meanings:

"Act" means the United States Food, Drug and cosmetic Act, as amended from time to time, and the regulations promulgated thereunder;

"**Active Materials**", **"Active Pharmaceutical Ingredients" or "API"** means the materials listed in a Product Agreement on Schedule D;

"**Active Materials Credit Value**" means the value of the Active Materials for certain purposes of this Agreement, as set forth in a Product Agreement on Schedule D;

"**Actual Annual Yield**" or "**AAY**" has the meaning specified in Section 2.2(a);

"**Actual Yearly Volume**" or "**AYV**" for each Product has the meaning specified in the applicable Product Agreement;

"**Affiliate**" means:

(a) a business entity which owns, directly or indirectly, a controlling interest in a party to this Agreement, by stock ownership or otherwise; or

(b) a business entity which is controlled by a party to this Agreement, either directly or indirectly, by stock ownership or otherwise; or

(c) a business entity, the controlling interest of which is, directly or indirectly, under common control with a party to this Agreement;

For this definition, "control" means the ownership of shares carrying at least a majority of the votes for the election of the directors of a corporation;

"Annual Product Review Report" means the annual product review report, which will be prepared by Patheon, as described in Title 21 of the United States Code of Federal Regulations, Section 211.180(e);

"**Annual Report"** means the annual report to the FDA, which is required to be prepared and filed by Client, regarding the Product as described in Title 21 of the United States Code of Federal Regulations, Section 314.81(b)(2);

"**Annual Volume**" means the minimum volume of Product to be manufactured in any Year of this Agreement as set forth in Schedule B;

"**Applicable Laws**" means all applicable federal, state and local laws, rules, regulations and requirements;

"**Authority**" means any governmental or regulatory authority, department, body or agency or any court, tribunal, bureau, commission or other similar body, whether federal, state, provincial, county or municipal;

"Batch" means a specific quantity of Active Material and Components that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture;

"Bill Back Items" means the expenses for all third party supplier fees for the purchase or use of columns, standards, non-standard tooling, non-standard pallets, non-standard PAPR or PPE suits (where applicable) and other project-specific items necessary for Patheon to perform the Manufacturing Services, and which are not included as Components, as may be specified in the Product Agreement for a Product;

"**Breach Notice**" has the meaning specified in Section 8.2(a);

"**Business Day**" means a day other than a Saturday, Sunday or a day that is a statutory holiday in the country where the Manufacturing Site is located, unless another country is specified in the Product Agreement;

"**Capital Equipment Agreement**" means a separate agreement that the parties may enter into that will address responsibility for the purchase of capital equipment and facility modifications that may be required to perform the Manufacturing Services under a particular Product Agreement;

"**cGMPs**" means, as applicable, current good manufacturing practices as described in the laws of the applicable jurisdiction, including without limitation:

(a) Parts 210 and 211 of Title 21 of the United States' Code of Federal Regulations;

(b) EC Directive 2003/94/EC; and

(c) Division 2 of Part C of the *Food and Drug Regulations* (Canada);

together with the latest Health Canada, FDA and EMA guidance documents pertaining to manufacturing and quality control practice, all as updated, amended and revised from time to time;

"Client Intellectual Property" means (a) Intellectual Property possessed, generated or derived by Client before entering into this Agreement and (b) Intellectual Property generated or derived by Patheon while performing any Manufacturing Services or otherwise generated or derived by Patheon in its business, to the extent this Intellectual Property is specific to, or dependent upon, Client's Active Material or Product or its development, manufacture, use and sale;

"**Client Property**" has the meaning specified in Section 8.5(d);

"**Client Requested Changes**" has the meaning specified in Section 4.4;

"**Client-Supplied Components**" means those Components to be supplied by Client or that have been supplied by Client, as specified in each Product Agreement;

"**Components**" means, collectively, all packaging components, raw materials, ingredients, and other materials (including labels, product inserts and other labelling for the Products) required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Confidential Information**" has the meaning specified in Section 11.1;

"**CTD**" has the meaning specified in Section 7.8(c);

"C-TPAT" has the meaning specified in Section 2.1(f);

"DEA" means the United States Drug Enforcement Administration or its counterparts in other countries;

"**Deficiencies**" have the meaning specified in Section 7.8(d);

"**Deficiency Notice**" has the meaning specified in Section 6.1(a);

"Delivery Date" means the date scheduled for shipment of Product under a Firm Order;

"Disclosing Party" has the meaning specified in Section 11.1;

"**EMA**" means the European Medicines Agency or any successor agency thereto;

"**FDA**" means the United States Food and Drug Administration or any successor agency thereto;

"**Firm Orders**" have the meaning specified in Section 5.1(c);

"**Force Majeure Event**" has the meaning specified in Section 13.7;

"**GST**" has the meaning specified in Section 13.16(a)(ii);

"**Health Canada**" means the section of the Canadian Government known as Health Canada and includes, among other departments, the Therapeutic Products Directorate and the Health Products and Food Branch Inspectorate or any successor agency thereto;

"**Importer of Record**" has the meaning specified in Section 3.2(a);

"**Initial Product Term**" has the meaning specified in Section 8.1;

"**Initial Set Exchange Rate**" means as of the Effective Date of a Product Agreement, the initial exchange rate set forth in the Product Agreement to convert one unit of the billing currency into the Patheon Manufacturing Site local currency, calculated as the daily average interbank exchange rate for conversion of one unit of the billing currency into the Patheon Manufacturing Site local currency during the 90 day period immediately preceding the Effective Date as published by OANDA.com "The Currency Site" under the heading "FxHistory: historical currency exchange rates" at www.OANDA.com/convert/fxhistory;

"**Initial Term**" has the meaning specified in Section 8.1;

"**Intellectual Property**" includes, without limitation, rights in patents, patent applications, formulae, trademarks, trademark applications, trade-names, Inventions, copyrights, industrial designs, and know how;

"**Invention**" means information about any innovation, improvement, development, discovery, computer program, device, trade secret, method, know-how, process, technique or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which it is contained and whether or not patentable or copyrightable;

"**Inventory**" means all inventories of Components and work-in-process produced or held by Patheon for the manufacture of the Products but, for greater certainty, does not include the Active Materials;

"**Laws**" means all laws, statutes, ordinances, regulations, rules, by-laws, judgments, decrees or orders of any Authority applicable to the activities hereunder and include, without limitation, cGMPs;

"Long Term Forecast" has the meaning specified in Section 5.1(a);

"**Manufacturing Services**" means all of the manufacturing, quality control, quality assurance, stability testing, packaging, and related services, as set forth in this Agreement, required to manufacture Product or Products using the Active Materials, Components, and Bill Back Items;

"**Manufacturing Site**" means the facility owned and operated by Patheon where the Manufacturing Services will be performed as identified in a Product Agreement;

"Materials" means all Components and Bill Back Items required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Maximum Credit Value**" means the maximum value of Active Materials that may be credited by Patheon under this Agreement, as set forth in a Product Agreement on Schedule D;

"**Minimum Order Quantity**" means the minimum number of Batches of a Product to be produced during the same cycle of manufacturing as set forth in a Product Agreement on Schedule B;

"**Obsolete Stock**" has the meaning specified in Section 5.2(b);

"**Patheon Competitor**" means a business that derives greater than [*] of its revenues from performing contract pharmaceutical development or commercial manufacturing services;

"Patheon Intellectual Property" means Intellectual Property generated or derived by Patheon in the course of performing the Manufacturing Services which are not related to or derived from the Client's Intellectual Property or specific to, or dependent upon, a Product and which have general application to manufacturing processes or formulation development of drug product or drug delivery. But this definition will not include any Intellectual Property allocated to or assigned to Jazz Pharmaceuticals or any of its Affiliates under any prior agreement entered into with Patheon or any of its Affiliates which will remain the exclusive property of Jazz Pharmaceuticals or its Affiliate;

"**PPI**" has the meaning specified in Section 4.2(a);

"**Patheon Requested Changes**" has the meaning specified in Section 4.4;

"Price" means, with respect to each Product, the price to be charged by Patheon for performing the Manufacturing Services for such Product, and includes the cost of Components (other than Client-Supplied Components), certain cost items as set forth in a Product Agreement on Schedule B, and annual stability testing costs as set forth in a Product Agreement on Schedule C;

"**Product(s)**" means the product(s) listed in a Product Agreement on Schedule A hereto;

"**Product Agreement**" means the document, signed by Patheon and Client or their respective Affiliates and issued under this Agreement generally in the form set forth in Appendix 1 (including Schedules A to D) under which Patheon will perform Manufacturing Services at a particular Manufacturing Site under the terms and conditions hereof;

"**Product Agreement Non-Renewal Notice Period**" will have the meaning specified in Section 8.1;

"**Product Claims**" have the meaning specified in Section 6.3(d);

"**Quality Agreement**" means the agreement between the parties entering a Product Agreement that sets out the quality assurance standards for the Manufacturing Services to be performed by Patheon for Client;

"**Recall**" has the meaning specified in Section 6.2(a);

"**Recipient**" has the meaning specified in Section 11.1;

"**Regulatory Approval**" has the meaning specified in Section 7.8(a);

"**Regulatory Authority**" means the FDA, EMA, and Health Canada and any other foreign regulatory agencies competent to grant marketing approvals for pharmaceutical products including the Products in the Territory;

"**Remediation Period**" has the meaning specified in Section 8.2(a);

"**Representatives**" means a party's directors, officers, employees, agents, consultants, or subcontractors;

"**Required Manufacturing Changes**" has the meaning specified in Section 4.4;

"Resident Jurisdiction" has the meaning specified in Section 13.16(a)(i);

"Set Exchange Rate" means the exchange rate to convert one unit of the billing currency into the Patheon Manufacturing Site local currency for each Year, calculated as the average daily interbank exchange rate for conversion of one unit of the billing currency into the Patheon Manufacturing Site local currency during the full year period (October 1st [preceding year] to September 30th) as published by OANDA.com "The Currency Site" under the heading "FxHistory: historical currency exchange rates" at www.OANDA.com/convert/fxhistory;

"**Shortfall Credit**" has the meaning specified in Section 2.2(b);

"**Specifications**" means the file, for each Product, which is given by Client to Patheon in accordance with the procedures listed in a Product Agreement on Schedule A and which contains documents relating to each Product, including, without limitation:

(a) specifications for Active Materials and Components including approved vendor;

(b) manufacturing specifications, directions, and processes;

(c) storage requirements;

(d) environmental, health and safety information for each Product including material safety data sheets; and

(e) the finished Product specifications, packaging specifications and shipping requirements for each Product;

all as updated, amended and revised from time to time by Client in accordance with the terms of this Agreement;

"**Target Yield**" has the meaning specified in Section 2.2(a);

"**Target Yield Determination Batches**" has the meaning specified in Section 2.2(a);

"**Tax**" or "**Taxes**" have the meaning specified in Section 13.6(a);

"**Technical Dispute**" has the meaning specified in Section 12.2;

"**Territory**" means the geographic area described in a Product Agreement where Products manufactured by Patheon will be distributed by Client;

"**Third Party Rights**" means the Intellectual Property of any third party;

"**VAT**" has the meaning specified in Section 13.16(d);

"**Year**" means in the first year of this Agreement or in the first year of a Product Agreement, the period from the Effective Date up to and including December 31 of the same calendar year, and thereafter will mean a calendar year; and

"**Yearly Forecast Volume**" or "**YFV**" has the meaning specified in Section 4.2.1;

1.4 Currency.

Unless otherwise agreed in a Product Agreement, all monetary amounts expressed in this Agreement are in United States Dollars (USD).

1.5 Sections and Headings.

The division of this Agreement into Articles, Sections, Subsections, an Appendix, Schedules and Exhibits and the insertion of headings are for convenience of reference only and will not affect the interpretation of this Agreement. Unless otherwise indicated, any reference in this Agreement to a Section, Appendix, Schedule or Exhibit refers to the specified Section, Appendix, Schedule or Exhibit

to this Agreement. In this Agreement, the terms "**this Agreement**", "**hereof**", "**herein**", "**hereunder**" and similar expressions refer to this Agreement as a whole and not to any particular part, Section, Appendix, Schedule or Exhibit of this Agreement.

1.6 **Singular Terms**.

Except as otherwise expressly stated or unless the context otherwise requires, all references to the singular will include the plural and vice versa.

1.7 **Appendix 1, Schedules and Exhibits**.

Appendix 1 (including the Schedules thereto) and the following Exhibits are attached to, incorporated in, and form part of this Agreement:

Appendix 1 Form of Product Agreement (Including Schedules A to D)

Exhibit A Technical Dispute Resolution
Exhibit B [Reserved]
Exhibit C Quarterly Active Materials Inventory Report
Exhibit D Report of Annual Active Materials Inventory Reconciliation and Calculation of Actual Annual Yield
Exhibit E Example of Price Adjustment Due to Currency Fluctuation

PATHEON'S MANUFACTURING SERVICES

2.1 Manufacturing Services.

Patheon will perform the Manufacturing Services for the Territory for the Price set forth in the applicable Product Agreement in Schedules B and C to manufacture Products for Client. Schedule B to a Product Agreement sets forth a list of cost items that are included or not included in the Price for Products; all cost items that are not included in the Price are subject to additional fees to be paid by Client. The Price may be adjusted as set forth in Article 4. Patheon may change the Manufacturing Site for the Products only with the prior written consent of Client. If the parties agree that a minimum percentage of any Product will be manufactured by Patheon, (a) this agreement will be set forth in the applicable Product Agreement; and (b) Client may establish other suppliers as additional manufacturers of each Product and may purchase each Product from these manufacturers, if Patheon does not, or cannot, meet all of Client's Firm Orders for the Product. Patheon will be entitled to any applicable manufacturing tax credits that arise from performing the Manufacturing Services under this Agreement. In performing the Manufacturing Services, Patheon and Client agree that:

(a) Conversion of Active Materials and Components. Patheon will convert each Active Material and the applicable Components into Product, as set forth in the applicable Product Agreement..

(b) Quality Control and Quality Assurance. Patheon will perform the quality control and quality assurance testing specified in the Quality Agreement. Batch review and release to Client will be the responsibility of Patheon's quality assurance group. Unless otherwise set forth in the Quality Agreement, Patheon will perform its batch review and release responsibilities in accordance with Patheon's standard operating procedures. Unless otherwise set forth in the applicable Product Agreement or Quality Agreement, each time Patheon ships Products to Client, it will give Client a certificate of analysis and certificate of compliance including a certification that the Batch has been evaluated by Patheon's Quality Control/Quality Assurance department and that the Product complies with the Specifications and was manufactured in accordance with cGMPs. Patheon will test each Batch of Product to be supplied pursuant to this Agreement in accordance with the methods for the Product set forth in the Specifications before delivery of the Batch to Client. Client reserves the right to test or have tested all Products supplied by Patheon and to reject Product that fails to comply with the applicable Specifications or Product that was not manufactured in accordance with cGMPs or Applicable Laws. Client will have sole responsibility for the release of Products to the market. The form and style of batch documents, including, but not limited to, Batch production records, lot packaging records, equipment set up control, operating parameters, and data printouts, raw material data, and laboratory notebooks are the exclusive property of Patheon. Specific Product related information contained in those Batch documents is Client Property.

(c) Components. Patheon will purchase and test all Components (with the exception of Client-Supplied Components) at Patheon's expense and as required by the Specifications. But Patheon may agree to test certain Client-Supplied Components as specified in the applicable Product Agreement. Client will have the right to specify the suppliers for the Components but if the supplier is not an approved supplier currently used by Patheon, it will be Client's responsibility to audit and approve the supplier. At Client's request and for an additional fee, Patheon may agree to audit and approve the supplier. Patheon will not change any Specifications or supplier of any Components without the prior written consent of Client.

(d) Active Material. Promptly following receipt of the Active Material to be supplied by Client, Patheon will test (pursuant to test methods and drug specifications to be provided by Client) and approve the Active Material as acceptable for performing Manufacturing Services under this Agreement and the applicable Product Agreement. Unless otherwise agreed in a Product Agreement, Patheon will notify Client in writing within [*] days of receipt of any failure of Active Material unless earlier notice is required by Applicable Law; absent this notice, the Active Material will be deemed to be accepted and approved by Patheon.

(e) Stability Testing. Patheon will conduct stability testing on the Products in accordance with the protocols set out in the Specifications for the fees and at the time periods set out in Schedule C to a Product Agreement. Patheon will not make any changes to these testing protocols or Specifications without prior written consent of Client. Patheon will promptly provide any and all data and results relating to the stability testing upon request by Client. If any Batch of a Product fails or is suspected to fail stability testing, Patheon will notify Client within [*], after which Patheon and Client will jointly determine the proceedings and methods to be undertaken to investigate the cause of the failure, including which party will bear the cost of the investigation. Patheon will not be liable for these costs unless it has failed to perform the Manufacturing Services in accordance with the Specifications and cGMPs. Patheon will give Client all stability test data and results at Client's request.

(f) Packaging and Artwork. Patheon will package the Products in accordance with the Specifications. Client will be responsible for the cost of artwork development. Patheon will determine and imprint the Batch numbers and expiration dates for each Product shipped. The Batch numbers expiration dates, and when agreed upon by the Parties, serial numbers will be affixed on the Products and on the shipping carton of each Product as outlined in the Specifications and as required by cGMPs. Client may, in its sole discretion, make changes to labels, product inserts, and other packaging for the Products. Those changes will be submitted by Client to all applicable Regulatory Authorities and other third parties responsible for the approval of the Products. Client will be responsible for the cost of labelling obsolescence when changes occur, as contemplated in Section 4.4. Patheon's name will not appear on the label or anywhere else on the Products unless: (i) required by any Laws; or (ii) Patheon consents in writing to the use of its name. At least [*] days prior to the Delivery Date of Product for which new or modified artwork is required, Client will provide at no cost to Patheon, final camera ready artwork for all packaging Components to be used in the manufacture of the Product that meet the Specifications. But if this new or modified artwork is required in connection with a Product launch or is due to changes in safety information or Regulatory Authority requirements, then Patheon will use commercially reasonable efforts to implement the changes to the artwork on an expedited basis. For the avoidance of doubt, the parties acknowledge and agree that Client will be responsible for complying with any and all regulatory requirements for the labeling of the Product.

(g) Active Materials and Client-Supplied Components. If Patheon has advised Client of the scheduled production date, then, at least [*] days before the scheduled production date, Client will deliver the Active Materials and any Client-Supplied Components to the Manufacturing Site [*] (Incoterms 2010), at no cost to Patheon, in sufficient quantity to enable Patheon to manufacture the desired quantities of Product and to ship Product on the Delivery Date. If the Active Materials and/or Client-Supplied Components are not received [*] days before the scheduled production date, Patheon may delay the shipment

of Product by the same number of days as the delay in receipt of the Active Materials and/or Client-Supplied Components. But if Patheon is unable to manufacture Product to meet this new shipment date due to prior third party production commitments, Patheon may delay the shipment until a later date as agreed to by the parties. All shipments of Active Material will be accompanied by certificate(s) of analysis from the Active Material manufacturer and Client, confirming the identity and purity of the Active Materials and its compliance with the Active Material specifications. For Active Materials or Client-Supplied Components which may be subject to import or export, Client agrees that it will use reasonable efforts to ensure that its vendors and carriers will comply with applicable requirements of the U.S. Customs and Border Protection Service and the Customs Trade Partnership Against Terrorism ("**C-TPAT**").

(h) Bill Back Items. Bill Back Items will be charged to Client at Patheon's cost plus a [*] handling fee.

(i) Validation Activities (if applicable). Patheon may assist in the development and approval of the validation protocols for analytical methods and manufacturing procedures (including packaging procedures) for the Products. The fees for this service are not included in the Price and will be set out separately in Schedule C to a Product Agreement.

(j) Additional Services. If Client requests services other than those expressly set forth herein or in any Product Agreement (such as qualification of a new packaging configuration or shipping studies, or validation of alternative Batch sizes), Patheon will provide a good faith and reasonable written quote of the fee for the additional services and Client will advise Patheon whether it wishes to have the additional services performed by Patheon. The scope of work and fees will be set forth in a separate statement of work signed by the parties, which will subject to the terms and conditions hereof. The title of this statement of work will reference the applicable Product Agreement and will be numbered sequentially. .

2.2 Active Material Yield.

(a) Reporting. Patheon will give Client a monthly inventory report of the Active Materials held by Patheon using the inventory report form set out in Exhibit C, which will contain the following information for the month:

Quantity Received: The total quantity of each Active Material that complies with the applicable Specifications and is received at the applicable Manufacturing Site during the applicable period.

Quantity Dispensed: The total quantity of each Active Material dispensed at the applicable Manufacturing Site during the applicable period. The Quantity Dispensed is calculated by [*]. The Quantity Dispensed will only include Active Materials received and dispensed in commercial manufacturing of Products and, for certainty, will not include any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv) Active Materials received or dispensed in technical transfer activities or development activities during the applicable period, including without

limitation, any regulatory, stability, validation or test Batches manufactured during the applicable period.

Quantity Converted: The total amount of Active Materials contained in the Products manufactured with the Quantity Dispensed (including any additional Products produced in accordance with Section 6.3(a) or 6.3(b)), delivered by Patheon, and not rejected, recalled or returned in accordance with Section 6.1or 6.2. Within [*] days after the end of each Year, Patheon will prepare an annual reconciliation of Active Materials on the reconciliation report form set forth in Exhibit D including the calculation of the "**Actual Annual Yield**" or "**AAY**" for the Product at the Manufacturing Site during the Year. AAY is the percentage of the Quantity Dispensed that was converted to Products and is calculated as follows:

$$\frac{\text{Quantity Converted during the Year}}{\text{Quantity Dispensed during the Year}} \times 100\%$$

After Patheon has produced a minimum of [*] successful commercial production Batches of Product and has produced commercial production Batches for at least [*] at the Manufacturing Site (collectively, the "**Target Yield Determination Batches**"), the parties will work in good faith to agree on the target yield for the Product at the Manufacturing Site (each, a "**Target Yield**"). The Target Yield will be revised annually as agreed by the parties to reflect the actual manufacturing experience.

(b) Shortfall Credit Calculation. The parties will agree in each Product Agreement to a specific Loss Tolerance Percentage, which will be used to calculate whether a shortfall in Active Material yield has occurred. If the Actual Annual Yield falls more than the agreed Loss Tolerance Percentage below the respective Target Yield in a Year, then the shortfall for the Year (the "**Shortfall**") for such Product will be calculated as follows:

[*]

(c) Credit for Shortfall. If there is a Shortfall for a Product in a Year, then Patheon will credit Client's account for the amount of the Shortfall not later than [*] days after the end of the Year. Each credit under this Section 2.2(c) will be summarized on the reconciliation report form set forth in Exhibit D. Upon expiration or termination of a Product Agreement, any remaining credit owing under this Section will be paid to Client. The Annual Shortfall, if any, will be disclosed by Patheon on the reconciliation report form.

(d) Maximum Credit. Patheon's liability for Active Materials calculated in accordance with this Section 2.2 **[for any Product]** in a Year will not exceed, in the aggregate, the Maximum Credit Value set forth in Schedule D to a Product Agreement.

(e) No Material Breach. If Patheon has used commercially reasonable efforts to achieve the Target Yield and if the Actual Yield is not less than 80% of the Target Yield, it will not be a material breach of this Agreement by Patheon under Section 8.2(a) if the Actual Annual Yield is less than the Target Yield.

ARTICLE 3

CLIENT'S OBLIGATIONS

3.1 **Payment**.

Client will pay Patheon for performing the Manufacturing Services according to the Prices specified in Schedules B and C in a Product Agreement. These Prices may be subject to adjustment under other parts of this Agreement. Client will also pay Patheon for any Bill Back Items.

3.2 **Active Materials and Qualification of Additional Sources of Supply.**

(a) Client will at its sole cost and expense deliver the Active Materials to Patheon in accordance with Section 2.1(g). If applicable, Patheon and Client will reasonably cooperate to permit the import of the Active Materials to the Manufacturing Site. Client's obligation will include obtaining the proper release of the Active Materials from the applicable Customs Agency and Regulatory Authority. Client or Client's designated broker will be the "**Importer of Record**" for Active Materials imported to the Manufacturing Site. [*] The Active Materials will be held by Patheon on behalf of Client as set forth in this Agreement. Title to the Active Materials will at all times remain the property of Client. Any Active Materials received by Patheon will only be used by Patheon to perform the Manufacturing Services. Client will be responsible for paying for all rejected Product that arises from defects in the Active Materials which could not be reasonably discoverable by Patheon using the test methods set forth in the Specifications.

