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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, 2016

or

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

For the transition period from to

Commission File Number: 001-33500

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, 2016, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $5,545,347,783 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 21,264,016 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 21, 2017, a total of 59,742,232 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 2017 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
2016 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 U.S. and/or other countries, including the following: Jazz Pharmaceuticals®, Xyrem® (sodium oxybate) oral solution, Erwinaze® (asparaginase *Erwinia chrysanthemi*), Erwinase®, Defitelio® (defibrotide sodium), Defitelio® (defibrotide), Prialt® (ziconotide) intrathecal infusion, CombiPlex® and Vyxeos™. This report also includes trademarks, service marks and trade names of other companies. Trademarks, service marks 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, and currently marketed 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 sodium)**, a product approved in the U.S. for the treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome, or SOS, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT, and in Europe (where it is marketed as Defitelio® (defibrotide)) for the treatment of severe VOD in adults and children undergoing 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 and new geographic markets;

- Acquiring or licensing rights to 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	Excessive sleepiness, or ES, in obstructive sleep apnea, or OSA	Patient enrollment in two Phase 3 trials completed in third quarter of 2016; expect preliminary data by end of first quarter of 2017; subject to results of trials, plan to submit a new drug application, or NDA, to the FDA in late 2017
JZP-110	ES in narcolepsy	Patient enrollment in Phase 3 trial completed in fourth quarter of 2016; expect preliminary data in second quarter of 2017; subject to results of trial, plan to submit an NDA to the FDA in late 2017
JZP-110	ES in Parkinson's disease	First patient enrolled in Phase 2 trial in first quarter of 2017
Xyrem	EDS and cataplexy in pediatric narcolepsy patients with cataplexy	Patient enrollment in Phase 3 trial completed in fourth quarter of 2016; subject to results of trial, expect to submit a supplemental NDA, or sNDA, and pediatric written request report to the FDA in fourth quarter of 2017
JZP-507	EDS and cataplexy in narcolepsy	Expect to submit an NDA to the FDA by first quarter of 2018
JZP-258	EDS and cataplexy in narcolepsy	Expect to initiate Phase 3 trial in the European Union, or EU, and U.S. in first quarter of 2017; subject to results of trial, expect to submit an NDA to the FDA in 2019
Oxybate once-nightly dosing	Narcolepsy	Program progressing; evaluation of deuterated oxybate and other formulation options continues as part of once-nightly development process
Hematology/Oncology		
Vyxeos (CPX-351)	High-risk acute myeloid leukemia, or AML	Initiated a rolling submission of an NDA to the FDA in third quarter of 2016; expect to complete the NDA submission by end of first quarter of 2017; expect to submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, in second half of 2017
Defibrotide	Prevention of VOD in high-risk patients following HSCT	First patient enrolled in Phase 3 trial in first quarter of 2017
Defibrotide	Prevention of acute Graft versus Host Disease, or aGvHD, following HSCT	Expect to initiate Phase 2 proof of concept trial in fourth quarter of 2017
Asparaginase	ALL and other hematologic disorders	Evaluation of early-stage product candidates

Our Commercialized Products

Xyrem

Xyrem is the only treatment approved by the FDA and marketed for both EDS and cataplexy in patients with narcolepsy. Sodium oxybate, the active pharmaceutical ingredient, or API, 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. We believe that fewer than half of those people have been definitively diagnosed with narcolepsy. In the fourth quarter of 2016, the average number of active Xyrem patients in the U.S. was approximately 12,900 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 2016, net product sales of Xyrem were $1,107.6 million, which represented 75% of our total net product sales.

We promote Xyrem in the U.S. through a specialty sales force of approximately 95 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 sent us notices that they had filed abbreviated new drug applications, or ANDAs, with the FDA seeking approval to market a generic version of Xyrem, and we filed patent lawsuits against each of these companies in the District Court for New Jersey, or District Court. In the second quarter of 2016, we settled two of these lawsuits, granting the settling ANDA applicants a license to manufacture, market and sell their generic versions of Xyrem on or after

December 31, 2025, or earlier depending on the occurrence of certain events. In 2016, the District Court consolidated all of our pending patent litigation against West-Ward Pharmaceuticals Corp., formerly known as Roxane Laboratories, Inc., or Roxane, with the exception of the case filed against Roxane in August 2016, and set the consolidated case for trial in the second quarter of 2017. In the first quarter of 2017, the District Court bifurcated and stayed the part of the consolidated case involving the patents on the Xyrem distribution system, or REMS patents. We cannot predict the timing or outcome of this or the other ANDA litigation proceedings against the remaining non-settling ANDA filers, which have been consolidated as one case in the District Court, with no trial date set. In July 2016, the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO, issued final decisions that the claims of six of seven REMS patents are unpatentable; if the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled, and we will