(b) If Client asks Patheon to qualify an additional source for an Active Material or any Component, Patheon may agree to evaluate the Active Material or Component to be supplied by the additional source to determine if it is suitable for use in the Product. The parties will agree on the scope of work to be performed by Patheon at Client's cost. For an Active Material, this work at a minimum will include: (i) laboratory testing to confirm the Active Material meets existing specifications; (ii) manufacture of an experimental Batch of Product that will be placed on three months accelerated stability; and (iii) manufacture of a mutually agreed upon number of full-scale validation Batches that will be placed on concurrent stability (one Batch may be the registration Batch if manufactured at full scale). Section 6.1(d) will apply to all Product manufactured using the newly approved Active Material or Component because of the limited material characterization that is performed on additional sources of supply.

(c) If will promptly advise Client if it encounters supply problems, including delays and/or delivery of non-conforming Active Material or Components from a Client designated additional source. Patheon and Client will cooperate to reduce or eliminate any supply problems from these additional sources of supply. Client will be obligated to re-qualify all Client designated sources of supply on an annual basis at its expense and will provide Patheon with copies of these annual re-qualifications. If Patheon agrees to qualify or re-qualify Client designated additional sources of supply on behalf of Client, it will do so at Client's expense.

ARTICLE 4

CONVERSION FEES AND COMPONENT COSTS

4.1 **First Year Pricing**.

The Price for the first Year will be listed in Schedules B and C in a Product Agreement and will be subject to the adjustments set forth in Sections 4.2 and 4.3. The Price may also be increased or decreased by Patheon at any time upon written notice to Client if there are changes to the underlying manufacturing, packaging or testing assumptions set forth in Schedule B of the Product Agreement that result in an increase or decrease in the cost of performing the Manufacturing Services.

4.2 **Price Adjustments – Subsequent Years' Pricing**.

After the first Year of the Product Agreement, Patheon may adjust the Price effective January 1st of each Year as follows:

(a) Manufacturing and Stability Testing Costs. For Products manufactured in the United States or Puerto Rico, the conversion component of the Price and the annual stability testing costs may be adjusted to the extent of the preliminary number for any change in the Producer Price Index pcu325412325412 for Pharmaceutical Preparation Manufacturing ("**PPI**") published by the United States Department of Labor, Bureau of Labor Statistics in August of the preceding Year compared to the final number for the same month of the Year prior to that, unless the parties otherwise agree in writing. On or before November 30 of each Year, Patheon will give Client a statement setting forth the calculation for the adjustment to be applied in calculating the Price for the next Year. For Products manufactured outside the United States or Puerto Rico, the conversion component of the Price and the annual stability testing costs may be adjusted to the extent of the corresponding changes using an inflation index to be agreed by the parties in the applicable Product Agreement.

(b) Component Costs. If Patheon incurs an increase in Component costs during the Year, it may increase the Price for the next Year to pass through the additional Component costs at Patheon's actual cost. [*] On or before November 30 of each Year, Patheon will give Client information about the increase or decrease in Component costs which will be applied to the calculation of the Price for the next Year together with reasonable documentation to demonstrate that the Price increase or decrease is justified. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers. Patheon will use commercially reasonable efforts to minimize Component costs.

(c) Pricing Basis. Client acknowledges that the Price in any Year is quoted based upon the Annual Volume specified in Schedule B to each Product Agreement. The Price is subject to change if [*].

[*].On or before November 30 of each Year, Patheon will give Client a statement setting forth the information to be applied in calculating those cost increases for the next Year. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(d) Adjustments Due to Currency Fluctuations. If the parties agree in a Product Agreement to invoice in a currency other than the local currency for the Manufacturing Site, Patheon will adjust the Price to reflect currency fluctuations. The adjustment will be calculated after all other annual Price adjustments under this Section 4.2 have been made. The adjustment will proportionately reflect the increase or decrease, if any, in the Set Exchange Rate compared to the Set Exchange Rate established for the prior Year or the Initial Set Exchange Rate, as the case may be. An example of the calculation of the price adjustment (for a Canadian Manufacturing Site invoiced in USD) is set forth in Exhibit E.

(e) Tier Pricing (if specified in a Product Agreement). If the pricing in Schedule B of a Product Agreement is set forth in Annual Volume tiers based upon Client's volume forecasts under Section 5.1(a), the parties will estimate the Price in any Year based on Client's [*] forecast provided pursuant to Section 5.1(a). Within [*] days of the end of each Year, the parties will reconcile the difference which may be payable by either party based on the Actual Ordered Product for the Year. If the Actual Ordered Product for the Year is in a tier with a higher cost than that used to calculate the Price for the Year, Client will pay Patheon the difference owed in accordance with Section 5.5. If the Actual Ordered Product for the year is in a tier with a lower cost than that used by the parties to estimate the Price for the year, Patheon will credit or refund, at Client's option, Client for the overpayment.

(f) For all Price adjustments under this Section 4.2, Patheon will deliver to Client on or before November 30 of each Year a revised Schedule B to the Product Agreement to be effective for Product delivered on or after the first day of the next Year. If in any Year Patheon would have been entitled to increase the Price based on any of the provisions of this Section 4.2 but Patheon did not exercise its right to do so, then at the expiry of any subsequent Year, Patheon will be entitled to make cumulative adjustments only for Product sold after the expiry of such Year, as set out in Section 4.2 to the extent of any permitted changes for all of the preceding Years since Patheon last adjusted the Price.

4.3 Price Adjustments – Current Year Pricing.

During any Year, the Prices set out in Schedule B of a Product Agreement will be adjusted as follows:

Extraordinary Increases in Component Costs. If, at any time, market conditions result in Patheon's cost of Components being materially greater or less than normal forecasted changes,

then the Price may be adjusted for any affected Product to solely to reflect the changes to the Component costs. Unless otherwise agreed in a Product Agreement, changes materially greater or less than normal forecasted increases will have occurred if: (i) the cost of a Component increases or decreases by [*] of the cost for that Component, as set forth in Schedule B to the applicable Product Agreement and subject to any prior adjustments made under Section 4.2(b); or (ii) the aggregate cost for all Components required to manufacture a Product increases or decreases by [*] of the total Component costs for the Product as set forth in Schedule B to applicable Product Agreement and subject to any prior adjustments made under Section 4.2(b). If Component costs have been previously adjusted to reflect an increase or decrease in the cost of one or more Components, the adjustments set out in (i) and (ii) above will operate based on the last cost adjustment for the Components.

For a Price adjustment under this Section 4.3, Patheon will deliver to Client a revised Schedule B to the Product Agreement and budgetary pricing information, adjusted Component costs or other documents reasonably sufficient to demonstrate that a Price adjustment is justified. Patheon will have no obligation to deliver any supporting documents that are subject to obligations of confidentiality between Patheon and its suppliers. The revised Price will be effective for any Product delivered on or after the first day of the month following Client's receipt of the revised Schedule B to the Product Agreement.

4.4 **Adjustments Due to Technical Changes or Regulatory Authority Requirements**.

For changes to the Specifications or manufacturing processes that are required by Applicable Laws ("**Required Manufacturing Changes**"), Patheon and Client will cooperate in making these changes and use commercially reasonable efforts to implement the changes promptly in a manner that minimizes any effect on the supply hereunder to Client of Product meeting Specifications. All costs associated with Required Manufacturing Changes directly related to the Manufacturing Site will be borne by Patheon. All other costs associated with Required Manufacturing Changes under this Agreement, including, without limitation, obsolete Components, Regulatory Filings, work in process, equipment and Product will be borne by Client. Amendments to the Specifications or the Quality Agreement requested by the Client that are not Required Manufacturing Changes ("**Client Requested Changes**") will only be implemented following a technical and cost review by Patheon and are subject to Client and Patheon reaching agreement as to revisions, if any, to the fees specified in Schedules B or C of the Product Agreement necessitated by the amendment. Amendments to the Specifications, the Quality Agreement or the Manufacturing Site requested by Patheon that are not Required Manufacturing Changes ("**Patheon Requested Changes**") will only be implemented following the approval of Client, this approval not to be unreasonably withheld, and the costs of the Patheon Requested Changes will be borne by Patheon. If Client accepts a proposed fee change, the proposed change in the Specifications will be implemented, and the fee change will become effective only for those orders of the Product that are manufactured in accordance with the revised Specifications. In addition, for Client Requested Changes, Client agrees to purchase, at Patheon's cost (including all costs incurred by Patheon in connection with the purchase and handling of the Inventory), all Inventory held under the "old" Specifications and purchased or maintained by Patheon in order to fill Firm Orders or in accordance with Section 5.2, to the extent that the Inventory can no longer be utilized under the revised Specifications. Open purchase orders for Components no longer required under any revised Specifications that were placed by Patheon in accordance with this Agreement with suppliers in order to fill Firm Orders or in accordance with Section 5.2 will be cancelled where possible, and where the orders are not subject to cancellation without penalty, will be assigned to and satisfied by Client.

4.5 Multi-Country Packaging Requirements.

If Client decides to have Patheon perform Manufacturing Services for the Product for countries outside the Territory, then Client will inform Patheon of the packaging requirements for each new country and Patheon will prepare a quotation for consideration by Client of any additional costs for Components (other than Client-Supplied Components) and the change over fees for the Product destined for each new country. The agreed additional packaging requirements and related packaging costs and change over fees will be set out in a written amendment to this Agreement.

ARTICLE 5

ORDERS, SHIPMENT, INVOICING, PAYMENT

5.1 Orders and Forecasts.

(a) Long Term Forecast. When each Product Agreement is executed, Client will give Patheon a non-binding [*] year forecast of Client's volume requirements for the Product for each Year during the term of the Product Agreement (the "**Long Term Forecast**"). The Long Term Forecast will thereafter be updated every six months (as of June 1 and December 1) during the Initial Product Term. If Patheon is unable to accommodate any portion of the Long Term Forecast, it will notify Client and the parties will agree on any revisions to the forecast.

(b) Rolling [*] Month Forecast. When each Product Agreement is executed, Client will give Patheon a non-binding [*] month forecast of the volume of Product that Client expects to order in the first [*] months of commercial manufacture of the Product. This forecast will then be updated by Client on or before the [*] day of each month on a rolling forward basis. Client will update the forecast forthwith if it determines that the volumes estimated in the most recent forecast are anticipated to change by more than [*]. The most recent [*] month forecast will prevail over prior forecasts.

(c) Firm Orders. On or before the [*] day of each month Client will issue firm written orders ("**Firm Orders**") for each Product from time to time at Client's discretion to be produced and delivered to Client on a date not less than [*] months from the [*] date of the month immediately following the date that the Firm Order is submitted unless otherwise agreed in a Product Agreement. Firm Orders submitted to Patheon will specify Client's purchase order number, quantities by Product, type of packaging, delivery schedule and any other elements necessary to ensure the timely production and shipment of each Product. The quantities of Product ordered in Firm Orders will be firm and binding on Client. Notwithstanding the foregoing, and subject to the availability of required Components, for each Product, Patheon will permit amendments and substitutions to Firm Orders issued by Client upon prior written notice to Patheon for Product packaging no more than [*] per Year. But Patheon will not accept these amendments or substitutions once manufacturing or packaging has commenced.

(d) Acceptance of Firm Order. Firm Orders placed with Patheon by Client pursuant to the provisions of Section 5.1(b) will be acknowledged by Patheon in writing within [*] days of receipt thereof. Patheon will use commercially reasonable efforts to ensure that all Product ordered by Client in accordance with this Agreement will be shipped in

accordance with the delivery dates specified in Client's purchase order but in no event will the actual delivery date be more or less than five days from the date of delivery specified in Client's purchase order. Patheon will notify Client promptly of any significant anticipated delay no later than [*] days prior to the delivery date.

(e) Cancellation of a Firm Order. Client may cancel a Firm Order upon written notice to Patheon within the first [*] days of the firm period if Patheon has not started the manufacturing process under the Firm Order before receipt of the cancellation notice. If Client cancels a Firm Order in any other circumstances, Client will pay Patheon [*] of the Price for the Firm Order.

(f) Controlled Substance Quota Requirements (if applicable). Client will give Patheon the information set forth below for obtaining any required DEA or equivalent agency quotas needed to perform the Manufacturing Services. Patheon will be responsible for management of DEA quota information in accordance with DEA regulations. Patheon and Client will cooperate to communicate the information and to assist each other in DEA information requirements related to the Product as follows: (i) as of [*] for the applicable Product, Client will provide to Patheon the next Year's annual quota requirements for the Product; (ii) as of [*], Client will provide to Patheon any changes to the next Year's quota requirements; (iii) Client will pro-actively communicate any changes to the quota requirements for the then-current Year reasonably in advance of the time for Patheon to file and finalize DEA filings supporting the changes; (iv) upon Patheon receiving the necessary forecast information from Client in order to request additional quota, Patheon will submit to the DEA, on a timely basis, all filings necessary to obtain DEA or equivalent agency quotas for Active Materials and will use commercially reasonable efforts to secure sufficient quota from the DEA so as to achieve Delivery Dates for Product as set forth in applicable purchase orders and forecasts submitted to Patheon by Client or its designee; and (v) Patheon will not be responsible for DEA's refusal or failure to grant sufficient quota for reasons beyond the reasonable control of Patheon, provided that Patheon has met its obligations above. PATHEON ACKNOWLEDGES THAT TIME IS OF THE ESSENCE IN PERFORMING ITS OBLIGATIONS UNDER THS PROVISION.

5.2 Reliance by Patheon.

(a) Client understands and acknowledges that Patheon will rely on the Firm Orders and rolling forecasts submitted under Sections 5.1(a), and (b) in ordering the Components (other than Client-Supplied Components) required to meet the Firm Orders. In addition, Client understands that to ensure an orderly supply of the Components, Patheon may want to purchase the Components in sufficient volumes to meet the production requirements for Products during part or all of the forecasted periods referred to in Section 5.1(a) or to meet the production requirements of any longer period agreed to by Patheon and Client. Accordingly, Client authorizes Patheon to purchase Components to satisfy the Manufacturing Services requirements for Products for the first [*] months contemplated in the most recent forecast given by Client under Section 5.1(a). Patheon may make other purchases of Components to meet Manufacturing Services requirements for longer periods if agreed to in writing by the parties. Client will give Patheon written authorization to order Components for any launch quantities of Product requested by Client which will be considered a Firm Order when accepted by Patheon.

(b) Client will reimburse Patheon for the cost of Components ordered by Patheon under Firm Orders or under Section 5.2(a) that are not included in finished Products manufactured for Client within [*] months after the forecasted month for which the purchases have been made (or for a longer period as

the parties may agree) or if the Components have expired or are rendered obsolete due to changes in artwork or applicable regulations during the period (collectively, "**Obsolete Stock**"). This reimbursement will include Patheon's cost to purchase and destroy the Obsolete Stock. If any non-expired Components are used in Products subsequently manufactured for Client or in third party products manufactured by Patheon, Client will receive credit for any costs of those Components previously paid to Patheon by Client.

(c) If Client fails to take possession or arrange for the destruction of non-expired Components within [*] months of purchase or, in the case of the delivery of conforming finished Product not accepted by Client within [*] of manufacture, Client will pay Patheon [*] per pallet, per month thereafter for storing the Components or finished Product. Storage fees for Components or Product which contain controlled substances or require refrigeration will be charged at [*] per pallet per month. Storage fees are subject to a one pallet minimum charge per month. Patheon may ship finished Product held by it longer than [*] to the Client at Client's expense on [*] days written notice to the Client.

5.3 Minimum Orders.

Client may only order Manufacturing Services for Batches of Products only in multiples of the Minimum Order Quantities as set out in Schedule B to each Product Agreement.

5.4 Delivery and Shipping.

Delivery of Products will be made [*] (Incoterms 2010) Patheon's shipping point unless otherwise agreed in a Product Agreement. Risk of loss or of damage to Products will remain with Patheon until Patheon loads the Products onto the carrier's vehicle for shipment at the shipping point at which time risk of loss or damage will transfer to Client. Patheon will, in accordance with Client's instructions and as agent for Client, arrange for shipping to be paid by Client. Client will arrange for insurance and will select the freight carrier used by Patheon to ship Products and may monitor Patheon's shipping and freight practices as they pertain to this Agreement. Products will be transported in accordance with the Specifications and Applicable Law.

5.5 Invoices and Payment.

Invoices will be sent by fax or email to the fax number or email address given by Client to Patheon in writing. Unless otherwise agreed in a Product Agreement, invoices will be issued when the Product is manufactured and released by Patheon to Client, and in the case of invoices for stability studies, within [*] days of completion of the applicable study. Patheon will also submit to Client, with each shipment of Products, a duplicate copy of the invoice covering the shipment. Patheon will also provide Client with an invoice covering any Inventory or Components which are to be purchased by Client under Section 5.2 of this Agreement. Each invoice will, to the extent applicable, identify Client's purchase order number, Product numbers, names and quantities, unit price, freight charges, and the total amount to be paid by Client. Unless otherwise agreed in a Product Agreement, Client will pay all invoices within [*] days of the date thereof. If any portion of an invoice is disputed, Client will pay Patheon for the undisputed amount and the parties will use good faith efforts to reconcile the disputed amount as soon as practicable. Any amounts that are disputed by Client will not be due until ten days following the resolution of the dispute. Interest on undisputed past due accounts will accrue at [*] per month which is equal to an annual rate of [*].

ARTICLE 6

PRODUCT CLAIMS AND RECALLS

6.1 Product Claims.

(a) Product Claims. Client has the right to reject any portion of any shipment of Product that deviates from the Specifications or was not manufactured in accordance with cGMPs or Applicable Laws without invalidating any remainder of the shipment. Client or its designee will inspect the Products manufactured by Patheon upon receipt and will use commercially reasonable efforts to give Patheon written notice (a "Deficiency Notice") of all claims for Products that deviate from the Specifications, cGMPs, or Applicable Laws within [*] days after Client's or its designee's receipt thereof (or, in the case of any defects not reasonably susceptible to discovery upon receipt of the Product, within [*] days after discovery by Client, but not after the expiration date of the Product). Should Client fail to give Patheon the Deficiency Notice within the applicable period, then the delivery will be deemed to have been accepted by Client on the [*] day after delivery or discovery, as applicable. Patheon will have no liability for any deviations for which it has not received notice within the applicable period.

(b) Determination of Deficiency. Upon receipt of a Deficiency Notice, Patheon will have [*] days to advise Client by notice in writing that it disagrees with the contents of the Deficiency Notice. If Client and Patheon fail to agree within [*] days after Patheon's notice to Client as to whether any Products identified in the Deficiency Notice deviate from the Specifications, cGMPs, or Applicable Laws, then the parties will mutually select an independent laboratory to evaluate if the Products deviate from the Specifications, cGMPs, or Applicable Laws. This evaluation will be binding on the parties. If the evaluation certifies that any Products deviate from the Specifications, cGMPs, or Applicable Laws, Client may reject those Products in the manner contemplated in this Section 6.1 and Patheon will be responsible for the cost of the evaluation. If the evaluation does not so certify for any of the Products, then Client will be deemed to have accepted delivery of the Products on the [*] day after delivery (or, in the case of any defects not reasonably susceptible to discovery upon receipt of the Product, on the [*] day after discovery thereof by Client, but not after the expiration date of the Product) and Client will be responsible for the cost of the evaluation.

(c) Shortages. If there is a shortage of Product in any shipment by Patheon, at Client's election, Patheon will use its commercially reasonable efforts to make up the shortage at the next scheduled delivery date. But if the shortage is more than [*] of the quantity ordered for any individual package configuration, Patheon will use its commercially reasonable efforts to make up the shortage as soon as practical after the shortage is reported to Patheon, but no later than [*] days thereafter.

(d) Product Rejection for Finished Product Specification Failure. Internal process specifications will be defined and agreed upon. If Patheon manufactures Product in accordance with the agreed upon process specifications, the batch production record, and Patheon's standard operating procedures for manufacturing, and a batch or portion of batch of Product does not meet a finished Product specification, Client will pay Patheon the applicable fee per unit for the non-conforming Product. The API in the non-conforming Product will be included in the "Quantity Converted" for purposes of calculating the "Actual Annual Yield" under Section 2.2(a). For avoidance of doubt, any dispute arising with respect to this Section shall be resolved in accordance with Section 12.2.

6.2 Product Recalls and Returns.

(a) Records and Notice. Patheon and Client will each maintain records necessary to permit a Recall of any Products delivered to Client or customers of Client. Each party will notify the other by

telephone (to be confirmed in writing) within [*] of any information which might affect the marketability, safety or effectiveness of the Products or which might result in the Recall or seizure of the Products. Upon receiving this notice or upon this discovery, each party will stop making any further shipments of any Products in its possession or control until a decision has been made whether a Recall or some other corrective action is necessary. The decision to initiate a Recall or to take some other corrective action, if any, will be made and implemented by Client. "**Recall**" will mean any action (i) by Client to recover title to or possession of quantities of the Products sold or shipped to third parties (including, without limitation, the voluntary withdrawal of Products from the market); or (ii) by any regulatory authorities to detain or destroy any of the Products. Recall will also include any action by either party to refrain from selling or shipping quantities of the Products to third parties which would be subject to a Recall if sold or shipped.

(b) Recalls. If (i) any Regulatory Authority issues a directive, order or, following the issuance of a safety warning or alert about a Product, a written request that any Product be Recalled, (ii) a court of competent jurisdiction orders a Recall, or (iii) Client determines that any Product should be Recalled or that a "Dear Doctor" letter is required relating the restrictions on the use of any Product, Patheon will co-operate as reasonably required by Client, having regard to all applicable laws and regulations.

(c) Product Returns. Client will have the responsibility for handling customer returns of the Products. Patheon will give Client any assistance that Client may reasonably require to handle the returns.

6.3 Patheon's Responsibility for Defective and Recalled Products.

(a) Defective Product. If Client rejects Products under Section 6.1 and the deviation is determined to have arisen from Patheon's failure to provide the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, Patheon will credit Client's account for Patheon's invoice price for the defective Products. If Client previously paid for the defective Products, Patheon will promptly, at Client's election, either: (i) refund the invoice price for the defective Products; (ii) offset the amount paid against other amounts due to Patheon hereunder; or (iii) replace the Products with conforming Products, without Client being liable for payment therefor under Section 3.1, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. If the defective Products were manufactured using Client-Supplied Components, then Patheon will, as determined by Client, (i) refund the value of these Client-Supplied Components to Client or (ii) offset the amount paid against other amounts due to Patheon hereunder. For greater certainty, Patheon's responsibility for any loss of Active Materials in defective Product will be captured and calculated in the Active Materials Yield under Section 2.2 and Client will receive a Shortfall Credit in connection therewith.

(b) Recalled Product. To the extent a Recall or return results from, or arises out of, a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, Patheon will be responsible for the documented out-of-pocket expenses of the Recall or return and will use its commercially reasonable efforts to replace the Recalled or returned Products with new Products, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. For greater certainty, Patheon's responsibility for any loss of Active Materials in Recalled Product will be captured and calculated in the Active Materials Yield under Section 2.2. If Patheon is unable to replace the Recalled or returned Products (except where this inability results from a failure to receive the required Active Materials and Client-Supplied Components due to the fault of Client), then at Client's request, Patheon will reimburse Client for the price that Client paid to Patheon for Manufacturing Services for the affected Products. Patheon will also be responsible for investigating all Recalls and returns (other than as a result of the

expiration of the Product) resulting from Patheon's failure to manufacture the Product in accordance with the Specifications, cGMPs, or Applicable Laws, at its own expense and Patheon will promptly report to Client in writing the results of this investigation. In all other circumstances, Recalls, returns, or other corrective actions will be made at Client's cost and expense.

(c) Except as set forth in Sections 6.3(a) and (b) above, Patheon will not be liable to Client nor have any responsibility to Client for any deficiencies in, or other liabilities associated with, any Product manufactured by it in accordance with this Agreement, (collectively, "**Product Claims**"). For greater certainty but not limitation, except as set forth in Sections 6.3(a) and (b) above, Patheon will have no obligation for any Product Claims to the extent the Product Claim (i) is caused by deficiencies in the Specifications, the safety, efficacy, or marketability of the Products or any distribution thereof after delivery in accordance with Section 5.4, (ii) results from a defect in a Component that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications prior to use of the applicable Component in the performance of the Manufacturing Services, (iii) results from a defect in the Active Materials, Client-Supplied Components or Components supplied by a Client designated additional source that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications, (iv) is caused by actions of third parties occurring after the Product is shipped by Patheon under Section 5.4, (v) is due to packaging design or labelling defects or omissions for which Patheon has no responsibility, (vi) is due to any unascertainable reason despite Patheon having performed the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, or (vii) is due to any breach by Client of its obligations under this Agreement.

6.4 Disposition of Defective or Recalled Products.

Client will not dispose of any damaged, defective, returned, or Recalled Products for which it intends to assert a claim against Patheon without Patheon's prior written authorization to do so. Alternatively, Patheon may instruct Client to return the Products to Patheon. Patheon will bear the cost of disposition for any damaged, defective, returned or Recalled Products for which it bears responsibility under Section 6.3. In all other circumstances, Client will bear the cost of disposition, including all applicable fees for Manufacturing Services, for any damaged, defective, returned, or Recalled Products.

6.5 Healthcare Provider or Patient Questions and Complaints.

Client will have the sole responsibility for responding to questions and complaints from its customers. Questions or complaints received by Patheon from Client's customers, healthcare providers or patients will be promptly referred to Client. Patheon will co-operate as reasonably required to allow Client to determine the cause of and resolve any questions and complaints. This assistance will include follow-up investigations, including testing. In addition, Patheon will give Client all necessary information in Patheon's possession or control that will enable Client to respond properly to questions or complaints about the Products as set forth in the Quality Agreement. If it is determined that the cause of the complaint resulted from a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws and any additional procedures agreed upon in writing by Patheon and Client or a breach of this Agreement by Patheon, all costs incurred under this Section 6.5 will be borne by Patheon. In all other circumstances, Client will bear the cost incurred under this Section 6.5.

6.6 Sole Remedy.

Except for the indemnity set forth in Section 10.3 and subject to the limitations set forth in Sections 10.1 and 10.2, the remedies described in this Article 6 will be Client's sole remedy for any failure

by Patheon to provide the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws or any additional procedures agreed upon in writing by Client and Patheon.

ARTICLE 7

CO-OPERATION

7.1 Quarterly Review.

Each party will forthwith upon execution of this Agreement appoint one of its employees to be a relationship manager responsible for liaison between the parties. The relationship managers will meet not less than quarterly to review the current status of the business relationship, including but not limited to, equipment and facilities updates, current and anticipated manufacturing capacity, planned work or changes to each Manufacturing Site and anticipated shut downs of each Manufacturing Site, and manage any issues that have arisen.

7.2 Governmental Agencies.

Subject to Section 7.8 and Article 11, each party may communicate with any governmental agency, including but not limited to governmental agencies responsible for granting Regulatory Approval for the applicable Product, regarding such Product if, in the opinion of that party's counsel, the communication is necessary to comply with the terms of this Agreement or the requirements of any law, governmental order or regulation. Unless, in the reasonable opinion of its counsel, there is a legal prohibition against doing so, each party will permit the other party to accompany and take part in any communications with the agency, and to receive copies of all communications from the agency.

7.3 Records and Accounting by Patheon.

Patheon will keep records of the manufacture, testing, and shipping of the Products, and retain samples of the Products as are necessary to comply with manufacturing regulatory requirements applicable to Patheon, as well as to assist with resolving Product complaints and other similar investigations. Unless otherwise agreed to in the Quality Agreement, copies of the records and samples will be retained for [*] following the date of Product expiry, or longer if required by Applicable Law, following which time Patheon may destroy such records or samples; provided, however, Patheon will notify Client in writing at least [*] days prior to such destruction and will retain or deliver such records or samples to Client, at Client’s option and expense, if Client so requests.

7.4 Inspection.

Client may inspect Patheon reports and records relating to this Agreement during normal business hours and with reasonable advance notice, but a Patheon representative must be present during the inspection.

7.5 Access.

Patheon will give Client reasonable access at agreed times to the areas of each Manufacturing Site in which a Product is manufactured, stored, handled, or shipped to permit Client to verify that the Manufacturing Services are being performed in accordance with the Specifications, cGMPs, and Applicable Laws. But, with the exception of “for-cause” audits, for each Product, Client will be limited each Year to [*], lasting no more than [*] days, and involving no more than [*] auditors. Client may request additional cGMP-type audits, additional audit days, or the participation

of additional auditors subject to payment to Patheon of a fee of [*] for each additional audit day and [*] per audit day for each additional auditor. Patheon agrees to permit Client to review Patheon's standard operating procedures for the manufacture of the Product and those associated with the general facilities, equipment or procedures required for compliance with cGMPs or DEA requirements. The right of access provided in this Section 7.5 will not include a right to access or inspect Patheon's financial records. Patheon will use commercially reasonable efforts to obtain the right for Client to have similar inspection rights for Patheon's third party Component suppliers. If deficiencies are found by Client during these inspections, the parties will promptly meet to discuss and resolve them and Client will be entitled to make reasonable follow up inspections to monitor correction of the deficiencies.

7.6 **Notification of Regulatory Inspections**.

Patheon will notify Client within [*] of any inspections by or communications with, any governmental agency involving the Products. Patheon will furnish to Client within [*] all material information supplied to, or supplied by the governmental agency or third party supplier to the extent that the report relates to a Product or the ability of Patheon to supply a Product. Patheon will promptly correct any deficiencies noted by any governmental agency in these inspections. Patheon will also notify Client of receipt of any form 483's or warning letters or any other significant regulatory action which Patheon's quality assurance group determines could impact the regulatory status of the Products.

7.7 **Reports**.

Upon request, Patheon will supply on an annual basis all Product data, including release test results, complaint test results, and all investigations (in manufacturing, testing, and storage), that Client reasonably requires in order to complete any filing under any applicable regulatory regime, including any Annual Report that Client is required to file with the FDA. Any additional report requested by Client beyond the scope of cGMPs and customary FDA requirements and beyond the scope of the reports provided by Section 2.2 will be subject to an additional fee to be agreed upon between Patheon and the Client.

7.8 **Regulatory Filings**.

(a) Regulatory Authority. Client will have the sole responsibility at Client's expense for filing all documents with all Regulatory Authorities and taking any other actions that may be required for the receipt and/or maintenance of Regulatory Authority approval for the commercial manufacture, distribution and sale of the Products ("**Regulatory Approval**"). Patheon will assist Client, to the extent consistent with Patheon's obligations under this Agreement, to obtain Regulatory Authority approval for the commercial manufacture, distribution and sale of all Products as quickly as reasonably possible.

(b) Verification of Data. Prior to filing any documents with any Regulatory Authority that incorporate data generated by Patheon, Client will give Patheon a copy of the documents incorporating this data to give Patheon the opportunity to verify the accuracy and regulatory validity of those documents as they relate to Patheon generated data. Patheon requires [*] days to perform this review but the parties may agree to a shorter time for the review as needed.

(c) Verification of CMC. Prior to filing with any Regulatory Authority any documentation which is or is equivalent to the Quality Module (Drug Product Section) of the Common Technical Document (all such documentation herein referred to as "**CTD**") related to any Marketing Authorization, such as a US New Drug Application, US Abbreviated New Drug Application, US Biologics Licence

Application, or EU Marketing Authorisation Application, Client will give Patheon a copy of the CTD as well as all supporting documents which have been relied upon to prepare the CTD. This disclosure will permit Patheon to verify that the CTD accurately describes the validation or scale-up work that Patheon has performed and the manufacturing processes that Patheon will perform under this Agreement. Patheon requires [*] days to perform this review but the parties may agree to a shorter time for the review as needed. Client will give Patheon copies of all relevant filings at the time of submission which contain CDT information regarding the Product.

(d) Deficiencies. If, in Patheon's good faith discretion, acting reasonably, Patheon determines that any of the information given by Client under clauses (b) and (c) above is inaccurate or deficient in any manner whatsoever (the "**Deficiencies**"), Patheon will notify Client in writing of the Deficiencies. The parties will work together to have the Deficiencies resolved prior to any pre-approval inspection.

(e) Client Responsibility. For clarity, in reviewing the documents referred to in clause (b) above, Patheon's role will be limited to verifying the accuracy of the description of the work undertaken or to be undertaken by Patheon. Subject to the foregoing, Patheon will not assume any responsibility for the accuracy of any application for receipt of an approval by a Regulatory Authority, except as to information provided by or verified by Patheon. Subject to Patheon's obligation to cooperate with Client pursuant to the terms and conditions of this Agreement, Client is solely responsible for the preparation and filing of the application for approval by the Regulatory Authority.

7.9 Inspection by Regulatory Authorities.

If Client does not give Patheon the documents requested under clauses (b) and (c) above within the time specified and if Patheon reasonably believes that Patheon's standing with a Regulatory Authority may be jeopardized, Patheon may, in its sole discretion, delay or postpone any inspection by the Regulatory Authority until Patheon has reviewed the requested documents and is satisfied with their contents, but this review must be completed within [*] days of Patheon's receipt of the documentation from Client.

ARTICLE 8

TERM AND TERMINATION

8.1 Initial Term.

This Agreement will become effective as of the Effective Date and will continue until **December 31, 2020** (the "**Initial Term**"), unless terminated earlier by one of the parties in accordance herewith. This Agreement will automatically renew after the Initial Term for successive terms of two Years each if there is a Product Agreement in effect, unless either party gives written notice to the other party of its intention to terminate this Agreement at least 18 months prior to the end of the then current term. In any event, the legal terms and conditions of this Agreement will continue to govern any Product Agreement in effect as provided in Section 1.2. Each Product Agreement will have an initial term of five years from the start of commercial manufacture at the Manufacturing Site for the Product unless the parties agree to a different number of years in the applicable Product Agreement (each, an "**Initial Product Term**"). Unless otherwise agreed in a particular Product Agreement, Product Agreements will automatically renew after the Initial Product Term for successive terms of two years each unless either party gives written notice to the other party of its intention to terminate the Product Agreement at least 18 months (the "**Product Agreement Non-Renewal Notice Period**") prior to the end of the then current term. [*].

[*].

8.2 Termination for Cause.

(a) Either party at its sole option may terminate this Agreement or a Product Agreement upon written notice where the other party has failed to remedy a material breach of any of its representations, warranties, or other obligations under this Agreement or the applicable Product Agreement within 60 days following receipt of a written notice (the "Remediation Period") of the breach from the aggrieved party that expressly states that it is a notice under this Section 8.2(a) (a "Breach Notice"). The aggrieved party's right to terminate this Agreement or the applicable Product Agreement under this Section 8.2(a) may only be exercised for a period of 60 days following the expiry of the Remediation Period (where the breach has not been remedied) and if the termination right is not exercised during this period then the aggrieved party will be deemed to have waived the breach of the representation, warranty, or obligation described in the Breach Notice. The termination of a Product Agreement under this Section 8.2(a) will not affect this Agreement or any other Product Agreements where there has been no material breach of the other Product Agreements.

(b) Either party at its sole option may immediately terminate this Agreement or a Product Agreement upon written notice, but without prior advance notice, to the other party if: (i) the other party is declared insolvent or bankrupt by a court of competent jurisdiction; (ii) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by the other party; or (iii) this Agreement or a Product Agreement is assigned by the other party for the benefit of creditors.

(c) Client may terminate a Product Agreement upon 30 days' prior written notice if any Authority takes any action, or raises any objection, that prevents Client from importing, exporting, purchasing, or selling the Product. But if this occurs, Client must still fulfill all of its obligations under Section 8.4 below and under any Capital Equipment Agreement regarding the applicable Product.

(d) Patheon may terminate this Agreement or a Product Agreement upon 12 months' prior written notice if Client assigns under Section 13.6 any of its rights under this Agreement or a Product Agreement to an assignee that (i), in the opinion of Patheon acting reasonably and in good faith, is unable to pay for Product it orders under this Agreement; or (ii) is a Patheon Competitor.

8.3 Termination by Client.

(a) The Client may terminate this Agreement or any Product Agreement at any time upon 12 months’ prior written notice to Patheon.

(b) For any Product that has not obtained Regulatory Authority approval at the time the applicable Product Agreement is executed, the Client may terminate the applicable Product Agreement at any time on 60 days prior written notice.

8.4 **Product Discontinuation**.

Except as provided in Section 8.2(c), Client may terminate a Product Agreement upon 90 days' prior written notice if it intends to no longer order Manufacturing Services for a Product due to this Product's discontinuance in the market.

8.5 **Obligations on Termination**.

If a Product Agreement expires, or is terminated in whole or in part for any reason:

(a) Client will take delivery of and pay for all undelivered Product that was manufactured and/or packaged in compliance with the Product Agreement and this Agreement under a Firm Order at the price in effect at the time the Firm Order was placed;

(b) Client will purchase, at Patheon's cost (plus a [*] handling fee for Components), the Inventory applicable to the Products which was purchased, produced or maintained by Patheon in reliance on Firm Orders or in accordance with Section 5.2 prior to notice of termination being given;

(c) Client will satisfy the purchase price payable under Patheon's orders with suppliers of Components, if the orders were made by Patheon in reliance on Firm Orders or in accordance with Section 5.2;

(d) Patheon will return to Client all unused Active Materials (with shipping and related expenses, if any, to be borne by Client).

(e) Client acknowledges that no Patheon Competitor will be permitted access to the Manufacturing Site; and

(f) Client will make commercially reasonable efforts, at its own expense, to remove from Patheon site(s), within [*] days, all unused Active Material and Client-Supplied Components, all applicable Inventory and Materials (whether current or obsolete), supplies, undelivered Product, chattels, equipment or other moveable property owned by Client, related to the Agreement and located at a Patheon site or that is otherwise under Patheon's care and control ("**Client Property**"). If Client fails to remove the Client Property within [*] days following the completion, termination, or expiration of the Product Agreement, Client will pay Patheon [*] per pallet, per month, [*] minimum (except that Client will pay [*] per pallet, per month, [*] minimum, for any of the Client Property that contains controlled substances, requires refrigeration or other special storage requirements) thereafter for storing the Client Property and will assume any third party storage charges invoiced to Patheon regarding the Client Property. Patheon will invoice Client for the storage charges as set forth in Section 5.5 of this Agreement.

(g) In connection with the expiration or termination of this Agreement or any Product Agreement hereunder, at Client's request, Patheon will provide assistance reasonably required to transfer the Manufacturing Services. Such assistance may include, without limitation, providing documents required for the Manufacturing Services, attending meetings (in person or via teleconference), and subject to the confidentiality provisions hereof, hosting a Manufacturing Site visit. Except in cases of termination by Client pursuant to Section 8.2, Client will reimburse Patheon for its costs incurred in providing

such assistance in accordance with a tech transfer plan and budget negotiated in good faith and agreed upon by the parties.

Any, termination or expiration of this Agreement or a Product Agreement will not affect any outstanding obligations or payments due prior to the termination or expiration, nor will it prejudice any other remedies that the parties may have under this Agreement or a Product Agreement or any related Capital Equipment Agreement. For greater certainty, the termination or expiration of this Agreement or of a Product Agreement for any reason will not affect the obligations and responsibilities of the parties under Articles 9, 10 and 11 and Sections 5.4, 5.5, 8.5, 13.1, 13.2 and 13.3, all of which survive any termination or expiration.

ARTICLE 9

REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1 **Authority**.

Each party covenants, represents, and warrants that it has the full right and authority to enter into this Agreement and that it is not aware of any impediment that would inhibit its ability to perform its obligations hereunder.

9.2 **Client Warranties**.

Client represents, and warrants that:

(c) Non-Infringement.

(i) Client has the right to disclose the Specifications to Patheon;

(ii) any Client Intellectual Property, used by Patheon in performing the Manufacturing Services according to the Specifications (A) is Client's or its Affiliate's property or is the subject of a license to Client, (B and to Client's knowledge, does not infringe and will not infringe any Third Party Rights;

(iii) there are no actions or other legal proceedings against Client pending or threatened in writing alleging that the any of the Specifications, any of the Active Materials or Components, or the sale, use, or other disposition of any Product made in accordance with the Specifications as contemplated by this Agreement and the applicable Product Agreement infringes the Intellectual Property rights of any Third Party;

(d) Quality and Compliance.

(i) the Specifications for each Product conforms to the applicable regulatory approval;

(ii) the Products, if labelled and manufactured in accordance with the Specifications and in compliance with applicable cGMPs and Applicable Laws may be lawfully sold and distributed in every jurisdiction in which Client markets the Products; ;

(iii) on the date of shipment, the API will conform to the specifications for the API that Client has given to Patheon and the API will be contained, packaged, and labelled in accordance with Applicable Law and the Specifications, and will conform to the affirmations of fact on the container.

9.3 Patheon Warranties.

Patheon covenants, represents, and warrants that:

(a) it will perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws and that any Product supplied by it hereunder at the time of shipment, will comply with the Specifications;

(b) Patheon is not aware of any Intellectual Property of any third party that is necessary for Patheon to manufacture any Product as contemplated hereby; and

(c) The Active Material will not be used for any purposes beyond or different from the scope of the Manufacturing Services or otherwise in violation of the terms and conditions of this Agreement. Patheon acknowledges that certain of the Products are controlled under the Controlled Substances Act and, as such, are subject to regulations and restrictions concerning sale and distribution. Patheon agrees to comply with these regulations and restrictions, as well as any reasonable instructions from Client with respect to the use and storage of the Products. Without limiting the foregoing, (a) Patheon will obtain and/or maintain in force during the term of the Agreement all licenses and authorizations from the Drug Enforcement Administration or any other regulatory or governmental agency which are necessary for it to manufacture and possess these Products; and (b) Patheon will keep these Products in a secure location with access limited to authorized employees.

(d) any Patheon Intellectual Property used by Patheon to perform the Manufacturing Services (i) is Patheon's or its Affiliate's unencumbered property, (ii) may be lawfully used by Patheon, and (iii) does not infringe and will not infringe any Third Party Rights.

9.4 Debarred Persons.

Patheon covenants that it will not in the performance of its obligations under this Agreement use the services of any person debarred or suspended under 21 U.S.C. §335(a) or (b). Patheon represents that it does not currently have, and covenants that it will not hire, as an officer or an employee any person who has been convicted of a felony under the laws of the United States for conduct relating to the regulation of any drug product under the *Federal Food, Drug, and Cosmetic Act* (United States).

9.5 Permits.

Client will be solely responsible for obtaining or maintaining, on a timely basis, any Regulatory Approvals for marketing the Products by Client or the Regulatory Approvals of the applicable Specifications, including, without limitation, all marketing and post-marketing approvals.

Patheon will be solely responsible for obtaining and maintain all permits, approvals and quotas necessary in order for Patheon to manufacture the Product in its facilities as contemplated hereby, and for those facilities themselves including all FDA Establishment Registrations or equivalent Registrations as applicable.

9.6 **Compliance with Laws**. Each party, in connection with its performance under this Agreement, will comply with all Applicable Laws.

9.7 **No Warranty**.

NEITHER PATHEON NOR THE CLIENT MAKES ANY WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, OTHER THAN THOSE EXPRESSLY SET FORTH IN THIS AGREEMENT. PATHEON MAKES NO WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE OR WARRANTY OF MERCHANTABILITY FOR THE PRODUCTS.

ARTICLE 10

REMEDIES AND INDEMNITIES

10.1 **Consequential Damages**.

Under no circumstances whatsoever will either party be liable to the other in contract, tort, negligence, breach of statutory duty, or otherwise for (i) any (direct or indirect) loss of profits, of production, of anticipated savings, of business, or goodwill or (ii) for any other liability, damage, costs, or expense of any kind incurred by the other party of an indirect or consequential nature, regardless of any notice of the possibility of these damages.

10.2 **Limitation of Liability**.

Except as set forth in the applicable Product Agreement, certain liabilities of Patheon are limited as set forth in subsections (a) through (c), below.

(a) Defective or Recalled Product. Patheon's maximum aggregate liability to Client for any obligation to (i) refund, offset or replace any defective Product under Section 6.3(a) or (ii) replace any recalled Products under Section 6.3(b), will not exceed [*] of the Price for the defective or recalled Product as applicable. This Section 10.2(a) shall not be subject to Section 10.2(c).

(b) Active Materials. Except as expressly set forth in Section 2.2, under no circumstances will Patheon be responsible for any loss or damage to the Active Materials. Patheon's maximum responsibility for loss or damage to the Active Materials will not exceed the Maximum Credit Value set forth in Schedule D of a Product Agreement.

(c) Maximum Liability. Except for Patheon's indemnity obligations under Section 10.3 and any liability arising from Patheon's breach of its confidentiality obligations under Article 11, or from its obligations related to Intellectual Property or from its willful misconduct, Patheon's maximum liability to Client under this Agreement or any Product Agreement for any reason whatsoever, including, without limitation, any liability arising under Section 6.3(b) relating to the expenses of a Recall or Product return, or Section 2.2 hereof or resulting from any and all breaches of its representations, warranties, or any other obligations under this Agreement or any Product Agreement will not exceed on a per Product basis [*] of revenues per Year to Patheon under the applicable Product Agreement.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

10.3 Patheon Indemnity.

(a) Patheon agrees to defend and indemnify Client, its Affiliates and their respective officers, employees, and agents against all losses, damages, costs, claims, demands, judgments and liability to, from and in favor of third parties (other than Affiliates) resulting from, or relating to any claim of (i) a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, (ii) Patheon's breach of its obligations under this Agreement or any Product Agreement, or (iii) Patheon's negligence, gross negligence or willful misconduct, each except to the extent that the losses, damages, costs, claims, demands, judgments, and liability are due to the negligence, gross negligence or wrongful act(s) of Client, its officers, employees, agents, or Affiliates.

(b) If a claim occurs, Client will: (a) promptly notify Patheon of the claim; (b) use commercially reasonable efforts to mitigate the effects of the claim; (c) reasonably cooperate with Patheon in the defense of the claim; and (d) permit Patheon to control the defense and settlement of the claim, all at Patheon's cost and expense.

10.4 Client Indemnity.

(a) Client agrees to defend and indemnify Patheon, its officers, employees, and agents against all losses, damages, costs, claims, demands, judgments and liability to, from and in favor of third parties (other than Affiliates) resulting from, or relating to any claim of (i) infringement or alleged infringement of any Third Party Rights in the Products, or any portion thereof, (ii) personal injury or property damage to the extent that the injury or damage is the result of a breach of this Agreement or any Product Agreement by Client, including, without limitation, any representation or warranty contained herein, (ii) product liability resulting in personal injury or property damage arising out of the Products that are labelled and manufactured in accordance with the Specifications and in compliance with applicable cGMPs and Applicable Laws or (iii) Client's negligence, gross negligence or willful misconduct, each except to the extent that the losses, damages, costs, claims, demands, judgments, and liability are due to the negligence, gross negligence or wrongful act(s) of Patheon, its officers, employees, or agents.

(b) If a claim occurs, Patheon will: (a) promptly notify Client of the claim; (b) use commercially reasonable efforts to mitigate the effects of the claim; (c) reasonably cooperate with Client in the defense of the claim; and (d) permit Client to control the defense and settlement of the claim, all at Client's cost and expense.

10.5 Reasonable Allocation of Risk.

This Agreement (including, without limitation, this Article 10) is reasonable and creates a reasonable allocation of risk having regard to the relative profits the parties each expect to derive from the Products. Patheon assumes only a limited degree of risk arising from the manufacture, distribution, and use of the Products because Client has developed and holds the marketing approval for the Products, Client requires Patheon to manufacture and label the Products strictly in accordance with the Specifications, and Client, not Patheon, is best positioned to inform and advise potential users about the circumstances and manner of use of the Products.

ARTICLE 11

CONFIDENTIALITY

11.1 Confidential Information.

"**Confidential Information**" means any information disclosed by the Disclosing Party to the Recipient (whether disclosed in oral, written, electronic or visual form), whether before the Effective Date or during the term hereof, that is non-public, confidential or proprietary including, without limitation, information relating to the Disclosing Party's patent and trademark applications, process designs, process models, drawings, plans, designs, data, databases and extracts therefrom, formulae, methods, know-how and other Intellectual Property, its clients or client confidential information, finances, marketing, products and processes and all price quotations, manufacturing or professional services proposals, information relating to composition, proprietary technology, and all other information relating to manufacturing capabilities and operations. In addition, all analyses, compilations, studies, reports or other documents prepared by any party's Representatives containing the Confidential Information will be considered Confidential Information. Samples or materials provided hereunder as well as any and all information derived from the approved analysis of the samples or materials will also constitute Confidential Information. For the purposes of this ARTICLE 11, a party or its Representative receiving Confidential Information under this Agreement is a "**Recipient**," and a party or its Representative disclosing Confidential Information under this Agreement is the **"Disclosing Party**."

11.2 Use of Confidential Information.

The Recipient will use the Disclosing Party's Confidential Information solely for the purpose of meeting its obligations under this Agreement. The Recipient will keep the Disclosing Party's Confidential Information strictly confidential. As Recipient, Client will use the Confidential Information of Patheon solely for the purpose of performing its obligations hereunder and for obtaining the benefits hereof. As Recipient, Patheon will use the Confidential Information of Client solely for the purpose of performing its obligations hereunder. Each Party will not disclose the Disclosing Party's Confidential Information in any manner whatsoever, in whole or in part, other than to those of its Representatives who (i) have a need to know the Confidential Information for the purpose of this Agreement; (ii) have been advised of the confidential nature of the Confidential Information and (iii) have obligations of confidentiality and non-use to the Recipient no less restrictive than those of this Agreement. Recipient will protect the Disclosing Party's Confidential Information disclosed to it by using all reasonable precautions to prevent the unauthorized disclosure, dissemination or use of the Confidential Information, which precautions will in no event be less than those exercised by Recipient with respect to its own confidential or proprietary Confidential Information of a similar nature.

11.3 Exclusions.

The obligations of confidentiality will not apply to the extent that the information:

(a) is or becomes publicly known through no breach of this Agreement by the Recipient or its Representatives;

(b) is in the Recipient's possession at the time of disclosure by the Disclosing Party other than as a result of the Recipient's breach of any legal obligation;

(c) is or becomes known to the Recipient on a non-confidential basis through disclosure by sources, other than the Disclosing Party, having the legal right to disclose the Confidential Information,

provided that the other source is not known by the Recipient to be bound by any obligations (contractual, legal, fiduciary, or otherwise) of confidentiality to the Disclosing Party with respect to the Confidential Information;

(d) is independently developed by the Recipient without use of or reference to the Disclosing Party's Confidential Information as evidenced by Recipient's written records; or

(e) is expressly authorized for release by the written authorization of the Disclosing Party.

Any combination of information which comprises part of the Confidential Information are not exempt from the obligations of confidentiality merely because individual parts of that Confidential Information were publicly known, in the Recipient's possession, or received by the Recipient, unless the combination itself was publicly known, in the Recipient's possession, or received by the Recipient.

11.4 Photographs and Recordings.

Neither party will take any photographs or videos of the other party's facilities, materials, Product, equipment or processes, nor use any other audio or visual recording equipment (such as camera phones) while at the other party's facilities, without that party's express written consent.

11.5 Permitted Disclosure.

Notwithstanding any other provision of this Agreement, the Recipient may disclose Confidential Information of the Disclosing Party to the extent required, in the reasonable opinion of counsel, in response to a valid order of a court or other governmental body or as required by law, regulation or stock exchange rule. But the Recipient will advise the Disclosing Party in advance of the disclosure to the extent practicable and permissible by the order, law, regulation or stock exchange rule and any other applicable law, will reasonably cooperate with the Disclosing Party, if requested, in seeking an appropriate protective order or other remedy, and will otherwise continue to perform its obligations of confidentiality set out herein. If any public disclosure is required by law, the parties will consult concerning the form of announcement prior to the public disclosure being made.

11.6 Return of Confidential Information.

Upon the written request of the Disclosing Party, the Recipient will promptly return the Disclosing Party's Confidential Information to the Disclosing Party or, if the Disclosing Party directs, destroy all of the Disclosing Party's Confidential Information disclosed in or reduced to tangible form including any copies thereof and any summaries, compilations, analyses or other notes derived from the Disclosing Party's Confidential Information except for one copy which may be maintained by the Recipient for its records. The retained copy will remain subject to all confidentiality provisions contained in this Agreement.

11.7 Remedies.

The parties acknowledge that monetary damages may not be sufficient to remedy a breach by either party of this Article 11 and agree that the non-breaching party will be entitled to seek specific performance, injunctive and/or other equitable relief to prevent breaches of this Article II and to specifically enforce the provisions hereof in addition to any other remedies available at law or in equity. These remedies will not be the exclusive remedies for breach of this Article 11 but will be in addition to any and all other remedies available at law or in equity.

ARTICLE 12

DISPUTE RESOLUTION

12.1 Commercial Disputes.

If any dispute arises out of or in connection with this Agreement or any Product Agreement (other than a dispute under Section 6.1(b) or a Technical Dispute, as defined herein), the parties will first try to resolve it amicably. In that regard, any party may send a notice of dispute to the other, and each party will appoint, within [*] Business Days from receipt of the notice of dispute, a single representative having full power and authority to resolve the dispute. The representatives will meet as necessary in order to resolve the dispute. If the representatives fail to resolve the matter within [*] from their appointment, or if a party fails to appoint a representative within the [*] Business Day period set forth above, the dispute will immediately be referred to the Chief Operating Officer or Executive Vice President (or another officer as he/she may designate) of each party who will meet and discuss as necessary to try to resolve the dispute amicably. Should the parties fail to reach a resolution under this Section 12.1, the dispute will be referred to a court of competent jurisdiction in accordance with Section 13.16.

12.2 Technical Dispute Resolution.

If a dispute arises (other than disputes under Sections (b) or 12.1) between the parties that is exclusively related to technical aspects of the manufacturing, packaging, labelling, quality control testing, handling, storage, or other activities under this Agreement (a "**Technical Dispute**"), the parties will make all reasonable efforts to resolve the dispute by amicable negotiations. In that regard, senior representatives of each party will, as soon as possible and in any event no later than [*] Business Days after a written request from either party to the other, meet in good faith to resolve any Technical Dispute. If the parties cannot agree that a dispute is a Technical Dispute, Section 12.1 will prevail. For greater certainty, the parties agree that the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

ARTICLE 13

MISCELLANEOUS

13.1 Inventions.

(a) For the term of this Agreement, Client hereby grants to Patheon a non-exclusive, paid-up, royalty-free, non-transferable license of Client's Intellectual Property which Patheon must use in order to perform the Manufacturing Services solely for the manufacture of the Products for Client.

(b) All Intellectual Property generated or derived by Patheon while performing the Manufacturing Services, to the extent it is specific to the development, manufacture, use, and sale of any of Client's Products that are the subject of the Manufacturing Services, will be the exclusive property of Client.

(c) All Patheon Intellectual Property will be the exclusive property of Patheon. Patheon hereby grants to Client a perpetual, irrevocable, non-exclusive, paid-up, royalty-free, transferable license to use the Patheon Intellectual Property used by Patheon to perform the Manufacturing Services to enable Client to manufacture the Product(s).

(d) Each party will be solely responsible for the costs of filing, prosecution, and maintenance of patents and patent applications on its own Inventions.

(e) Either party will give the other party written notice, as promptly as practicable, of all Inventions which can reasonably be deemed to constitute improvements or other modifications of the Products or processes or technology owned or otherwise controlled by the party.

(f) Each party agrees and acknowledges that it will not acquire by virtue of this Agreement any interest in or any trademarks or trade names of the other party but Client will have the right to identify Patheon as the manufacturer of the Products.

13.2 Intellectual Property.

Neither party has, nor will it acquire, any interest in any of the other party's Intellectual Property unless otherwise expressly agreed to in writing. Neither party will use any Intellectual Property of the other party, except as specifically authorized by the other party or as required for the performance of its obligations under this Agreement. Each party agrees to execute all applications, assignments or other instruments reasonably requested by the other party, in order for that party to establish its ownership of the Intellectual Property and to obtain whatever protection for the Intellectual Property, including patent and copyright rights, in any and all countries on the Intellectual Property as the requesting party will determine. Each party further agrees to cooperate fully with the other party in the process of securing and enforcing the other party's rights to the Intellectual Property, as applicable.

13.3 Insurance.

Each party will maintain commercial general liability insurance, including blanket contractual liability insurance covering the obligations of that party under this Agreement through the term of this Agreement and for a period of three years thereafter. This insurance will have policy limits of not less than (i) [*] for each occurrence for personal injury or property damage liability; and (ii) [*] in the aggregate per annum for product and completed operations liability. If requested each party will give the other a certificate of insurance evidencing the above and showing the name of the issuing company, the policy number, the effective date, the expiration date, and the limits of liability. The insurance certificate will further provide for a minimum of [*] days' written notice to the insured of a cancellation of, or material change in, the insurance. If a party is unable to maintain the insurance policies required under this Agreement through no fault of its own, then the party will forthwith notify the other party in writing and the parties will in good faith negotiate appropriate amendments to the insurance provision of this Agreement in order to provide adequate assurances.

13.4 Independent Contractors.

The parties are independent contractors and this Agreement and any Product Agreement will not be construed to create between Patheon and Client any other relationship such as, by way of example only, that of employer-employee, principal agent, joint-venturer, co-partners, or any similar relationship, the existence of which is expressly denied by the parties.

13.5 **No Waiver**.

Neither party's failure to require the other party to comply with any provision of this Agreement or any Product Agreement will be deemed a waiver of the provision or any other provision of this Agreement or any Product Agreement, with the exception of Sections 6.1 and 8.2 of this Agreement.

13.6 **Assignment**.

(a) Patheon may not assign this Agreement or any Product Agreement or any of its associated rights or obligations without the written consent of Client, this consent not to be unreasonably withheld. Patheon may subcontract any part of the Manufacturing Services under a Product Agreement to any of its Affiliates but Patheon will remain fully liable to Client for the Affiliate's performance.

(b) Subject to Section 8.2(d), Client may assign this Agreement or any Product Agreement or any of its associated rights or obligations without approval from Patheon. But Client will give Patheon prompt written notice of any assignment, any assignee will covenant in writing with Patheon to be bound by the terms of this Agreement or the Product Agreement.

(c) Despite the foregoing provisions of this Section 13.6, either party may assign this Agreement or any Product Agreement to any of its Affiliates or to a successor to or purchaser of all or substantially all of its business, but the assignee must execute an agreement with the non-assigning party whereby it agrees to be bound hereunder.

13.7 **Force Majeure**.

Neither party will be liable for the failure to perform its obligations under this Agreement or any Product Agreement if the failure is caused by an event beyond that party's reasonable control, including, but not limited to, strikes or other labor disturbances, lockouts, riots, quarantines, communicable disease outbreaks, wars, acts of terrorism, fires, floods, storms, interruption of or delay in transportation, lack of or inability to obtain fuel, power or components, or compliance with any order or regulation of any government entity acting within colour of right (a "**Force Majeure Event**"). A party claiming a right to excused performance under this Section 13.7 will immediately notify the other party in writing of the extent of its inability to perform, which notice will specify the event beyond its reasonable control that prevents the performance. Neither party will be entitled to rely on a Force Majeure Event to relieve it from an obligation to pay money (including any interest for delayed payment) which would otherwise be due and payable under this Agreement or any Product Agreement.

13.8 **Additional Product**.

Additional Products may be added to, or existing Products deleted from, any Product Agreement by amendments to the Product Agreement including Schedules A, B, C, and D as applicable.

13.9 **Notices**.

Unless otherwise agreed in a Product Agreement, any notice, approval, instruction or other written communication required or permitted hereunder will be sufficient if made or given to the other party by personal delivery, by telecopy, facsimile communication, or internationally-recognized overnight courier or by sending the same by first class mail, postage prepaid to the respective addresses, telecopy or facsimile numbers set forth below:

If to Client:

Jazz Pharmaceuticals Ireland Limited
Fourth Floor, Connaught House
One Burlington Road
Dublin 4, Ireland

Attention: Head of Supply Chain

Facsimile No.: [*]

With a copy to:

Jazz Pharmaceuticals
3180 Porter Drive
Palo Alto, CA 94304
Attention: Legal
Facsimile No.: [*]

If to Patheon:

Patheon Pharmaceuticals Inc.
2110 East Galbraith Road
Cincinnati, OH 45237-1625
Attention: [*]
Facsimile No.: [*]

With a copy to:

Patheon Inc.
4721 Emperor Boulevard
Research Triangle Park,
NC 27703
Attention: [*]
Telecopier No.: [*]

or to any other addresses, telecopy or facsimile numbers given to the other party in accordance with the terms of this Section 13.9. Notices or written communications made or given by personal delivery, telecopy, or facsimile, will be deemed to have been sufficiently made or given when sent (receipt acknowledged), or if mailed, five days after being deposited in the United States, Canada, or European Union mail, postage prepaid or upon receipt, whichever is sooner.

13.10 **Severability**.

If any provision of this Agreement or any Product Agreement is determined by a court of competent jurisdiction to be invalid, illegal, or unenforceable in any respect, that determination will not impair or affect the validity, legality, or enforceability of the remaining provisions, because each provision is separate, severable, and distinct.

13.11 Entire Agreement.

This Agreement, together with the applicable Product Agreements and Quality Agreements constitute the full, complete, final and integrated agreement between the parties relating to the subject matter hereof and supersedes all previous written or oral negotiations, commitments, agreements, transactions, or understandings concerning the subject matter hereof. Any modification, amendment, or supplement to this Agreement or any Product Agreement must be in writing and signed by authorized representatives of both parties. In case of conflict, the prevailing order of documents will be this Agreement, the Product Agreement, and the Quality Agreement but the Product Agreement will prevail where it specifically states the intent to prevail over this Agreement. If a topic or subject is addressed in two or more of the foregoing agreements, and it is possible to meet the obligations under both or all of these agreements without violating the terms of either or any agreement, then the terms of both or all of the agreements will apply and be met.

13.12 Other Terms.

No terms, provisions or conditions of any purchase order or other business form or written authorization used by Client or Patheon will have any effect on the rights, duties, or obligations of the parties under or otherwise modify this Agreement or any Product Agreement, regardless of any failure of Client or Patheon to object to the terms, provisions, or conditions unless the document specifically refers to this Agreement or the applicable Product Agreement and is signed by both parties.

13.13 No Third Party Benefit or Right.

For greater certainty, nothing in this Agreement or any Product Agreement will confer or be construed as conferring on any third party any benefit or the right to enforce any express or implied term of this Agreement or any Product Agreement.

13.14 Execution in Counterparts.

This Agreement and any Product Agreement may be executed in two or more counterparts, by original or facsimile or “pdf” signature, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

13.15 Use of Client Name.

Patheon will not make any use of Client’s name, trademarks or logo or any variations thereof, alone or with any other word or words, without the prior written consent of Client.

13.16 Taxes.

(a) Client will bear all taxes, duties, levies and similar charges (and any related interest and penalties) ("**Tax**" or "**Taxes**"), however designated, imposed as a result of the provision by the Patheon of Services under this Agreement, except:

(i) any Tax based on net income or gross income that is imposed on Patheon by its jurisdiction of formation or incorporation ("**Resident Jurisdiction**");

(ii) any Tax based on net income or gross income that is imposed on Patheon by jurisdictions other than its Resident Jurisdiction if this tax is based on a permanent establishment of Patheon; and

(iii) any Tax that is recoverable by Patheon in the ordinary course of business for purchases made by Patheon in the course of providing its Services, such as Value Added Tax (as more fully defined in subparagraph (d) below), Goods & Services Tax ("**GST**") and similar taxes.

(b) If Client is required to bear a tax, duty, levy or similar charge under this Agreement by any state, federal, provincial or foreign government, including, but not limited to, Value Added Tax, Client will pay the tax, duty, levy or similar charge and any additional amounts to the appropriate taxing authority as are necessary to ensure that the net amounts received by Patheon hereunder after all such payments or withholdings equal the amounts to which Patheon is otherwise entitled under this Agreement as if the tax, duty, levy or similar charge did not exist.

(c) Patheon will not collect an otherwise applicable tax if Client's purchase is exempt from Patheon's collection of the tax and a valid tax exemption certificate is furnished by Client to Patheon.

(d) If subparagraph 13.16(a)(iii) does not apply, any payment due under this Agreement for the provision of Services to Client by Patheon is exclusive of value added taxes, turnover taxes, sales taxes or similar taxes, including any related interest and penalties (hereinafter all referred to as "**VAT**"). If any VAT is payable on a Service supplied by Patheon to Client under this Agreement, this VAT will be added to the invoice amount and will be for the account of (and reimbursable to Patheon by) Client. If VAT on the supplies of Patheon is payable by Client under a reverse charge procedure (i.e., shifting of liability, accounting or payment requirement to recipient of supplies), Client will ensure that Patheon will not effectively be held liable for this VAT by the relevant taxing authorities or other parties. Where applicable, Patheon will use its reasonable commercial efforts to ensure that its invoices to Client are issued in such a way that these invoices meet the requirements for deduction of input VAT by Client, if Client is permitted by law to do so.

(e) Any Tax that Client pays, or is required to pay, but which Client believes should properly be paid by Patheon pursuant hereto may not be offset against sums due by Client to Patheon whether due pursuant to this Agreement or otherwise.

13.17 **Governing Law**.

This Agreement and any Product Agreement, unless otherwise agreed by the parties in the Product Agreement, will be construed and enforced in accordance with the laws of the State of New York and the laws of the United States of America applicable therein. The UN Convention on Contracts for the International Sale of Goods will not apply to this Agreement.

[Signature page to follow]

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Agreement as of the Effective Date.

PATHEON PHARMACEUTICALS INC.

By: /s/ Francis P. McCune

Name: Francis P. McCune

Title: Secretary

JAZZ PHARMACEUTICALS IRELAND LIMITED

By: /s/ Shawn Mindus

Name: Shawn Mindus

Title: VP, Head of Ireland Finance

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

APPENDIX 1

FORM OF PRODUCT AGREEMENT

(Includes Schedules A to D)

PRODUCT AGREEMENT

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated October 1, 2015 between **Patheon Pharmaceuticals Inc.**, and **Jazz Pharmaceuticals Ireland Limited** (the "**Master Agreement**"), and is entered into **[insert effective date]** (the "**Effective Date**"), between Patheon Pharmaceuticals Inc., **[or applicable Patheon Affiliate]**, a corporation existing under the laws of the State of Delaware **[or applicable founding jurisdiction for Patheon Affiliate]**, having a principal place of business at 2110 East Galbraith Road, Cincinnati, OH 45237-1625 **[or Patheon Affiliate address]** ("**Patheon**") and **[insert Client name, legal entity, founding jurisdiction and address]** ("**Client**").

The terms and conditions of the Master Agreement are incorporated herein except to the extent this Product Agreement expressly references the specific provision in the Master Agreement to be modified by this Product Agreement. All capitalized terms that are used but not defined in this Product Agreement will have the respective meanings given to them in the Master Agreement.

The Schedules to this Product Agreement are incorporated into and will be construed in accordance with the terms of this Product Agreement.

1. **Product List and Specifications** (See Schedule A attached hereto)
2. **Minimum Order Quantity, Annual Volume, and Price** (See Schedule B attached hereto)
3. **Annual Stability Testing and Validation Activities (if applicable)** (See Schedule C attached hereto)
4. **Active Materials, Active Materials Credit Value, and Maximum Credit Value** (See Schedule D attached hereto)
5. **Business Day** (if different from a Business Day at the Manufacturing Site under the definition in Section 1.3 of the Master Agreement)
6. **Manufacturing Site**: (insert address of Patheon Manufacturing Site where the Manufacturing Services will be performed)
7. **Territory**: (insert the description of the Territory here)
8. **Loss Tolerance Percentage** (per Section 2.2(b) of the Master Agreement)
9. **Extraordinary Increase in Component Cost materiality percentage** (if different from the [*] that is stated in Section 4.3 of the Master Agreement)
10. **Yearly Forecasted Volume:** (insert for sterile products if applicable under Section 4.2.1)

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

11. **Delivery Date Under Firm Order (**if different from the three month period set forth in Section 5.1(c) of the Master Agreement)

12. **Payment Terms**: (if different from Section 5.5 of the Master Agreement)

13. **Governing Law**: (if applicable under Section 13.17 of the Master Agreement)

14. **Inflation Index:** (if applicable under Section 4.2(a) of the Master Agreement for Products manufactured outside of the Unites States or Puerto Rico)

15. **Currency**: (if applicable under Section 1.4 of the Master Agreement)

16. **Initial Set Exchange Rate**: (if applicable under Section 4.2(d) of the Master Agreement)

17. **Initial Product Term:** (if applicable under Section 8.1 of the Master Agreement)

18. **Notices**: (if applicable under Section 13.9 of the Master Agreement)

19. **Other Modifications to the Master Agreement**: (if applicable under Section 1.2 of the Master Agreement)

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Product Agreement as of the Effective Date set forth above.

PATHEON PHARMACEUTICALS INC. [or applicable Patheon Affiliate]

By: _____

Name: _____

Title: _____

JAZZ PHARMACEUTICALS IRELAND LIMITED [or applicable Jazz Affiliate]

By: _____

Name: _____

Title: _____

SCHEDULE A

PRODUCT LIST AND SPECIFICATIONS

Product List

[insert product list]

Specifications

Prior to the start of commercial manufacturing of Product under this Agreement Client will give Patheon the originally executed copies of the Specifications as approved by the applicable Regulatory Authority. If the Specifications received are subsequently amended, then the parties will follow the process set forth in the Quality Agreement.

SCHEDULE B

MINIMUM ORDER QUANTITY, ANNUAL VOLUME, AND PRICE

[*]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

[*]

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SCHEDULE C

ANNUAL STABILITY TESTING [and VALIDATION ACTIVITIES (if applicable)]

Patheon and Client will agree in writing on any stability testing to be performed by Patheon on the Products. This agreement will specify the commercial and Product stability protocols applicable to the stability testing and the fees payable by Client for this testing.

[NTD: Schedule C should clearly indicate when and/or under what conditions Patheon's responsibility to perform stability testing will end]

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SCHEDULE D

ACTIVE MATERIALS

Active Materials	Supplier
Ÿ	Ÿ
Ÿ	Ÿ

ACTIVE MATERIALS CREDIT VALUE

The Active Materials Credit Value will be as follows:

PRODUCT	ACTIVE MATERIALS	ACTIVE MATERIALS CREDIT VALUE
		[*]

MAXIMUM CREDIT VALUE

Patheon's liability for Active Materials calculated in accordance with Section 2.2 of the Master Agreement **[for any Product]** in a Year will not exceed, in the aggregate, the maximum credit value set forth below:

PRODUCT	MAXIMUM CREDIT VALUE

[End of Product Agreement]

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EXHIBIT A

TECHNICAL DISPUTE RESOLUTION

Technical Disputes which cannot be resolved by negotiation as provided in Section 12.2 will be resolved in the following manner:

1. **Appointment of Expert**. Within [*] Business Days after a party requests under Section 12.2 that an expert be appointed to resolve a Technical Dispute, the parties will jointly appoint a mutually acceptable expert with experience and expertise in the subject matter of the dispute. If the parties are unable to so agree within the [*] Manufacturing Site Business Day period, or in the event of disclosure of a conflict by an expert under Paragraph 2 hereof which results in the parties not confirming the appointment of the expert, then an expert (willing to act in that capacity hereunder) will be appointed by an experienced arbitrator on the roster of the American Arbitration Association.

2. **Conflicts of Interest**. Any person appointed as an expert will be entitled to act and continue to act as an expert even if at the time of his appointment or at any time before he gives his determination, he has or may have some interest or duty which conflicts or may conflict with his appointment if before accepting the appointment (or as soon as practicable after he becomes aware of the conflict or potential conflict) he fully discloses the interest or duty and the parties will, after the disclosure, have confirmed his appointment.

3. **Not Arbitrator**. No expert will be deemed to be an arbitrator and the provisions of the American Arbitration Act or of any other applicable statute (foreign or domestic) and the law relating to arbitration will not apply to the expert or the expert's determination or the procedure by which the expert reaches his determination under this Exhibit A.

4. **Procedure**. Where an expert is appointed:

(a) Timing. The expert will be so appointed on condition that (i) he promptly fixes a reasonable time and place for receiving representations, submissions or information from the parties and that he issues the authorizations to the parties and any relevant third party for the proper conduct of his determination and any hearing and (ii) he renders his decision (with full reasons) within [*] Business Days (or another other date as the parties and the expert may agree) after receipt of all information requested by him under Paragraph 4(b) hereof.

(b) Disclosure of Evidence. The parties undertake one to the other to give to any expert all the evidence and information within their respective possession or control as the expert may reasonably consider necessary for determining the matter before him which they will disclose promptly and in any event within [*] Business Days of a written request from the relevant expert to do so.

(c) Advisors. Each party may appoint any counsel, consultants and advisors as it feels appropriate to assist the expert in his determination and so as to present their respective cases so that at all times the parties will co-operate and seek to narrow and limit the issues to be determined.

(d) Appointment of New Expert. If within the time specified in Paragraph 4(a) above the expert will not have rendered a decision in accordance with his appointment, a new expert may (at the request of either party) be appointed and the appointment of the

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existing expert will thereupon cease for the purposes of determining the matter at issue between the parties save this if the existing expert renders his decision with full reasons prior to the appointment of the new expert, then this decision will have effect and the proposed appointment of the new expert will be withdrawn.

(e) Final and Binding. The determination of the expert will, except for fraud or manifest error, be final and binding upon the parties.

(f) Costs. Each party will bear its own costs for any matter referred to an expert hereunder and, in the absence of express provision in the Agreement to the contrary, the costs and expenses of the expert will be shared equally by the parties.

For greater certainty, the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including this Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

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EXHIBIT B

[Reserved]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

EXHIBIT C

QUARTERLY ACTIVE MATERIALS INVENTORY REPORT

TO: JAZZ PHARMACEUTICALS IRELAND LIMITED

FROM: PATHEON PHARMACEUTICALS INC. [or applicable Patheon entity]

RE: Active Materials quarterly inventory report under Section 2.2(a) of the Master Manufacturing Services Agreement dated October 1, 2015 (the "**Agreement**")

Reporting quarter: _____

Active Materials on hand at beginning of quarter: _____ kg (A)

Active Materials on hand at end of quarter: _____ kg (B)

Quantity Received during quarter: _____ kg (C)

[*]

Quantity Converted during quarter: _____ kg
(total Active Materials in Products produced and not rejected, recalled or returned)

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

PATHEON PHARMACEUTICALS INC.
[or applicable Patheon Affiliate]

DATE: _____

Per: _____
Name:
Title:

---

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

EXHIBIT D

REPORT OF ANNUAL ACTIVE MATERIALS INVENTORY RECONCILIATION

AND CALCULATION OF ACTUAL ANNUAL YIELD

TO: JAZZ PHARMACEUTICALS IRELAND LIMITED

FROM: PATHEON PHARMACEUTICALS INC. [or applicable Patheon entity]

RE: Active Materials annual inventory reconciliation report and calculation of Actual Annual Yield under Section 2.2(a) of the Master Manufacturing Services Agreement dated October 1, 2015 (the "Agreement")

Reporting Year ending:	_____		
Active Materials on hand at beginning of Year:	_____	kg	(A)
Active Materials on hand at end of Year:	_____	kg	(B)
Quantity Received during Year:	_____	kg	(C)
[*]			
Quantity Converted during Year: (total Active Materials in Products produced and not rejected, recalled or returned)	_____	kg	(E)
Active Materials Credit Value:	$ _____	/kg	(F)
Target Yield:	_____	%	(G)
Actual Annual Yield: ((E / D) * 100)	_____	%	(H)

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

[*]

Based on the foregoing reimbursement calculation Patheon will reimburse Client the amount of $_____.

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

DATE: _____

PATHEON PHARMACEUTICALS INC.
[or applicable Patheon Affiliate]

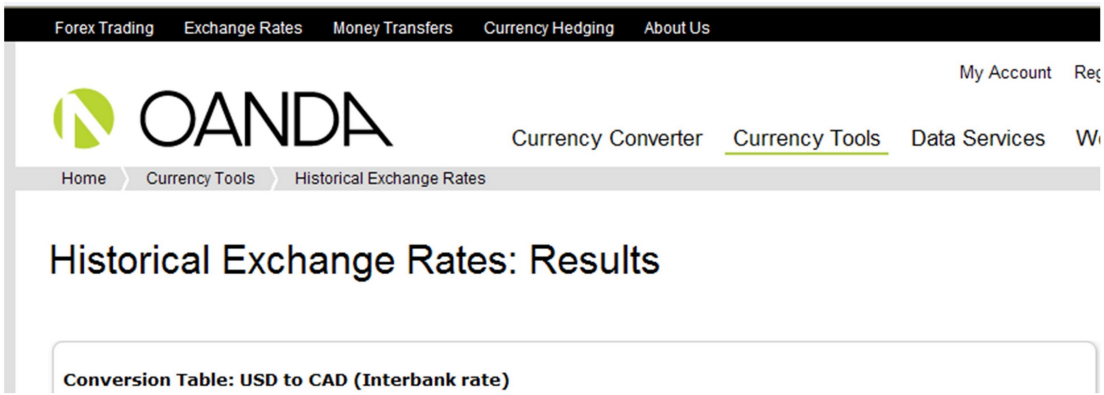
Per: _____
Name:
Title:

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

EXHIBIT E

EXAMPLE OF PRICE ADJUSTMENT DUE TO CURRENCY FLUCTUATION

Section 4.2(d)



Time period: 10/01/11 to 09/30/12.

Average (365 days):	0.998	-- "Set Exchange Rate"

SAMPLE EXCHANGE CALCULATION

Initial Exchange Rate:	1.000	CAD/USD
Set Exchange Rate:	0.998	CAD/USD

Initial Price:	3.59	
Revised Price (FX):	3.70	(Material price and PPI adjustments)

Calculation:

[Revised Price (After FX)] = [Revised Price (Before FX)] X [Initial Exchange Rate] / [Set Exchange Rate]

= 3.70 X [1.000 / 0.998]

= 3.71

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 10.22B

JAZZ PHARMACEUTICALS PLC

CASH BONUS PLAN

(U.S. AFFILIATES)

1. Purpose of the Plan.

The Jazz Pharmaceuticals plc Cash Bonus Plan (U.S. Affiliates) (the "***Plan***") is designed to provide meaningful incentive, on an annual basis, for employees of U.S. Affiliates of Jazz Pharmaceuticals plc (the "***Company***").

2. Eligibility.

In order to be eligible to participate in the Plan for a Plan Year, an employee (a) must be an active regular employee of a U.S. Affiliate of the Company whose Employment Start Date is October 31 of the Plan Year or earlier and (b) must not be eligible to participate in a commercial (including sales) or other similar incentive compensation plan. Employees who are not expressly classified by the U.S. Affiliate as "regular" employees, such as temporary or contract employees and interns, are not eligible to be Participants.

In order to be eligible to receive a Bonus for a Plan Year, a Participant must (i) continue to be an active regular employee of a U.S. Affiliate of the Company in good standing from the date his/her participation in the Plan commences for the Plan Year until the date Bonuses are paid for the Plan Year, except as provided in Section 6, and (ii) act in accordance with the Company's Code of Conduct, compliance policies and procedures, and those of the Participant's employer, and applicable laws and regulations during the Plan Year.

3. Target Bonus Ranges.

A Participant's Target Bonus Range generally will be based on the Participant's position and/or responsibility level. The Target Bonus Range for Participants and the amount of Bonus actually paid to a Participant in a Plan Year under the Plan may vary from year to year and between positions, and among positions at the same level. However, as a general guideline, the Target Bonus Ranges which will typically be assigned to various categories of employees (and varying depending on responsibility levels within each category) are as follows:

Position	**Target Bonus Range (Percent of Base Salary)**
Chairman of the Board, Chief Executive Officer, President	100%
Executive Vice President	55%

Senior Vice President who is an Executive Committee Member or is a Section 16 Officer	45%
Senior Vice President who is not an Executive Committee Member or a Section 16 Officer	40%
Vice President	25-35%
Senior Director/Executive Director	20-30%
Associate Director/Director	15-25%
Managers (all levels)	10-20%
Other	5-15%

If a Participant moves to a position and/or responsibility level with a higher Target Bonus Range during a Plan Year, the Participant's Target Bonus Range will be reset at such higher level for the entire Plan Year. If a Participant moves to a position and/or responsibility level with a lower Target Bonus Range during a Plan Year, the Participant's Target Bonus Range will be reset at the lower level for the entire Plan Year.

4. Bonus Pool and Bonuses.

Following the end of a Plan Year, the Board or the Compensation Committee will determine, in its sole discretion, the Bonus Pool for the Plan Year to be allocated for the payment of Bonuses to Participants. The Bonus Pool will be calculated by multiplying

(a) the sum of the following amounts for each Participant:

(i) the Base Salary for such Participant, multiplied by

(ii) a percentage within such Participant's applicable Target Bonus Range (as determined by the Company on an individual or category level within the ranges set forth in the table above), provided that in the case of any Participant who is an executive officer of Jazz Pharmaceuticals plc, such Participant's Target Bonus Range will be determined by the Board or the Compensation Committee;

with

(b) the percentage set by the Board or the Compensation Committee based upon its determination of the Company's success in achieving the objectives established by the Board or the Compensation Committee for funding the Bonus Pool for the Plan Year (the "***Bonus Pool Objectives***").

The Bonus Pool Objectives are related to the achievement of the overall corporate objectives established for the applicable Plan Year by the Board or the Compensation Committee (the "***Corporate Objectives***").

5. Bonus.

Except as provided in Section 6, a Participant's Bonus for a Plan Year will be based upon the following criteria: (a) the Company's success in achieving the Corporate Objectives established for the Plan Year, (b) the Participant's success in achieving his/her individual objectives established for the Plan Year (if applicable) and the Participant's contribution to the Company's success in achieving the Corporate Objectives, in each case while demonstrating Company values, and (c) the Participant's compliance with Company policies and those of Participant's employer. Except as provided in Section 6, the amount of Bonus actually paid to each Participant will be an amount equal to such Participant's Base Salary multiplied by a percentage within the applicable Target Bonus Range (as may be adjusted up or down for each Participant by the Board, the Compensation Committee or the Company's management, as appropriate, based on the criteria set forth above). Each Participant's Bonus for a Plan Year will be approved by the Chief Executive Officer or his or her delegate, except that in the case of any Participant who is an executive officer of Jazz Pharmaceuticals plc, such Participant's Bonus will be approved by the Board or the Compensation Committee.

The total of all Bonuses paid under this Plan in any Plan Year may not exceed the Bonus Pool for such Plan Year unless such excess amount is specifically approved by the Board or the Compensation Committee. Except as provided in Section 6, no amounts will be payable to any Participant hereunder until the Bonus Pool and such Participant's Bonus have been determined as described above. Except as provided in Section 6, no Participant is entitled to any particular bonus, or any bonus, unless approved as described above.

6. Termination of Employment; Death; Retirement; Permanent Disability.

No Bonus will be paid to any Participant whose employment with a U.S. Affiliate of the Company terminates prior to the date Bonuses for a Plan Year are scheduled to be paid pursuant to Section 7, unless (a) such termination is due to the Participant's death, retirement or Permanent Disability, (b) the Board, the Compensation Committee, or the Company's management in appropriate circumstances in management's discretion determines that the Participant will be eligible to receive a Bonus, or (c) such condition is prohibited by regulations, laws, employment agreements or employment contracts applicable to a particular Participant.

In the case of a Participant whose employment with a U.S. Affiliate of the Company terminates (including due to death, retirement or Permanent Disability) prior to the date Bonuses for a Plan Year are scheduled to be paid and who becomes entitled to receive a Bonus pursuant to the foregoing paragraph, the amount of such Participant's Bonus for the Plan Year will be determined by the Board, the Compensation Committee, or the Company's management and may be prorated or otherwise determined based on the number of months employed during the Plan Year, performance or any other factors as decided by the Board, the Compensation Committee or the Company's management, as appropriate.

Any Participant whose employment with a U.S. Affiliate of the Company terminates (including due to death, retirement or Permanent Disability) prior to the date Bonuses for a Plan Year are scheduled to be paid and who becomes entitled to receive a Bonus pursuant to this Section 6 will be paid such Bonus at the time determined by the Company's management, which will in no event be later than the time at which other Participants' Bonuses for the Plan Year are scheduled to be paid pursuant to Section 7.

7. Payment of Bonuses.

Bonuses for a Plan Year will be paid in cash to a Participant (or his/her beneficiary, in the event of death) by March 15th of the following year, except (i) as is otherwise determined in the sole discretion of the Board, the Compensation Committee or the Company's management, as appropriate, or (ii) as may be necessary or advisable to comply with regulations, laws, employment agreements or employment contracts applicable to a particular Participant; *provided*, *however*, that in all cases, the payment date of any Bonus for any Participant who is subject to Section 409A of the Internal Revenue Code of 1986, as amended, or any state law of similar effect ("***Section 409A***") will be designed to either comply with Section 409A or satisfy an exemption from application of Section 409A, and the Plan will be administered and interpreted to the greatest extent possible in compliance with Section 409A or in accordance with such exemption, as applicable. Benefits under this Plan are not transferable, and the Plan is unfunded.

8. Withholding of Taxes.

Bonuses will be subject to income and employment tax withholding as required by applicable law.

9. Plan Amendments.

This Plan may be revised, modified, or terminated at any time in the sole discretion of the Board or the Compensation Committee. Without limiting the foregoing, the Plan may be revised, modified, or terminated with respect to a Participant or specific group of Participants as may be necessary or advisable to comply with the laws and regulations of the jurisdiction where such Participant or specific group of Participants are employed or where such Participant or specific group of Participants are tax residents.

10. No Employment Rights.

Nothing contained in this Plan is intended to confer any right upon any employee to continued employment with the Company or any U.S. Affiliate or other affiliate thereof.

11. Plan Administration.

This Plan will be administered by the Board or the Compensation Committee. The Board and the Compensation Committee shall have the sole discretion and authority to administer and interpret the Plan, and the decisions of the Board and the Compensation Committee shall in every case be final and binding on all persons having an interest in the Plan. Notwithstanding the foregoing, certain aspects of the Plan may be administered by the Chief Executive Officer or the Company's

management, as specifically provided in the Plan, and in such event, the Chief Executive Officer or the Company's management shall have the sole discretion and authority to administer and interpret such aspects of the Plan, and the decisions of the Chief Executive Officer or the Company's management shall in such cases be final and binding.

12. Definitions.

"***Base Salary***" for a Participant means the total amount of base salary or base pay actually paid to the Participant during the period of his/her participation in the Plan for the Plan Year, rather than the Participant's base salary level or base pay level at any particular point during the Plan Year (*e.g.*, the Base Salary for a Participant whose base salary or base pay is adjusted during the Plan Year, for a Participant who is hired during the Plan Year, or for a Participant whose employment terminates during the Plan Year will be the total amount of base salary or base pay actually paid to the Participant during the period of his/her participation in the Plan for the Plan Year). Base Salary does not include any expense reimbursements, relocation payments, incentive compensation or bonuses, amounts received as a result of equity awards, overtime or shift differential payments or similar one-time or unusual payments. Any salary or pay earned for periods during which a Participant is on disciplinary action are excluded from Base Salary.

"***Board***" means the Board of Directors of Jazz Pharmaceuticals plc.

"***Bonus***" means a Participant's actual bonus for a Plan Year as determined in accordance with Section 5 or Section 6, if applicable.

"***Bonus Pool***" for a Plan Year means the aggregate dollar amount set by the Board or the Compensation Committee for the payment of Bonuses for such Plan Year to Participants as set forth in Section 4.

"***Chief Executive Officer***" means the Chief Executive Officer of Jazz Pharmaceuticals plc.

"***Compensation Committee***" means the Compensation Committee of the Board.

"***Employment Start Date***" means the first business day on which a Participant is an active regular employee of a U.S. Affiliate of the Company, on the U.S. Affiliate's payroll, as applicable.

"***Executive Committee Member***" means an employee of the Company who serves as a member of the Company's executive committee, as determined by the Chief Executive Officer from time to time.

"***Participant***" means an active regular employee of a U.S. Affiliate of the Company who meets all of the eligibility requirements set forth in Section 2.

"***Permanent Disability***" means that a Participant has become permanently disabled under any policy or program of disability income insurance then in force covering such Participant.

"***Plan***" means this Jazz Pharmaceuticals plc Cash Bonus Plan (U.S. Affiliates).

"***Plan Year***" means the calendar year.

"***Section 16 Officer***" means an individual who has been designated by the Board as an "officer" of Jazz Pharmaceuticals plc for the purposes of Section 16 of the Securities Exchange Act of 1934, as amended, and Rule 16a-1(f) thereunder.

"***Target Bonus Range***" means, for a Participant for a Plan Year, the percentage or range of percentages of Base Salary, based on such Participant's position and/or responsibility level in a Plan Year, that represents the amount of Bonus that such Participant may receive for such Plan Year, as may be adjusted with respect to such Participant for such Plan Year in the discretion of the Board, the Compensation Committee or the Chief Executive Officer or his or her delegate, as applicable.

"***U.S. Affiliate***" means any "parent" or "subsidiary" of the Company, as such terms are defined in Rule 405 of the Securities Act of 1933, as amended, that is organized under the laws of the United States.

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As approved by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on 13 February 2013, as amended on 4 November 2015.

Exhibit 10.22D

JAZZ PHARMACEUTICALS

CASH BONUS PLAN

(IRELAND AND OTHER SPECIFIED AFFILIATES)

(Calendar Year 2016)

1. Purpose of the Plan.

The Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2016) (the "***Plan***") is designed to provide meaningful incentive, on an annual basis, for employees of Jazz Pharmaceuticals plc (the "***Company***") and employees of the Company's Ireland and Other Specified Affiliates for the Plan Year beginning 1 January 2016 and ending 31 December 2016.

2. Eligibility.

In order to be eligible to participate in the Plan for a Plan Year, an employee (a) must be an employee of the Company or an Ireland and Other Specified Affiliate (each, including Ireland, a "***Specified Affiliate***") whose Employment Start Date is 31 October of the Plan Year or earlier, and (b) must not be eligible to participate in a commercial (including sales) or other similar incentive compensation plan. Additionally, with respect to Gentium S.p.A. and Jazz Pharmaceuticals Italy S.p.A., only employees who are classified as "dirigenti" under Italian employment laws are eligible to participate in the Plan. Employees who are interns are not eligible to be Participants, to the extent permissible under applicable local law.

In order to be eligible to receive a Bonus for a Plan Year, a Participant must (i) continue to be an employee of the Company or a Specified Affiliate in good standing, as determined at the discretion of the employer, from the date his/her participation in the Plan commences for the Plan Year until the Bonus Payment Date (as defined in Section 7) for the Plan Year, except as provided in Section 6, (ii) act in accordance with the Company's Code of Conduct, compliance policies and procedures, and those of the Participant's employer, and applicable laws and regulations during the Plan Year, and (iii) not be serving a notice period as of the Bonus Payment Date for the Plan Year.

The Plan will automatically expire at the end of the indicated Plan Year, and no new plan will be implemented unless the Company announces otherwise.

3. Target Bonus Ranges.

The Target Bonus Range for Participants and the amount of Bonus actually paid to a Participant in a Plan Year under the Plan may vary from year to year and between positions, and among positions at the same level. No Participant has any contractual or otherwise acquired rights to a Target Bonus Range pursuant to any previous target bonus range (whether set forth in a written plan or otherwise). The Board or the Compensation Committee retains the sole discretion to determine the Target Bonus Ranges that apply to Participants, and such determination may include (but is not required) consideration of a Participant's position and/or responsibility level. Participants in Italy who are classified as "dirigenti" under Italian employment laws will be

provided written notice specifying such Participant's Target Bonus Range and the below table does not apply to such Participants. For other Participants, the following table provides a general guideline as to the Target Bonus Ranges which may typically be assigned to various categories of employees (and varying depending on responsibility levels within each category):

Position	Target Bonus Range (Percent of Base Salary)
Chairman of the Board, Chief Executive Officer, President	100%
Executive Vice President	55%
Senior Vice President who is an Executive Committee Member or is a Section 16 Officer	45%
Senior Vice President who is not an Executive Committee Member or a Section 16 Officer	40%
Vice President	25-35%
Senior Director/Executive Director	20-30%
Associate Director/Director	15-25%
Managers (all levels)	10-20%
Other	5-15%

As additional general guidelines, if a Participant moves to a position and/or responsibility level with a higher Target Bonus Range during a Plan Year, the Participant's Target Bonus Range will be reset at such higher level for the entire Plan Year; and if a Participant moves to a position and/or responsibility level with a lower Target Bonus Range during a Plan Year, the Participant's Target Bonus Range will be reset at the lower level for the entire Plan Year, to the extent permissible under applicable local law.

4. Bonus Pool and Bonuses.

Following the end of a Plan Year, the Board or the Compensation Committee will determine, in its sole discretion, the Bonus Pool for the Plan Year to be allocated for the payment of Bonuses to Participants. The Bonus Pool will be calculated by multiplying

(a) the sum of the following amounts for each Participant:

(i) the Base Salary for such Participant, multiplied by

(ii) a percentage within such Participant's applicable Target Bonus Range (as determined by the Company on an individual or category level within the ranges set forth in the table above), provided that in the case of any Participant who is an executive officer of Jazz Pharmaceuticals

plc, such Participant's Target Bonus Range will be determined by the Board or the Compensation Committee;

with

(b) the percentage set by the Board or the Compensation Committee based upon its determination of the Company's success in achieving the objectives established by the Board or the Compensation Committee for funding the Bonus Pool for the Plan Year (the "Bonus Pool Objectives").

The Bonus Pool Objectives are related to the achievement of the overall corporate objectives established for the applicable Plan Year by the Board or the Compensation Committee (the "Corporate Objectives").

At the discretion of the Board or the Compensation Committee, the Bonus Pool will be reduced by the amount of bonuses that are required to be paid to any Participants under applicable collective bargaining agreements, labor union arrangements, or the like, if any.

5. Bonus.

Except as provided in Section 6, a Participant's Bonus (on a gross basis) for a Plan Year will be based upon the following criteria: (a) the Company's success in achieving the Corporate Objectives established for the Plan Year, (b) the Participant's success in achieving his/her individual objectives established for the Plan Year (if applicable) and the Participant's contribution to the Company's success in achieving the Corporate Objectives, in each case while demonstrating Company values, and (c) the Participant's compliance with Company policies and those of Participant's employer as evaluated at the discretion of the employer. Applying these criteria, a participant may (or may not) be entitled to any Bonus. In the event that a Participant is to receive a Bonus, except as provided in Section 6, the amount of Bonus actually paid to each Participant will be an amount equal to such Participant's Base Salary multiplied by a percentage within the applicable Target Bonus Range (as may be adjusted up or down for each Participant by the Board, the Compensation Committee or the Company's management, as appropriate, based on the criteria set forth above, and will be reduced by the amount of any bonuses that are required to be paid to the Participant under applicable collective bargaining agreements, labor union arrangements, or the like). Each Participant's Bonus for a Plan Year will be approved by the Chief Executive Officer or his or her delegate, except that in the case of any Participant who is an executive officer of Jazz Pharmaceuticals plc, such Participant's Bonus will be approved by the Board or the Compensation Committee.

The total of all Bonuses paid under this Plan in any Plan Year may not exceed the Bonus Pool for such Plan Year unless such excess amount is specifically approved by the Board or the Compensation Committee. Except as provided in Section 6, no amounts will be payable to any Participant hereunder until the Bonus Pool and such Participant's Bonus have been determined as described above. Except as provided in Section 6, no Participant is entitled to any particular bonus, or any bonus, unless approved as described above.

6. Termination of Employment; Death; Retirement; Permanent Disability.

No Bonus, prorated or otherwise, will be paid to any Participant whose employment with the Company or a Specified Affiliate terminates prior to the date Bonuses for a Plan Year are scheduled to be paid pursuant to Section 7, unless (a) such termination is due to the Participant's death, retirement or Permanent Disability, (b) the Board, the Compensation Committee, or the Company's management in appropriate circumstances in management's discretion determines that the Participant will be eligible to receive a Bonus, or (c) such condition is prohibited by regulations, laws, employment agreements or employment contracts applicable to a particular Participant.

In the case of a Participant whose employment with the Company or a Specified Affiliate terminates (including due to death, retirement or Permanent Disability) prior to the Bonus Payment Date and who becomes entitled to receive a Bonus pursuant to the foregoing paragraph, the amount of such Participant's Bonus for the Plan Year will be determined by the Board, the Compensation Committee, or the Company's management, and may be prorated or otherwise determined based on the number of months employed during the Plan Year, performance or any other factors as decided by the Board, the Compensation Committee or the Company's management, as appropriate, to the extent permissible under applicable local law.

Any Participant whose employment with the Company or a Specified Affiliate terminates (including due to death, retirement or Permanent Disability) prior to the Bonus Payment Date and who becomes entitled to receive a Bonus pursuant to this Section 6 will be paid such Bonus at the time determined by the Company's management, which will in no event be later than the Bonus Payment Date.

Unless otherwise required under applicable local law, payments under this Plan shall not be included in calculation of any payment in lieu of notice, severance pay, termination, indemnity or similar pay.

7. Payment of Bonuses.

Bonuses for a Plan Year will be paid in cash to a Participant (or his/her beneficiary, in the event of death) by March 15th of the following year (the "Bonus Payment Date"), except (i) as is otherwise determined in the sole discretion of the Board, the Compensation Committee or the Company's management, as appropriate, or (ii) as may be necessary or advisable to comply with regulations, laws, employment agreements or employment contracts applicable to a particular Participant. Benefits under this Plan are not transferable, to the extent permissible under applicable local law.

8. Withholding of Taxes and Mandatory Contributions.

Bonuses will be subject to applicable tax and social security withholding as required by applicable local laws.

9. Plan Amendments.

This Plan may be revised, modified, or terminated at any time in the sole discretion of the Board or the Compensation Committee. Without limiting the foregoing, the Plan may be revised,

modified, or terminated with respect to a Participant or specific group of Participants as may be necessary or advisable to comply with the laws and regulations of the jurisdiction where such Participant or specific group of Participants are employed or where such Participant or specific group of Participants are tax residents.

10. No Employment Rights; No Acquired Rights.

Nothing contained in this Plan is intended to confer any right upon any employee to continued employment with the Company or any Specified Affiliate or other affiliate thereof.

Any payment of Bonuses would be on a voluntary and discretionary basis, without creating any contractual or other acquired right to participate with respect to a similar (or any other) bonus plan or to receive any similar awards (or benefits in lieu) in the future.

11. Plan Administration.

This Plan will be administered by the Board or the Compensation Committee. The Board and the Compensation Committee shall have the sole discretion and authority to administer and interpret the Plan, and the decisions of the Board and the Compensation Committee shall in every case be final and binding on all persons having an interest in the Plan. Notwithstanding the foregoing, certain aspects of the Plan may be administered by the Chief Executive Officer or the Company's management, as specifically provided in the Plan, and in such event, the Chief Executive Officer or the Company's management shall have the sole discretion and authority to administer and interpret such aspects of the Plan, and the decisions of the Chief Executive Officer or the Company's management shall in such cases be final and binding.

12. Definitions.

"***Base Salary***" for a Participant means the total amount of base salary or base pay actually paid to the Participant during the period of his/her participation in the Plan for the Plan Year, rather than the Participant's base salary level or base pay level at any particular point during the Plan Year (*e.g.*, the Base Salary for a Participant whose base salary or base pay is adjusted during the Plan Year, for a Participant who is hired during the Plan Year, or for a Participant whose employment terminates during the Plan Year will be the total amount of base salary or base pay actually paid to the Participant during the period of his/her participation in the Plan for the Plan Year). Base Salary does not include any benefits, expense reimbursements, relocation payments, incentive compensation or bonuses, amounts received as a result of equity awards, overtime or shift differential payments or similar one-time or unusual payments. Any salary or pay earned for periods during which a Participant is on disciplinary action or serving a notice period are excluded from Base Salary to the extent permissible under applicable local law.

"***Board***" means the Board of Directors of Jazz Pharmaceuticals plc.

"***Bonus***" means a Participant's actual bonus for a Plan Year as determined in accordance with Section 5 or Section 6, if applicable.

"***Bonus Pool***" for a Plan Year means the aggregate dollar amount set by the Board or the Compensation Committee for the payment of Bonuses for such Plan Year to Participants as set forth in Section 4.

"***Chief Executive Officer***" means the Chief Executive Officer of Jazz Pharmaceuticals plc.

"***Compensation Committee***" means the Compensation Committee of the Board.

"***Employment Start Date***" means the first business day on which a Participant is an employee of the Company or a Specified Affiliate, on the Company's or such Affiliate's payroll, as applicable.

"***Executive Committee Member***" means an employee of the Company who serves as a member of the Company's executive committee, as determined by the Chief Executive Officer from time to time.

"***Ireland and Other Specified Affiliate***" means any "parent" or "subsidiary" of the Company that is organized under the laws of Ireland, under the laws of any other country within Europe, or under the laws of Canada. In addition, the Board or the Compensation Committee can designate any other "parent" or "subsidiary" of the Company to be included within this definition.

"***Participant***" means an employee of the Company or an Ireland and Other Specified Affiliate who meets all of the eligibility requirements set forth in Section 2.

"***Permanent Disability***" means that a Participant has become permanently disabled under any policy or program of disability income insurance then in force covering such Participant.

"***Plan***" means this Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2016).

"***Plan Year***" means the calendar year beginning 1 January 2016 and ending 31 December 2016, after which the Plan should expire.

"***Section 16 Officer***" means an individual who has been designated by the Board as an "officer" of Jazz Pharmaceuticals plc for the purposes of Section 16 of the Securities Exchange Act of 1934, as amended, and Rule 16a-1(f) thereunder.

"***Target Bonus Range***" means, for a Participant for a Plan Year, the percentage or range of percentages of Base Salary that represents the amount of Bonus that such Participant may receive for such Plan Year, as may be adjusted with respect to such Participant for such Plan Year in the discretion of the Board, the Compensation Committee or the Chief Executive Officer or his or her delegate, as applicable.

*****

As approved by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on 4 November 2015.

AGREEMENT AND ACCEPTANCE

I acknowledge that this Cash Bonus Plan for the Plan Year beginning 1 January 2016 and ending 31 December 2016 supersedes and replaces all prior agreements, representations or understandings, whether written, oral or implied, between the Company, my employer and me, with respect to this subject matter. Further, I acknowledge that I have read, understand, and agree to comply with all of the terms and conditions of this Cash Bonus Plan.

Employee Signature:

Date:

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
EXECUTIVE CHANGE IN CONTROL AND SEVERANCE BENEFIT PLAN

SECTION 1. INTRODUCTION.

The Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (the "***Plan***") was originally established effective as of May 1, 2007 (the "***Effective Date***") and was amended and restated effective as of February 17, 2009, October 24, 2011, February 14, 2012, April 24, 2012, July 31, 2013 and February 10, 2016.

The purpose of the Plan is to provide for the payment of severance benefits to certain eligible executive employees of U.S. Affiliates of Jazz Pharmaceuticals plc in the event that such employees are subject to a Covered Termination. Except as provided in Section 6(a)(iv), this Plan shall supersede any individual agreement between the Company or any Affiliate and a Participant, and any other plan, policy or practice, whether written or unwritten, maintained by the Company or any Affiliate with respect to a Participant (other than any such plan, policy or practice that provides for benefits upon the Participant's death or Disability), in each case to the extent that such agreement, plan, policy or practice provides for benefits upon a Covered Termination. This Plan document also constitutes the Summary Plan Description for the Plan.

SECTION 1. DEFINITIONS.

For purposes of the Plan, the following terms are defined as follows:

(a) "***Affiliate***" means, at the time of determination, any "parent" or "subsidiary" of the Company as such terms are defined in Rule 405 of the Securities Act of 1933, as amended, and any "holding company" or "subsidiary" of the Company as such terms are defined in Section 8 and 7 respectively of the Companies Act. The Plan Administrator shall have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(b) "***Base Salary***" means a Participant's annual base pay (excluding incentive pay, premium pay, commissions, overtime, bonuses and other forms of variable compensation).

(c) "***Board***" means the Board of Directors of the Company.

(d) "***Bonus Multiplier***" means the quotient obtained by dividing the number of full months that a Participant is employed by the Company or an Affiliate during the calendar year in which the Participant's Covered Termination occurs by twelve (12).

(e) "***Bonus Percentage***" means the greater of:

(i) the highest amount of any annual bonus paid to a Participant by the Company or an Affiliate for (x) either of the last two (2) calendar years prior to the date of the Participant's Covered Termination or (y) either of the last two (2) calendar years prior to the

Change in Control, in each case expressed as a percentage of the Participant's Base Salary for the applicable year; or

(ii) the higher of the Participant's target bonus for (x) the calendar year in which the Participant's Covered Termination occurs or (y) the calendar year in which the Change in Control occurs, in each case expressed as a percentage of the Participant's Base Salary for such year. For purposes of the foregoing and this Plan, in the case of any Participant with a title of Vice President on the date of the Participant's Covered Termination, the Participant's target bonus for the calendar year in which the Participant's Covered Termination occurs or for the calendar year in which the Change in Control occurs shall mean, in each case, thirty percent (30%) of the Participant's Base Salary for such year, notwithstanding any contrary provision set forth in any bonus or other plan maintained by the Company or an Affiliate.

(f) ***"Cause"*** means the occurrence of any one or more of the following: (i) the Participant's unauthorized use or disclosure of the confidential information or trade secrets of the Company or an Affiliate which use or disclosure causes material harm to the Company or an Affiliate; (ii) the Participant's material breach of any written agreement between the Participant and the Company or an Affiliate, or the Participant's material violation of any statutory duty owed to the Company or an Affiliate, in either case which remains uncured for ten (10) business days after receiving written notification of the breach or violation from the Board or its designee; (iii) the Participant's material failure to comply with the written policies or rules of the Company or an Affiliate which remains uncured for ten (10) business days after receiving written notification of the failure from the Board or its designee; (iv) the Participant's conviction of, or plea of "guilty" or "no contest" to, any crime involving fraud, dishonesty or moral turpitude under the laws of any United States federal, state or local authority or any foreign governmental authority; (v) the Participant's gross misconduct, including but not limited to attempted or actual commission of, participation or cooperation in, fraud or act of dishonesty against the Company or an Affiliate; (vi) the Participant's continuing failure to perform assigned duties after receiving written notification of the failure from the Board or its designee; or (vii) the Participant's failure to reasonably cooperate in good faith with a governmental or internal investigation of the Company or any of its Affiliates, directors, officers or employees, if the Board or its designee has requested the Participant's cooperation.

(g) "***Change in Control***" means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than thirty percent (30%) of the combined voting power of the Company's then outstanding securities. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur on account of the acquisition of securities of the Company directly from the Company;

(ii) there is consummated a compromise or arrangement sanctioned by the Irish courts under the Companies Act, a scheme, contract or offer which has become binding on all shareholders of the Company pursuant to Section 457 of the Companies Act or a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC))

Regulations 2006 (as may be amended, updated or replaced from time to time), an offer or reverse takeover transaction which has been completed pursuant to the Irish Takeover Panel Act, 1997, Takeover Rules, 2013, or a reorganization, merger, statutory share exchange, consolidation or similar transaction involving (directly or indirectly) the Company (each, a "***Business Combination***") and (A) immediately after the consummation of such Business Combination, the shareholders of the Company immediately prior thereto do not Own, directly or indirectly, either outstanding voting securities representing more than fifty percent (50%) of the combined outstanding voting power of the surviving Entity or ultimate parent of the surviving Entity in such Business Combination in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such Business Combination, (B) an Exchange Act Person becomes the Owner, directly or indirectly, of securities representing more than thirty percent (30%) of the combined voting power of the surviving Entity or ultimate parent of the surviving Entity through the Business Combination, or (C) at least a majority of the members of the board of directors of the ultimate parent (or if there is no parent, the surviving Entity) immediately following such Business Combination were not Incumbent Board Members (as defined below) at the time the Board approved the execution of the definitive agreement providing for such Business Combination;

(iii) the shareholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation;

(iv) there is consummated a sale, lease, exclusive license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, exclusive license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than fifty percent (50%) of the combined voting power of the voting securities of which are Owned by shareholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, exclusive license or other disposition; or

(v) individuals who, on February 10, 2016, are members of the Board (the "***Incumbent Board Members***") cease for any reason to constitute at least a majority of the members of the Board; *provided, however*, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the Incumbent Board Members then still in office, such new member shall, for purposes of the Plan, be considered as an Incumbent Board Member, but excluding for purposes of the Plan any such individual whose initial assumption of office occurs as a result of either an actual or threatened election contest or other actual or threatened solicitation of proxies or consents by or on behalf of any person or Entity other than the Board.

(h) "***COBRA***" means the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended.

(i) "***Code***" means the Internal Revenue Code of 1986, as amended.

(j) "***Companies Act***" means the Companies Act 2014 of Ireland, together with all statutory modifications and re-enactments thereof and all statutes and statutory instruments which are to be read as one with, or construed or read together as one with, the aforementioned enactments and every statutory modification and re-enactment thereof for the time being in force.

(k) "***Company***" means:

(i) prior to a Change in Control, Jazz Pharmaceuticals plc; and

(ii) on or after a Change in Control, (A) Jazz Pharmaceuticals plc in the event that the surviving Entity resulting from a Change in Control is Jazz Pharmaceuticals plc, (B) the surviving Entity resulting from a Change in Control in the event that such surviving Entity is not Jazz Pharmaceuticals plc, (C) any Entity to which the assets of Jazz Pharmaceuticals plc and its Subsidiaries are sold, leased, exclusively licensed or otherwise disposed of in the event of a Change in Control under Section 2(g)(iv), or (D) any other successor to Jazz Pharmaceuticals plc in the event of a Change in Control, as applicable;

provided, however, that in the event Jazz Pharmaceuticals plc completes a reorganization that is not in connection with a Change in Control that results in Jazz Pharmaceuticals plc no longer being the ultimate parent company and reporting company under the Exchange Act, then "Company" means the ultimate parent that directly or indirectly holds Jazz Pharmaceuticals plc.

(l) "***Constructive Termination***" means a termination of a Participant's employment with the Company or an Affiliate as a result of the Participant's resignation of such employment for Good Reason; *provided, however*, that in order for such termination to constitute a Constructive Termination, the Participant must (i) provide written notice to the Company's General Counsel (or equivalent position) within thirty (30) days after the first occurrence of the action or event constituting Good Reason setting forth the basis for such resignation, (ii) allow the Company at least thirty (30) days from receipt of such written notice to cure such action or event, and (iii) if such action or event is not reasonably cured within such period, resign from all positions the Participant then holds with the Company and any Affiliate effective not later than ninety (90) days after the expiration of such cure period.

(m) "***Covered Termination***" means either (i) an Involuntary Termination Without Cause, or (ii) a Constructive Termination, in each case effective upon or within twelve (12) months following a Change in Control.

(n) "***Disability***" means, with respect to a Participant, the inability of the Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than twelve (12) months, as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and shall be reasonably determined by the Board or its designee on the basis of such medical evidence as the Board or its designee deems warranted under the circumstances.

(o) "***Entity***" means a corporation, partnership, limited liability company, or other entity.

(p) "***ERISA***" means the Employee Retirement Income Security Act of 1974, as amended.

(q) "***Exchange Act***" means the Securities Exchange Act of 1934, as amended.

(r) "***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, or (iv) an Entity Owned, directly or indirectly, by the shareholders of the Company in substantially the same proportions as their Ownership of shares of the Company.

(s) "***Final Base Salary***" means the higher of a Participant's Base Salary in effect (x) on the date of the Participant's Covered Termination (without giving effect to any reduction in Base Salary that would constitute Good Reason for Constructive Termination) or (y) immediately prior to the Change in Control; *provided, however*, that if the Participant has, during the twelve (12) months prior to the date of the Participant's Covered Termination or the Change in Control, as applicable, taken a voluntary pay reduction, then the Participant's Final Base Salary will be determined without regard to such voluntary pay reduction.

(t) "***Good Reason***" means the occurrence of any one or more of the following actions or events effected without a Participant's written consent:

(i) one or more reductions in the Participant's Base Salary that results in a total reduction in the Participant's Base Salary, as in effect immediately prior to the Change in Control or any higher Base Salary in effect following the Change in Control, by more than ten percent (10%);

(ii) a relocation of the Participant's principal place of employment that increases the Participant's one-way commute by more than thirty-five (35) miles;

(iii) a substantial reduction in the Participant's authority, duties or responsibilities (and not simply a change in reporting relationships) as in effect immediately prior to the Change in Control; provided that if (i) the Participant continues to hold the same position but the size of the Participant's employing Entity (or the business unit to which the Participant is assigned) has decreased significantly or (ii) neither the Company nor the Participant's employing Entity continues to be a publicly-traded corporation, the Participant's authority, duties and responsibilities will be considered to be substantially reduced;

(iv) a reduction in the Participant's title (*i.e.*, the Participant no longer has a "Vice President," "Senior Vice President," "Executive Vice President," "Chief Executive Officer", "Executive Chairman" or "President" title, as applicable to the Participant); or

(v) required travel by the Participant on the Company's or an Affiliate's business is substantially increased compared with the Participant's business travel obligations prior to the Change in Control.

(u) "***Involuntary Termination Without Cause***" means a termination by the Company or an Affiliate of a Participant's employment for any reason other than for Cause. For purposes of the foregoing and the Plan, a termination of employment of a Participant due to the Participant's death or Disability shall constitute an Involuntary Termination Without Cause.

(v) "***Own***," "***Owned***," "***Owner***," "***Ownership***" A person or Entity shall be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(w) "***Participant***" means an individual who is an employee of a U.S. Affiliate and who has been designated a "Participant" by the Plan Administrator in its sole discretion (either by a specific written designation or by virtue of being a member of a class of employees who have been so designated).

(x) "***Plan Administrator***" means the Board or any committee duly authorized by the Board to administer the Plan. The Plan Administrator may, but is not required to be, the Compensation Committee of the Board. The Board may at any time administer the Plan, in whole or in part, notwithstanding that the Board has previously appointed a committee to act as the Plan Administrator.

(y) "***Release***" has the meaning set forth in Section 5(a).

(z) "***Stock Award***" means any option, right or other stock award described in Section 4(c).

(aa) "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation shall have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other Entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than fifty percent (50%).

(bb) "***U.S. Affiliate***" means any Affiliate incorporated in the United States of America.

SECTION 3. ELIGIBILITY FOR BENEFITS.

(a) General Rules. Subject to the limitations set forth in this Section 3, Section 5 and Section 6, in the event of a Participant's Covered Termination, the Company shall provide the benefits described in Sections 4(a), 4(b) and 4(c) to the Participant.

(b) Exceptions to Benefit Entitlement. A Participant will not receive benefits under the Plan (or will receive reduced benefits under the Plan) in the following circumstances, as determined by the Plan Administrator in its sole discretion:

(i) The Participant's employment with the Company or an Affiliate terminates or is terminated for any reason other than a Covered Termination.

(ii) The Participant voluntarily terminates employment with the Company or an Affiliate in order to accept employment with another Entity that is controlled (directly or indirectly) by the Company or is otherwise an Affiliate.

(iii) The Participant does not confirm in writing that he or she is and shall be subject to the Employee Confidential Information and Inventions Agreement (or other similar agreement with a different name relating to confidentiality obligations) entered into by the Participant in connection with his or her employment with the applicable Affiliate (the "***Employee Confidentiality Agreement***") and the Company's *Code of Conduct* as then in effect during any notice or post-termination period.

(iv) The Participant does not confirm in writing that he or she is and shall be subject to the obligations described in Section 3(c).

(v) Following the Participant's Covered Termination but prior to the date benefits under the Plan are scheduled to commence, the Participant commences employment with the Company or an Affiliate for an identical or substantially equivalent or comparable position as the Participant's position with the Company or an Affiliate on the date of the Participant's Covered Termination. For purposes of the foregoing, a "substantially equivalent or comparable position" is one that provides the Participant substantially the same level of responsibility and Base Salary as the Participant's position with the Company or an Affiliate on the date of the Participant's Covered Termination.

(vi) Prior to the date of the Participant's Covered Termination, the Participant is offered an identical or substantially equivalent or comparable position in the U.S. with the Company or an Affiliate as the Participant's then current position with the Company or an Affiliate. For purposes of the foregoing, a "substantially equivalent or comparable position" is one that provides the Participant substantially the same level of responsibility and Base Salary as the Participant's then current position; *provided*, *however*, that a Participant shall not be considered to be offered a "substantially equivalent or comparable position" if a resignation by the Participant would constitute a Constructive Termination.

(vii) The Participant has failed to execute or has revoked the Release described in Section 5(a).

(viii) The Participant fails to return all Company Property. For this purpose, "***Company Property***" means all documents (and all copies thereof) and other property of the Company or an Affiliate which the Participant had in his or her possession at any time, including, but not limited to, files, notes, drawings, records, plans, forecasts, reports, studies, analyses, proposals, agreements, financial information, research and development information, sales and marketing information, operational and personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, but not limited to, computers, printers, facsimile machines, mobile telephones and other mobile devices, and servers), credit cards, entry cards, identification badges and keys, and any materials of any kind which is owned by the Company or an Affiliate or contain or embody any proprietary or confidential information of the Company or an Affiliate (and all reproductions thereof in whole or in part).

(c) Termination of Benefits. A Participant's right to receive benefits under this Plan shall terminate immediately if, at any time prior to or during the period for which the Participant is receiving benefits hereunder, the Participant, without the prior written approval of the Plan Administrator:

(i) willfully breaches a material provision of the Participant's *Employee Confidentiality Agreement* or the Company's *Code of Conduct*;

(ii) encourages or solicits any then current employees or independent contractors of the Company or an Affiliate to end their service with the Company or an Affiliate for any reason or interferes in any other manner with the service relationships existing between the Company or an Affiliate and its then current employees or independent contractors; or

(iii) induces any then current clients, customers, suppliers, vendors, distributors, licensors, licensees of the Company or an Affiliate, or other third party in a similar relationship to the Company or an Affiliate, to terminate their existing business relationship with the Company or an Affiliate or interferes in any other manner with any existing business relationship between the Company or an Affiliate and any then current client, customer, supplier, vendor, distributor, licensor, licensee or other third party.

SECTION 4. AMOUNT OF BENEFITS.

Subject to the limitations set forth in Section 3, Section 5 and Section 6, in the event of a Participant's Covered Termination, the Participant shall be entitled to receive the benefits described in Sections 4(a), 4(b) and 4(c).

(a) Cash Severance Payment. The Company shall make a cash severance payment to the Participant in an amount equal to the sum of:

(i) the Participant's Final Base Salary multiplied by the percentage set forth below that applies to the Participant, plus

(ii) the product of (A) the Participant's Final Base Salary, (B) the Participant's Bonus Percentage and (C) the percentage set forth below that applies to the Participant, plus

(iii) the product of (A) the Participant's Final Base Salary, (B) the Participant's Bonus Percentage and (C) the Participant's Bonus Multiplier;

provided, *however*, that the amount of such cash severance payment shall be reduced by the amount of any payment made to or earned by the Participant on or prior to the date of the Participant's Covered Termination for performance for the calendar year in which the Covered Termination occurs under any bonus (including sales or incentive compensation) plan maintained by the Company or an Affiliate (which, for purposes of clarification and as determined by the Plan Administrator, shall not include any one-time or extraordinary bonus payments made to or earned by the Participant outside of a plan for performance for such calendar year). Such cash severance payment shall be paid in accordance with Section 6.

If the Participant is at the time of the Covered Termination a:	**Applicable Percentage:**
Vice President	100 %
Senior Vice President, Executive Vice President, or above (but not Chief Executive Officer, Executive Chairman or President)	150 %
Chief Executive Officer, Executive Chairman or President	200 %

(b) Health Continuation Coverage.

(i) Provided that the Participant is eligible to continue coverage under a health, dental or vision insurance plan sponsored by the Company or an Affiliate upon the Participant's Covered Termination pursuant to COBRA and the Participant makes an election to continue such coverage pursuant to COBRA within the time period prescribed under COBRA, the Participant shall be entitled to payment by the Company of all of the applicable COBRA premiums for such health, dental or vision insurance plan coverage from the date of the Participant's Covered Termination through the earliest of (A) a period of twelve (12) months following such date in the case of a Vice President, eighteen (18) months following such date in the case of a Senior Vice President, Executive Vice President, or above (but not the Chief Executive Officer, Executive Chairman or President), and twenty-four (24) months following such date in the case of the Chief Executive Officer, Executive Chairman or President, (B) the Participant's death or (C) the effective date of the Participant's coverage by a health, dental or vision insurance plan of a subsequent employer (such period from the date of the Participant's

Covered Termination through the earliest of (A) through (C), the "***COBRA Payment Period***"), with such coverage counted as coverage pursuant to COBRA. Such COBRA premium payments shall be inclusive of premiums for the Participant's eligible dependents for such health, dental or vision insurance plan coverage as in effect immediately prior to the date of the Participant's Covered Termination, provided that such dependents continue to be eligible for such coverage during the COBRA Payment Period.

(ii) No COBRA premium payments (or any other payments for health, dental or vision insurance plan coverage by the Company or an Affiliate) shall be made following the Participant's death or the effective date of the Participant's coverage by a health, dental or vision insurance plan of a subsequent employer. Each Participant shall be required to provide written notification to the Plan Administrator immediately if the Participant becomes covered by a health, dental or vision insurance plan of a subsequent employer.

(iii) No provision of this Plan will affect the continuation coverage rules under COBRA, except that the Company's payment of any applicable COBRA premiums will be credited as payment by the Participant for purposes of the Participant's payment required under COBRA. Therefore, the period during which the Participant may elect to continue the Company's or its Affiliate's health, dental or vision insurance plan coverage at his or her own expense under COBRA, the length of time during which COBRA coverage will be made available to the Participant, and all other rights and obligations of the Participant under COBRA (except the Company's obligation, if any, to pay COBRA premiums under this Section 4(b)) will be applied in the same manner that such rules would apply in the absence of this Plan. Upon the conclusion of any COBRA Payment Period, the Participant will be responsible for the entire payment of premiums required under COBRA for the remainder of the COBRA period.

(iv) For purposes of this Section 4(b), (i) references to COBRA shall be deemed to refer also to analogous provisions of state law, and (ii) any applicable insurance premiums that are paid by the Company shall not include any amounts payable by a Participant under an Internal Revenue Code Section 125 health care reimbursement plan, which amounts, if any, are the sole responsibility of the Participant.

(v) Notwithstanding the foregoing but subject to Section 6, if at any time the Plan Administrator determines, in its sole discretion, that its payment of COBRA premiums on the Participant's behalf would result in a violation of applicable law (including, without limitation, Section 2716 of the Public Health Service Act), then in lieu of paying COBRA premiums pursuant to this Section 4(b), the Company will pay to the Participant, on the last day of each remaining month of the COBRA Payment Period, a fully taxable cash payment equal to the COBRA premiums for such month, subject to applicable tax withholding (such amount, the "***Special Severance Payment***"), and such Special Severance Payment will be made without regard to the Participant's payment of COBRA premiums and without regard to the expiration of the COBRA period prior to the end of the COBRA Payment Period.

(vi) Such COBRA premium payments and Special Severance Payments, if any, shall be paid in accordance with Section 6.

(c) Stock Award Vesting Acceleration. The vesting (and exercisability, if applicable) of all outstanding options to purchase the Company's ordinary shares, stock appreciation rights or similar rights or other rights with respect to the Company's ordinary shares, and any other stock awards granted to the Participant pursuant to any equity incentive plan of the Company that are held by the Participant on the date of the Participant's Covered Termination shall be accelerated in full.

(d) Other Employee Benefits. All other benefits (such as life insurance, disability coverage and 401(k) plan coverage) provided by the Company or an Affiliate shall terminate as of the date of the Participant's Covered Termination (except to the extent that a conversion privilege may be available thereunder).

(e) Additional Benefits. Notwithstanding the foregoing, the Plan Administrator may, in its sole discretion, provide benefits in addition to those pursuant to Sections 4(a), 4(b) and 4(c) to one or more Participants chosen by the Plan Administrator, in its sole discretion, and the provision of any such benefits to a Participant shall in no way obligate the Company to provide such benefits to any other Participant, even if similarly situated.

SECTION 5. LIMITATIONS ON BENEFITS.

(a) Release. In order to be eligible to receive benefits under the Plan, a Participant must (i) execute and return to the Company within the applicable time period set forth therein a general waiver and release in substantially the form attached hereto as **EXHIBIT A**, **EXHIBIT B**, or **EXHIBIT C**, as appropriate (a "***Release***"), and (ii) not revoke the Release within the revocation period (if any) set forth therein; *provided, however*, that in no event may the applicable time period or revocation period extend beyond sixty (60) days following the date of the Participant's Covered Termination. The Plan Administrator, in its sole discretion, may modify the form of the Release to comply with applicable law and shall determine the form of the Release, which may be incorporated into a separation agreement or other agreement with the Participant.

(b) Certain Reductions. The Plan Administrator, in its sole discretion, shall have the authority to reduce or otherwise adjust a Participant's benefits under the Plan, in whole or in part, by any other severance benefits, pay and benefits in lieu of notice, or other similar benefits payable to the Participant by the Company or an Affiliate that become payable in connection with the Participant's termination of employment with the Company or an Affiliate pursuant to (i) any applicable legal requirement, including, without limitation, the Worker Adjustment and Retraining Notification Act (the "***WARN Act***"), the California Plant Closing Act or any other similar state law, or (ii) any policy or practice of the Company or an Affiliate providing for the Participant to remain on payroll for a limited period of time after being given notice of the termination of the Participant's employment. The benefits provided under this Plan are intended to satisfy, in whole or in part, any and all statutory obligations of the Company and its Affiliates that may arise out of a Participant's termination of employment, and the Plan Administrator shall so construe and implement the terms of the Plan. Any reductions that the Company determines to make pursuant to this Section 5(b) shall be made such that any benefit under the Plan shall be reduced solely by any similar type of benefit under such legal requirement, policy or practice

(*i.e.*, any cash severance benefits under the Plan shall be reduced solely by any cash severance benefits under such legal requirement, policy or practice, and any continued health insurance benefits under the Plan shall be reduced solely by any continued health insurance benefits under such legal requirement, policy or practice). The Plan Administrator's decision to apply such reductions to the benefits of one Participant under the Plan and the amount of such reductions shall in no way obligate the Plan Administrator to apply the same reductions in the same amounts to the benefits of any other Participant under the Plan, even if similarly situated. In the Plan Administrator's sole discretion, such reductions may be applied on a retroactive basis, with benefits previously paid being re-characterized as payments or other benefits pursuant to the Company's or an Affiliate's statutory or other obligations.

(c) Parachute Payments.

(i) Except as otherwise provided in a written agreement between a Participant and the Company or an Affiliate, if any payment or benefit a Participant will or may receive from the Company or otherwise (a "***280G Payment***") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "***Excise Tax***"), then any such 280G Payment pursuant to this Plan (a "***Payment***") shall be equal to the Reduced Amount. The "***Reduced Amount***" shall be either (x) the largest portion of the Payment that would result in no portion of the Payment (after reduction) being subject to the Excise Tax or (y) the largest portion, up to and including the total, of the Payment, whichever amount (*i.e.*, the amount determined by clause (x) or by clause (y)), after taking into account all applicable federal, state and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in the Participant's receipt, on an after-tax basis, of the greater economic benefit notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in a Payment is required pursuant to the preceding sentence and the Reduced Amount is determined pursuant to clause (x) of the preceding sentence, the reduction shall occur in the manner (the "***Reduction Method***") that results in the greatest economic benefit for the Participant. If more than one method of reduction will result in the same economic benefit, the items so reduced will be reduced pro rata (the "***Pro Rata Reduction Method***").

(ii) Notwithstanding any provision of Section 5(c)(i) to the contrary, if the Reduction Method or the Pro Rata Reduction Method would result in any portion of the Payment being subject to taxes pursuant to Section 409A of the Code and the regulations and other guidance thereunder and any state law of similar effect (collectively, "***Section 409A***") that would not otherwise be subject to taxes pursuant to Section 409A, then the Reduction Method and/or the Pro Rata Reduction Method, as the case may be, shall be modified so as to avoid the imposition of taxes pursuant to Section 409A as follows: (A) as a first priority, the modification shall preserve, to the greatest extent possible, the greatest economic benefit for the Participant as determined on an after-tax basis; (B) as a second priority, Payments that are contingent on future events (*e.g.*, being terminated without Cause) shall be reduced (or eliminated) before Payments that are not contingent on future events; and (C) as a third priority, Payments that are "deferred compensation" within the meaning of Section 409A shall be reduced (or eliminated) before Payments that are not "deferred compensation" within the meaning of Section 409A.

(iii) The independent registered public accounting firm engaged by the Company for general audit purposes as of the day prior to the effective date of the event described in Section 280G(b)(2)(A)(i) of the Code shall perform the foregoing calculations. If the independent registered public accounting firm so engaged by the Company is serving as accountant or auditor for the individual, entity or group effecting such event, the Company shall appoint a nationally recognized independent registered public accounting firm to make the determinations required hereunder. The Company shall bear all expenses with respect to the determinations by such independent registered public accounting firm required to be made hereunder. The Company shall use commercially reasonable efforts to cause the independent registered public accounting firm engaged to make the determinations hereunder to provide its calculations, together with detailed supporting documentation, to the Company and the Participant within thirty (30) calendar days after the date on which the Participant's right to a 280G Payment becomes reasonably likely to occur (if requested at that time by the Company or the Participant) or such other time as requested by the Company or the Participant.

(iv) If the Participant receives a Payment for which the Reduced Amount was determined pursuant to clause (x) of Section 5(c)(i) and the Internal Revenue Service determines thereafter that some portion of the Payment is subject to the Excise Tax, the Participant agrees to promptly return to the Company a sufficient amount of the Payment (after reduction pursuant to clause (x) of Section 5(c)(i)) so that no portion of the remaining Payment is subject to the Excise Tax. For the avoidance of doubt, if the Reduced Amount was determined pursuant to clause (y) of Section 5(c)(i), the Participant shall have no obligation to return any portion of the Payment pursuant to the preceding sentence.

(d) Mitigation. Except as otherwise specifically provided herein, a Participant shall not be required to mitigate damages or the amount of any payment provided under this Plan by seeking other employment or otherwise, nor shall the amount of any payment provided for under this Plan be reduced by any compensation earned by a Participant as a result of employment by another employer or any retirement benefits received by the Participant after the date of the Participant's Covered Termination, except for health continuation coverage provided pursuant to Section 4(b).

(e) Non-Duplication of Benefits. Except as otherwise specifically provided for herein, no Participant is eligible to receive benefits under this Plan or pursuant to other contractual obligations more than one time. This Plan is designed to provide certain severance benefits to Participants pursuant to the terms and conditions set forth in this Plan. The payments pursuant to this Plan are in addition to, and not in lieu of, any unpaid salary, bonuses, incentive compensation or benefits to which a Participant may be entitled for the period ending with the date of the Participant's Covered Termination.

SECTION 6. TIME OF PAYMENT AND FORM OF BENEFITS.

(a) General Rules. Except as otherwise set forth in the Plan, in the event of a Participant's Covered Termination, benefits under the Plan shall be paid to the Participant in accordance with the following:

(i) Any cash severance payment under the Plan shall be paid to the Participant in a single lump sum payment on the sixtieth (60^{th}) day following the date of the Participant's Covered Termination.

(ii) Any COBRA premium payments under the Plan shall be paid on a monthly basis during the COBRA Payment Period; *provided, however*, that the first such payment shall be paid on the sixtieth (60^{th}) day following the date of the Participant's Covered Termination, in an amount equal to the aggregate amount of COBRA premium payments that the Company would have paid through such sixtieth (60^{th}) day had such payments commenced on the date of the Participant's Covered Termination, with the balance of such payments paid thereafter on the foregoing monthly schedule.

(iii) Any Special Severance Payments, if applicable, under the Plan shall be paid on a monthly basis in accordance with Section 4(b)(v); *provided, however*, that if any Special Severance Payment(s) is payable with respect to the first sixty (60) days following the date of the Participant's Covered Termination, such Special Severance Payment(s) shall be paid on the sixtieth (60^{th}) day following the date of the Participant's Covered Termination, with the balance of such payments paid thereafter on the foregoing monthly schedule.

(iv) The vesting (and exercisability, if applicable) of any Stock Award shall be accelerated pursuant to Section 4(c) on the sixtieth (60^{th}) day following the date of the Participant's Covered Termination. In order to give effect to the intent of this provision, in the event of a Participant's Covered Termination, notwithstanding anything to the contrary set forth in any applicable equity incentive plan of the Company or any agreement evidencing a Stock Award, in no event will any portion of the Participant's Stock Award be forfeited or terminate any earlier than the sixtieth (60^{th}) day following the date of the Participant's Covered Termination; *provided, however*, that no provision in the Plan shall affect any provision in any applicable equity incentive plan of the Company or any agreement evidencing a Stock Award that provides for the acceleration of vesting (and exercisability, if applicable) of such Stock Award.

In no event shall payment of any benefit under the Plan be made unless (A) the Participant's Covered Termination constitutes a "separation from service" (as defined in Treasury Regulation Section 1.409A-1(h) without regard to any alternative definition thereunder ("***Separation from Service***")) and (B) the Participant has executed and returned a Release and the revocation period (if any) with respect to such Release has expired in accordance with Section 5(a) prior to the sixtieth (60^{th}) day following the date of the Participant's Covered Termination.

(b) Application of Section 409A. It is intended that all of the benefits payable under this Plan satisfy, to the greatest extent possible, the exemptions from the application of Section 409A provided under Treasury Regulations 1.409A-1(b)(4), 1.409A-1(b)(5) and 1.409A-1(b)(9), and that this Plan will be construed to the greatest extent possible as consistent with those provisions, and to the extent not so exempt, this Plan (and any definitions hereunder) will be construed in a manner that complies with Section 409A. For purposes of Section 409A (including, without limitation, for purposes of Treasury Regulation Section 1.409A-2(b)(2)(iii)), a Participant's right to receive any installment payments under this Plan (whether severance

payments, reimbursements or otherwise) shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment hereunder shall at all times be considered a separate and distinct payment. Notwithstanding anything to the contrary herein, if the Plan Administrator determines that a Participant is, upon his or her Separation from Service, a "specified employee" for purposes of Section 409A, then, solely to the extent necessary to avoid adverse personal tax consequences under Section 409A, (i) the commencement of any benefit payments under the Plan shall be delayed until the earlier of (A) six (6) months and one (1) day after the Participant's Separation from Service (or such longer period as is required under Section 409A) and (B) the date of the Participant's death (such applicable date, the "***Delayed Initial Payment Date***"), and (ii) the Company shall (A) pay the Participant a lump sum amount equal to the sum of any benefit payments that the Participant otherwise would have received through the Delayed Initial Payment Date if the commencement of such benefit payments had not been delayed pursuant to this paragraph and (B) commence paying the balance, if any, of such benefit payments in accordance with the applicable payment schedule.

(c) Application of Section 252 and 253 of the Companies Act. This Plan is entered into for the benefit of Participants in the ordinary course of their employment. It is not intended to provide for any payment by way of compensation for loss of office or consideration for or in connection with the retirement from office of a director of the Company in connection with the transfer of the whole or any part of the undertaking or property of the Company within the meaning of Section 252 of the Companies Act nor to provide for a payment giving rise to a duty of a director of the Company pursuant to Section 253 of the Companies Act.

(d) Tax Withholding. All payments under the Plan will be subject to all applicable tax withholding obligations of the Company and any Affiliate, including, without limitation, obligations to withhold for federal, state and local income and employment taxes.

(e) Indebtedness of Participants. If a Participant is indebted to the Company or an Affiliate on the date of his or her Covered Termination, the Plan Administrator reserves the right to offset any severance payments under the Plan by the amount of such indebtedness.

SECTION 7. RIGHT TO INTERPRET PLAN; AMENDMENT AND TERMINATION.

(a) Exclusive Discretion. The Plan Administrator shall have the exclusive discretion and authority to establish rules, forms, and procedures for the administration of the Plan, and to construe and interpret the Plan and to decide any and all questions of fact, interpretation, definition, computation or administration arising in connection with the operation of the Plan, including, but not limited to, the eligibility to participate in the Plan and amount of benefits paid under the Plan. The rules, interpretations, computations and other actions of the Plan Administrator shall be binding and conclusive on all persons.

(b) Amendment or Termination. The Company reserves the right to amend or terminate this Plan, or the benefits provided hereunder, at any time; *provided*, *however*, that no such amendment or termination shall occur following a Change in Control or a Covered Termination as to any Participant who would be adversely affected by such amendment or

termination unless such Participant consents in writing to such amendment or termination. Any action amending or terminating the Plan shall be in writing and executed by a duly authorized officer of the Company.

SECTION 8. NO IMPLIED EMPLOYMENT CONTRACT.

The Plan shall not be deemed (i) to give any employee or other person any right to be retained in the employ of the Company or an Affiliate, or (ii) to interfere with the right of the Company or an Affiliate to discharge any employee or other person at any time, with or without advance notice, and with or without cause, which right is hereby reserved.

SECTION 9. LEGAL CONSTRUCTION.

This Plan is intended to be governed by and shall be construed in accordance with ERISA and, to the extent not preempted by ERISA, the laws of the State of California.

SECTION 10. CLAIMS, INQUIRIES AND APPEALS.

(a) Claims for Benefits and Inquiries. Any claim for benefits, inquiries about the Plan or inquiries about present or future rights under the Plan must be submitted to the Plan Administrator in writing by a claimant (or his or her authorized representative). The Plan Administrator is set forth in Section 12(d). Certain capitalized terms used in this Section 10 are defined in Section 10(e) below.

(b) Denial of Claims. The Plan Administrator shall make a benefit determination and communicate its decision, electronically or in writing, to the claimant in accordance with its claim practices, which shall comply with Department of Labor regulations.

(i) Claims other than Disability Claims. In the event that any claim for benefits that is not a Disability Claim is denied in whole or in part, the Plan Administrator must provide the claimant with notice of the Adverse Benefit Determination within a reasonable period of time, but not later than ninety (90) days after the Plan Administrator's receipt of the written claim for benefits, unless the Plan Administrator determines that special circumstances require an extension of time for processing the claim. If the Plan Administrator determines that an extension of time for processing is required, written notice of the extension shall be furnished to the claimant prior to the termination of the initial ninety (90) day period. In no event shall such extension exceed a period of ninety (90) days from the end of such initial period. The extension notice shall indicate the special circumstances requiring an extension of time and the date by which the Plan Administrator expects to render the benefit determination.

(ii) Disability Claims. In the event that any claim for benefits that is a Disability Claim is denied in whole or in part, the Plan Administrator must provide the claimant with notice of the Adverse Benefit Determination within a reasonable period of time, but not later than forty-five (45) days after the Plan Administrator's receipt of the written claim for benefits. This period may be extended for up to thirty (30) days, provided that the Plan Administrator both (i) determines that such an extension is necessary due to matters beyond the

control of the Plan and (ii) notifies the claimant, prior to the expiration of the initial forty-five (45) day period, of the circumstances requiring the extension of time and the date by which the Plan Administrator expects to render a decision. If, prior to the end of the first thirty (30) day extension period, the Plan Administrator determines that, due to matters beyond the control of the Plan, a decision cannot be rendered within the first thirty (30) day extension period, the period for making the determination may be extended for up to an additional thirty (30) days, provided that the Plan Administrator notifies the claimant, prior to the expiration of the first thirty (30) day extension period, of the circumstances requiring the extension and the date as of which the Plan Administrator expects to render a decision. Any notice of extension under this paragraph shall specifically explain the standards on which entitlement to a benefit is based, the unresolved issues that prevent a decision on the claim, and the additional information needed to resolve those issues, and the claimant shall be afforded at least forty-five (45) days within which to provide the specified information.

(iii) Content of Notice of Adverse Benefit Determination. The Plan Administrator shall provide the claimant with written or electronic notification of any Adverse Benefit Determination. Any electronic notification shall comply with the standards imposed by Section 2520.104b-1(c) of Part 29 of the Code of Federal Regulations. Any notice of Adverse Benefit Determination shall set forth in a manner calculated to be understood by the claimant:

(1) The specific reason or reasons for the Adverse Benefit Determination;

(2) Reference to the specific Plan provision(s) on which the Adverse Benefit Determination is based;

(3) A description of any additional material or information necessary for the claimant to perfect the claim and an explanation of why such material or information is necessary;

(4) A description of the Plan's review procedures and the time limits applicable to such procedures, including a statement of the claimant's right to bring a civil action under Section 502(a) of ERISA following an Adverse Benefit Determination on review; and

(5) In the case of an Adverse Benefit Determination involving a Disability Claim:

a. If an internal rule, guideline, protocol, or other similar criterion was relied upon in making the Adverse Benefit Determination, either the specific rule, guideline, protocol, or other similar criterion, or a statement that such a rule, guideline, protocol, or other similar criterion was relied upon in making the Adverse Benefit Determination and that a copy of such rule, guideline, protocol, or other criterion will be provided free of charge to the claimant upon request; or

b. If the Adverse Benefit Determination is based on a medical necessity or experimental treatment or similar exclusion or limit, either (i) an explanation of the

scientific or clinical judgment for the determination, applying the terms of the Plan to the claimant's medical circumstances, or (ii) a statement that such explanation will be provided free of charge upon request.

(c) Request for a Review. Each claimant (or his or her authorized representative) shall have a reasonable opportunity to appeal an Adverse Benefit Determination by filing a written request for review with the Plan Administrator.

(i) Claims other than Disability Claims. In the case of a request for review not involving a Disability Claim, the written request for review must be furnished to the Plan Administrator within sixty (60) days following the claimant's receipt of the notice of an Adverse Benefit Determination. The claimant shall be provided with an opportunity to submit written comments, documents, records, and other information relating to the claimant's claim for benefits. The Plan Administrator shall provide the claimant, upon request and free of charge, reasonable access to, and copies of, all Relevant Records. The Plan Administrator's review of the claimant's appeal shall take into account all comments, documents, records, and other information submitted by the claimant relating to the claim, without regard to whether such information was submitted or considered in the initial benefit determination. If the claimant fails to request a review within the above-stated period, the claimant shall have waived the right to a review of the denial of his or her claim.

(ii) Disability Claims. In the case of a request for review involving a Disability Claim, the written request for review must be furnished to the Plan Administrator within one hundred eighty (180) days following the claimant's receipt of the notice of an Adverse Benefit Determination. The claimant shall be provided with an opportunity to submit written comments, documents, records, and other information relating to the claimant's claim for benefits. The Plan Administrator shall provide the claimant, upon request and free of charge, reasonable access to, and copies of, all Relevant Records. The Plan Administrator's review of the claimant's appeal shall take into account all comments, documents, records, and other information submitted by the claimant relating to the claim, without regard to whether such information was submitted or considered in the initial benefit determination. Further, the Plan Administrator's review of the claimant's appeal shall not afford deference to the initial Adverse Benefit Determination and shall be conducted by an appropriate named fiduciary of the Plan who is neither the individual who made the initial Adverse Benefit Determination that is the subject of the appeal, nor the subordinate of such individual. If the claimant fails to request a review within the above-stated period, the claimant shall have waived the right to a review of the denial of his or her claim.

If the appeal involves an Adverse Benefit Determination that is based in whole or in part on a medical judgment, including determinations with regard to whether a particular treatment, drug, or other item is experimental, investigational, or not medically necessary or appropriate, the appropriate named fiduciary shall consult with a Health Care Professional who has appropriate training and experience in the field of medicine involved in the medical judgment. Such Health Care Professional shall be an individual who is neither an individual who was consulted in connection with the initial Adverse Benefit Determination that is the subject of the appeal, nor the subordinate of any such individual.

The Plan Administrator shall provide the claimant with the identification of medical or vocational experts whose advice was obtained on behalf of the Plan in connection with the claimant's initial Adverse Benefit Determination, without regard to whether the advice was relied upon in making the Adverse Benefit Determination.

(iii) Timing of Notice of Benefit Determination on Review. The Plan Administrator shall notify a claimant of its decision on review within a reasonable period of time, but not later than sixty (60) days after the Plan Administrator's receipt of the claimant's request for review, unless the Plan Administrator determines that special circumstances require an extension of time for processing the claim. If the Plan Administrator determines that an extension of time for processing is required, written notice of the extension shall be furnished to the claimant prior to the termination of the initial sixty (60) day period. In no event shall such extension exceed a period of sixty (60) days from the end of the initial sixty (60) day period. The extension notice shall indicate the special circumstances requiring an extension of time and the date by which the Plan Administrator expects to render the determination on review. Notwithstanding the foregoing, if a claimant's request for review involves a Disability Claim, the references to sixty (60) days in this paragraph shall be replaced by forty-five (45) days.

(iv) Contents of Notice of Benefit Determination on Review. The Plan Administrator shall provide a claimant with written or electronic notification of its benefit determination on review. Any electronic notification shall comply with the standards imposed by Section 2520.104b-1(c) of Part 29 of the Code of Federal Regulations. In the case of an Adverse Benefit Determination, the notification shall set forth, in a manner calculated to be understood by the claimant:

(1) The specific reason or reasons for the Adverse Benefit Determination;

(2) Reference to the specific Plan provision(s) on which the benefit determination is based;

(3) A statement that the claimant is entitled to receive, upon request and free of charge, reasonable access to, and copies of, all Relevant Records;

(4) A statement describing any voluntary appeal procedures offered by the Plan and the claimant's right to obtain the information about such procedures described in Section 2560.503-1(c)(3)(iv) of Part 29 of the Code of Federal Regulations;

(5) A statement of the claimant's right to bring an action under Section 502(a) of ERISA; and

(6) In the case of an Adverse Benefit Determination involving a Disability Claim:

a. If an internal rule, guideline, protocol, or other similar criterion was relied upon in making the Adverse Benefit Determination, either the specific rule,

guideline, protocol, or other similar criterion, or a statement that such rule, guideline, protocol, or other similar criterion was relied upon in making the Adverse Benefit Determination and that a copy of the rule, guideline, protocol, or other similar criterion will be provided free of charge to the claimant upon request;

b. If the Adverse Benefit Determination is based on a medical necessity or experimental treatment or similar exclusion or limit, either (i) an explanation of the scientific or clinical judgment for the determination, applying the terms of the Plan to the claimant's medical circumstances, or (ii) a statement that such explanation will be provided free of charge upon request; and

c. The following statement: "You and your Plan may have other voluntary alternative dispute resolution options, such as mediation. One way to find out what may be available is to contact your local U.S. Department of Labor Office and your State insurance regulatory agency."

(d) Calculating Time Periods.

(i) Calculating Time Periods for Initial Benefit Determination. The period of time within which a benefit determination is required to be made shall begin at the time a claim is filed, without regard to whether all the information necessary to make a benefit determination accompanies the filing. In the case of a Disability Claim, in the event that a period of time for making the benefit determination is extended due to a claimant's failure to submit information necessary to decide a claim, the period for making the benefit determination shall be tolled from the date on which the notification of the extension is sent to the claimant until the date on which the claimant responds to the request for additional information.

(ii) Calculating Time Periods for Benefit Determination on Review. The period of time within which a benefit determination on review is required to be made shall begin at the time an appeal is filed, without regard to whether all the information necessary to make a benefit determination on review accompanies the filing. In the event that the period of time for making the benefit determination on review is extended due to a claimant's failure to submit information necessary to decide a claim, the period for making the benefit determination on review shall be tolled from the date on which the notification of the extension is sent to the claimant until the date on which the claimant responds to the request for additional information.

(e) Definitions for Claims and Appeals Procedures.

(i) "***Adverse Benefit Determination***" means any of the following: a denial, reduction, or termination of, or a failure to provide or make payment (in whole or in part) for, a benefit, including any such denial, reduction, termination, or failure to provide or make payment that is based on a determination of an individual's eligibility to participate in the Plan.

(ii) "***Disability Claim***" means a claim for benefits under the Plan based on a Participant's Covered Termination due to the Participant's Disability.

(iii) "***Health Care Professional***" means a physician or other health care professional who is licensed, accredited, or certified to perform specified health services consistent with applicable state law.

(iv) "***Relevant Records***" means any document, record, or other information that:

(1) the Plan Administrator relied upon in making the benefit determination for the claimant's claim;

(2) was submitted, considered, or generated in the course of making the benefit determination for the claimant's claim, without regard to whether such document, record, or other information was relied upon in making the benefit determination;

(3) demonstrates compliance with the administrative processes and safeguards required pursuant to Department of Labor regulations in making the benefit determination for the claimant's claim; or

(4) in the case of a Disability Claim, constitutes a statement of policy or guidance with respect to the Plan concerning the denied treatment option or benefit for the claimant's diagnosis, without regard to whether such advice or statement was relied upon in making the benefit determination.

(f) Exhaustion of Remedies. No legal action for benefits under the Plan may be brought until the claimant (i) has submitted a written claim for benefits in accordance with the procedures described by Section 10(a) above, (ii) has been notified by the Plan Administrator that the claim is denied, (iii) has filed a written request for a review of the claim in accordance with the appeal procedure described in Section 10(c) above, and (iv) has been notified that the Plan Administrator has denied the appeal. Notwithstanding the foregoing, if the Plan Administrator does not respond to a claimant's claim or appeal within the relevant time limits specified in this Section 10, the claimant may bring legal action for benefits under the Plan pursuant to Section 502(a) of ERISA.

SECTION 11. BASIS OF PAYMENTS TO AND FROM PLAN.

The Plan shall be unfunded, and all benefits hereunder shall be paid only from the general assets of the Company.

SECTION 12. OTHER PLAN INFORMATION.

(a) Employer and Plan Identification Numbers. The Employer Identification Number assigned to the Company (which is the "Plan Sponsor" as that term is used in ERISA) by the Internal Revenue Service is 98-1032470. The Plan Number assigned to the Plan by the Plan Sponsor pursuant to the instructions of the Internal Revenue Service is 502.

(b) Ending Date for Plan's Fiscal Year. The date of the end of the fiscal year for the purpose of maintaining the Plan's records is December 31.

(c) Agent for the Service of Legal Process. The agent for the service of legal process with respect to the Plan is:

Jazz Pharmaceuticals plc
Attn: General Counsel
c/o Jazz Pharmaceuticals, Inc.
3180 Porter Drive
Palo Alto, CA 94304

(d) Plan Sponsor and Administrator. The "Plan Sponsor" of the Plan is:

Jazz Pharmaceuticals plc
Attn: General Counsel
c/o Jazz Pharmaceuticals, Inc.
3180 Porter Drive
Palo Alto, CA 94304

The "Plan Administrator" of the Plan is as set forth in Section 2(x). The Plan Sponsor's and Plan Administrator's telephone number is (650) 496-3777. The Plan Administrator is the named fiduciary charged with the responsibility for administering the Plan.

SECTION 13. STATEMENT OF ERISA RIGHTS.

Participants in this Plan (which is a welfare benefit plan sponsored by Jazz Pharmaceuticals plc) are entitled to certain rights and protections under ERISA. If you are a Participant, you are considered a participant in the Plan for the purposes of this Section 13 and, under ERISA, you are entitled to:

(a) Receive Information About Your Plan and Benefits

(i) Examine, without charge, at the Plan Administrator's office and at other specified locations, such as worksites, all documents governing the Plan and a copy of the latest annual report (Form 5500 Series), if applicable, filed by the Plan with the U.S. Department of Labor and available at the Public Disclosure Room of the Employee Benefits Security Administration;

(ii) Obtain, upon written request to the Plan Administrator, copies of documents governing the operation of the Plan and copies of the latest annual report (Form 5500 Series), if applicable, and an updated (as necessary) Summary Plan Description. The Plan Administrator may make a reasonable charge for the copies; and

(iii) Receive a summary of the Plan's annual financial report, if applicable. The Plan Administrator is required by law to furnish each participant with a copy of this summary annual report.

(b) Prudent Actions By Plan Fiduciaries. In addition to creating rights for Plan participants, ERISA imposes duties upon the people who are responsible for the operation of the

employee benefit plan. The people who operate the Plan, called “fiduciaries” of the Plan, have a duty to do so prudently and in the interest of you and other Plan participants and beneficiaries. No one, including your employer, your union or any other person, may fire you or otherwise discriminate against you in any way to prevent you from obtaining a Plan benefit or exercising your rights under ERISA.

(c) Enforce Your Rights.

(i) If your claim for a Plan benefit is denied or ignored, in whole or in part, you have a right to know why this was done, to obtain copies of documents relating to the decision without charge, and to appeal any denial, all within certain time schedules.

(ii) Under ERISA, there are steps you can take to enforce the above rights. For instance, if you request a copy of Plan documents or the latest annual report from the Plan, if applicable, and do not receive them within 30 days, you may file suit in a federal court. In such a case, the court may require the Plan Administrator to provide the materials and pay you up to $110 a day until you receive the materials, unless the materials were not sent because of reasons beyond the control of the Plan Administrator.

(iii) If you have a claim for benefits which is denied or ignored, in whole or in part, you may file suit in a state or federal court.

(iv) If you are discriminated against for asserting your rights, you may seek assistance from the U.S. Department of Labor, or you may file suit in a federal court. The court will decide who should pay court costs and legal fees. If you are successful, the court may order the person you have sued to pay these costs and fees. If you lose, the court may order you to pay these costs and fees, for example, if it finds your claim is frivolous.

(d) Assistance With Your Questions. If you have any questions about the Plan, you should contact the Plan Administrator. If you have any questions about this statement or about your rights under ERISA, or if you need assistance in obtaining documents from the Plan Administrator, you should contact the nearest office of the Employee Benefits Security Administration, U.S. Department of Labor, listed in your telephone directory or the Division of Technical Assistance and Inquiries, Employee Benefits Security Administration, U.S. Department of Labor, 200 Constitution Avenue N.W., Washington, D.C. 20210. You may also obtain certain publications about your rights and responsibilities under ERISA by calling the publications hotline of the Employee Benefits Security Administration.

SECTION 14. GENERAL PROVISIONS.

(a) Notices. Any notice, demand or request required or permitted to be given by the Company, an Affiliate or a Participant pursuant to the terms of this Plan shall be in writing and shall be deemed given when delivered personally or deposited in the U.S. mail, First Class with postage prepaid, and addressed to the parties, in the case of the Company or an Affiliate, at the address set forth in Section 12(d) and, in the case of a Participant, at the address as set forth in the Company’s or Affiliate’s employment file maintained for the Participant as previously

furnished by the Participant or such other address as a party may request by notifying the other in writing.

(b) Transfer and Assignment. The rights and obligations of a Participant under this Plan may not be transferred or assigned without the prior written consent of the Company. This Plan shall be binding upon (i) any surviving Entity resulting from a Change in Control in the event that such surviving Entity is not Jazz Pharmaceuticals plc, (ii) any Entity to which the assets of Jazz Pharmaceuticals plc and its Subsidiaries are sold, leased, exclusively licensed or otherwise disposed of in the event of a Change in Control under Section 2(g)(iv), and (iii) any other Entity or person who is a successor by merger, acquisition, consolidation or otherwise to the business formerly carried on by Jazz Pharmaceuticals plc, in each case without regard to whether or not such Entity or person actively assumes the obligations hereunder.

(c) Waiver. Any party's failure to enforce any provision or provisions of this Plan shall not in any way be construed as a waiver of any such provision or provisions, nor prevent any party from thereafter enforcing each and every other provision of this Plan. The rights granted the parties herein are cumulative and shall not constitute a waiver of any party's right to assert all other legal remedies available to it under the circumstances.

(d) Severability. Should any provision of this Plan be declared or determined to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired.

(e) Section Headings. Section headings in this Plan are included for convenience of reference only and shall not be considered part of this Plan for any other purpose.

SECTION 15. EXECUTION.

To record the adoption of the Plan as set forth herein as of the Effective Date, the assumption of the Plan by Jazz Pharmaceuticals plc as of January 18, 2012, and the amendment and restatement of the Plan, Jazz Pharmaceuticals plc has caused its duly authorized officer to execute the same as of February 10, 2016.

JAZZ PHARMACEUTICALS PLC

By: /s/ Suzanne Sawochka Hooper

Title: Executive Vice President & General Counsel

The Executive Change in Control and Severance Benefit Plan was established effective as of May 1, 2007.

The Executive Change in Control and Severance Benefit Plan was amended and restated by the Board of Directors of Jazz Pharmaceuticals, Inc. on February 17, 2009.

The Executive Change in Control and Severance Benefit Plan was amended and restated by the Board of Directors of Jazz Pharmaceuticals, Inc. on October 24, 2011.

The Amended and Restated Executive Change in Control and Severance Benefit Plan was assumed by Jazz Pharmaceuticals plc effective as of January 18, 2012.

The Amended and Restated Executive Change in Control and Severance Benefit Plan was amended and restated by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on February 14, 2012.

The Amended and Restated Executive Change in Control and Severance Benefit Plan was amended and restated by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on April 24, 2012.

The Amended and Restated Executive Change in Control and Severance Benefit Plan was amended and restated by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on July 31, 2013.

The Amended and Restated Executive Change in Control and Severance Benefit Plan was amended and restated by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on February 10, 2016.

EXHIBIT A

RELEASE AGREEMENT (“*RELEASE*”)

I understand and agree completely to the terms set forth in the Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (the “*Plan*”).

I understand that this Release, together with the Plan, constitutes the complete, final and exclusive embodiment of the entire agreement between the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company that is not expressly stated therein. Certain capitalized terms used in this Release are defined in the Plan.

I hereby confirm my obligations under my *Employee Confidential Information and Inventions Agreement* with the Company.

I hereby represent that I have been paid all compensation owed and for all hours worked, I have received all the leave and leave benefits and protections for which I am eligible, pursuant to the federal Family and Medical Leave Act, the California Family Rights Act, or any other applicable law or leave of absence policy, and I have not suffered any on-the-job injury for which I have not already filed a claim for workers compensation benefits.

In exchange for the consideration provided to me by this Release that I am not otherwise entitled to receive, I hereby generally and completely release Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., my employer entity (if not Jazz Pharmaceuticals, Inc.), and their respective current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, parent and subsidiary entities, insurers, affiliates, and assigns (collectively, the “***Released Parties***”) of and from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring prior to my signing this Release (collectively, the “***Released Claims***”).

The Released Claims include, but are not limited to: (1) all claims arising out of or in any way related to my employment, or the termination of that employment; (2) all claims related to my compensation or benefits from my employer (or any parent or subsidiary entities or affiliates of my employer), including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in Jazz Pharmaceuticals plc or any of its parent or subsidiary entities or affiliates; (3) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (4) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (5) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys’ fees, or other claims

arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the federal Age Discrimination in Employment Act of 1967 (as amended) ("***ADEA***"), the California Labor Code (as amended), the California Fair Employment and Housing Act (as amended), the Pennsylvania Equal Pay Law, the Pennsylvania Wage Payment and Collection Law, the City of Philadelphia Fair Practices Code, and the Pennsylvania Human Relations Act.

Notwithstanding the foregoing, the following are not included in the Released Claims (the "***Excluded Claims***"): (1) any rights or claims for indemnification I may have pursuant to any written indemnification agreement with any of the Released Parties to which I am a party, the charter, bylaws, or operating agreements of the Released Parties, or under applicable law; or (2) any rights which are not waivable as a matter of law. In addition, nothing in this Release prevents me from filing, cooperating with, or participating in any proceeding before the Equal Employment Opportunity Commission, the Department of Labor, or any other government agency, except that I hereby waive my right to any monetary benefits in connection with any such claim, charge or proceeding. I hereby represent and warrant that, other than the Excluded Claims, I am not aware of any claims I have or might have against any of the Released Parties that are not included in the Released Claims.

I acknowledge that I am knowingly and voluntarily waiving and releasing any rights I may have under the ADEA. I also acknowledge that the consideration given for the Released Claims is in addition to anything of value to which I was already entitled. I further acknowledge that I have been advised by this writing, as required by the ADEA, that: (1) the Released Claims do not apply to any rights or claims that arise after the date I sign this Release; (2) I should consult with an attorney prior to signing this Release (although I may choose voluntarily not to do so); (3) I have twenty-one (21) days to consider this Release (although I may choose to voluntarily to sign it sooner); (4) I have seven (7) days following the date I sign this Release to revoke it by providing written notice to the General Counsel of my employer or of Jazz Pharmaceuticals plc; and (5) this Release will not be effective until the date upon which the revocation period has expired unexercised, which will be the eighth day after I sign this Release (the "***Release Effective Date***").

I acknowledge that I have read and understand Section 1542 of the California Civil Code which reads as follows: **"A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her must have materially affected his or her settlement with the debtor."** I hereby expressly waive and relinquish all rights and benefits under that section and any law of any jurisdiction of similar effect with respect to my release of any claims hereunder, including but not limited to any unknown or unsuspected claims.

I acknowledge that I must sign and return this Release to the Company so that it is received not later than twenty-one (21) days following the date it is provided to me.

EXECUTIVE

Name: _____

Date: _____

EXHIBIT B

RELEASE AGREEMENT (“*RELEASE*”)

I understand and agree completely to the terms set forth in the Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (the “*Plan*”).

I understand that this Release, together with the Plan, constitutes the complete, final and exclusive embodiment of the entire agreement between the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company that is not expressly stated therein. Certain capitalized terms used in this Release are defined in the Plan.

I hereby confirm my obligations under my *Employee Confidential Information and Inventions Agreement* with the Company.

I hereby represent that I have been paid all compensation owed and for all hours worked, I have received all the leave and leave benefits and protections for which I am eligible, pursuant to the federal Family and Medical Leave Act, the California Family Rights Act, or any other applicable law or leave of absence policy, and I have not suffered any on-the-job injury for which I have not already filed a claim for workers compensation benefits.

In exchange for the consideration provided to me by this Release that I am not otherwise entitled to receive, I hereby generally and completely release Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., my employer entity (if not Jazz Pharmaceuticals, Inc.), and their respective current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, parent and subsidiary entities, insurers, affiliates, and assigns (collectively, the “***Released Parties***”) of and from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring prior to my signing this Release (collectively, the “***Released Claims***”).

The Released Claims include, but are not limited to: (1) all claims arising out of or in any way related to my employment, or the termination of that employment; (2) all claims related to my compensation or benefits from my employer (or any parent or subsidiary entities or affiliates of my employer), including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in Jazz Pharmaceuticals plc or any of its parent or subsidiary entities or affiliates; (3) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (4) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (5) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys’ fees, or other claims

arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the federal Age Discrimination in Employment Act of 1967 (as amended) ("***ADEA***"), the California Labor Code (as amended), the California Fair Employment and Housing Act (as amended), the Pennsylvania Equal Pay Law, the Pennsylvania Wage Payment and Collection Law, the City of Philadelphia Fair Practices Code, and the Pennsylvania Human Relations Act.

Notwithstanding the foregoing, the following are not included in the Released Claims (the "***Excluded Claims***"): (1) any rights or claims for indemnification I may have pursuant to any written indemnification agreement with any of the Released Parties to which I am a party, the charter, bylaws, or operating agreements of the Released Parties, or under applicable law; or (2) any rights which are not waivable as a matter of law. In addition, nothing in this Release prevents me from filing, cooperating with, or participating in any proceeding before the Equal Employment Opportunity Commission, the Department of Labor, or any other government agency, except that I hereby waive my right to any monetary benefits in connection with any such claim, charge or proceeding. I hereby represent and warrant that, other than the Excluded Claims, I am not aware of any claims I have or might have against any of the Released Parties that are not included in the Released Claims.

I acknowledge that I am knowingly and voluntarily waiving and releasing any rights I may have under the ADEA. I also acknowledge that the consideration given for the Released Claims is in addition to anything of value to which I was already entitled. I further acknowledge that I have been advised by this writing, as required by the ADEA, that: (1) the Released Claims do not apply to any rights or claims that arise after the date I sign this Release; (2) I should consult with an attorney prior to signing this Release (although I may choose voluntarily not to do so); (3) I have forty-five (45) days to consider this Release (although I may choose to voluntarily to sign it sooner); (4) I have seven (7) days following the date I sign this Release to revoke it by providing written notice to the General Counsel of my employer or of Jazz Pharmaceuticals plc; and (5) this Release will not be effective until the date upon which the revocation period has expired unexercised, which will be the eighth day after I sign this Release (the "***Release Effective Date***").

I have received with this Release a written disclosure of all of the information required by the ADEA, including without limitation a list of the job titles and ages of all employees who were terminated in this group termination and the ages of all employees in the same job classification or organizational unit who were not terminated, along with information on the eligibility factors used to select employees for the group termination and any time limits applicable to this group termination program.

I acknowledge that I have read and understand Section 1542 of the California Civil Code which reads as follows: **"A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her must have materially affected his or her settlement with the debtor."** I hereby expressly waive and relinquish all rights and benefits under that section and any law of

any jurisdiction of similar effect with respect to my release of any claims hereunder, including but not limited to any unknown or unsuspected claims.

I acknowledge that I must sign and return this Release to the Company so that it is received not later than forty-five (45) days following the date this Release and the ADEA disclosure form is provided to me.

EXECUTIVE

Name: _____

Date: _____

EXHIBIT C

RELEASE AGREEMENT (“*RELEASE*”)

I understand and agree completely to the terms set forth in the Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (the “*Plan*”).

I understand that this Release, together with the Plan, constitutes the complete, final and exclusive embodiment of the entire agreement between the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company that is not expressly stated therein. Certain capitalized terms used in this Release are defined in the Plan.

I hereby confirm my obligations under my *Employee Confidential Information and Inventions Agreement* with the Company.

I hereby represent that I have been paid all compensation owed and for all hours worked, I have received all the leave and leave benefits and protections for which I am eligible, pursuant to the federal Family and Medical Leave Act, the California Family Rights Act, or any other applicable law or leave of absence policy, and I have not suffered any on-the-job injury for which I have not already filed a claim for workers compensation benefits.

In exchange for the consideration provided to me by this Release that I am not otherwise entitled to receive, I hereby generally and completely release Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., my employer entity (if not Jazz Pharmaceuticals, Inc.), and their respective current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, parent and subsidiary entities, insurers, affiliates, and assigns (collectively, the “***Released Parties***”) of and from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring prior to my signing this Release (collectively, the “***Released Claims***”).

The Released Claims include, but are not limited to: (1) all claims arising out of or in any way related to my employment, or the termination of that employment; (2) all claims related to my compensation or benefits from my employer (or any parent or subsidiary entities or affiliates of my employer), including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in Jazz Pharmaceuticals plc or any of its parent or subsidiary entities or affiliates; (3) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (4) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (5) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys’ fees, or other claims

arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the California Labor Code (as amended), the California Fair Employment and Housing Act (as amended), the Pennsylvania Equal Pay Law, the Pennsylvania Wage Payment and Collection Law, the City of Philadelphia Fair Practices Code, and the Pennsylvania Human Relations Act.

Notwithstanding the foregoing, the following are not included in the Released Claims (the "***Excluded Claims***"): (1) any rights or claims for indemnification I may have pursuant to any written indemnification agreement with any of the Released Parties to which I am a party, the charter, bylaws, or operating agreements of the Released Parties, or under applicable law; or (2) any rights which are not waivable as a matter of law. In addition, nothing in this Release prevents me from filing, cooperating with, or participating in any proceeding before the Equal Employment Opportunity Commission, the Department of Labor, or any other government agency, except that I hereby waive my right to any monetary benefits in connection with any such claim, charge or proceeding. I hereby represent and warrant that, other than the Excluded Claims, I am not aware of any claims I have or might have against any of the Released Parties that are not included in the Released Claims.

I acknowledge that I have read and understand Section 1542 of the California Civil Code which reads as follows: **"A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her must have materially affected his or her settlement with the debtor."** I hereby expressly waive and relinquish all rights and benefits under that section and any law of any jurisdiction of similar effect with respect to my release of any claims hereunder, including but not limited to any unknown or unsuspected claims.

I acknowledge that I must sign and return this Release to the Company so that it is received not later than fourteen (14) days following the date it is provided to me.

EXECUTIVE

Name: _____

Date: _____

EXHIBIT 21.1

Subsidiaries of the Registrant

Name of Subsidiary	State or Jurisdiction of Incorporation or Organization
Jazz Pharmaceuticals Ireland Limited	Ireland
Jazz Financing I Limited	Ireland
Jazz Capital Limited	Ireland
Jazz Pharmaceuticals, Inc.	Delaware
Jazz Pharmaceuticals Holdings Inc.	Delaware
Jazz Pharmaceuticals Europe Holdings Limited	Gibraltar
EUSA Pharma SAS	France
EUSA Pharma Holdings SAS	France
Jazz Pharmaceuticals Lux S.à.r.l.	Luxembourg
Jazz Pharmaceuticals Italy S.r.l.	Italy
Gentium S.r.l.	Italy

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Jazz Pharmaceuticals plc:

We consent to the incorporation by reference in the registration statements (No. 333-202269, No. 333-194131, No. 333-186886 and No. 333-179075) on Form S-8 of Jazz Pharmaceuticals plc of our reports dated February 23, 2016, with respect to the consolidated balance sheets of Jazz Pharmaceuticals plc as of December 31, 2015 and 2014, and the related consolidated statements of income, comprehensive income (loss), shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2015, and the related financial statement schedule, and the effectiveness of internal control over financial reporting as of December 31, 2015, which reports appear in the December 31, 2015 annual report on Form 10-K of Jazz Pharmaceuticals plc.

/s/ KPMG

Dublin, Ireland
February 23, 2016

Exhibit 31.1

CERTIFICATION

I, Bruce C. Cozadd, certify that:

1. I have reviewed this Annual Report on Form 10-K of Jazz Pharmaceuticals public limited company;

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

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

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

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

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

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

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

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

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

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

Date: February 23, 2016

By: /s/ Bruce C. Cozadd

Bruce C. Cozadd
Chairman and Chief Executive Officer and Director

Exhibit 31.2

CERTIFICATION

I, Matthew P. Young, certify that:

1. I have reviewed this Annual Report on Form 10-K of Jazz Pharmaceuticals public limited company;

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

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

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

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

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

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

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

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

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

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

Date: February 23, 2016

By: /s/ Matthew P. Young

Matthew P. Young
Executive Vice President and Chief Financial Officer

Exhibit 32.1

CERTIFICATION[(1)]

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), Bruce C. Cozadd, Chief Executive Officer of Jazz Pharmaceuticals public limited company (the "Company"), and Matthew P. Young, Executive Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2015, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Date: February 23, 2016

/s/ Bruce C. Cozadd

Bruce C. Cozadd
Chairman and Chief Executive Officer and Director

/s/ Matthew P. Young

Matthew P. Young
Executive Vice President and Chief Financial Officer

(1) This certification accompanies the Annual Report on Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Jazz Pharmaceuticals public limited company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing. A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to Jazz Pharmaceuticals public limited company and will be retained by Jazz Pharmaceuticals public limited company and furnished to the Securities and Exchange Commission or its staff upon request.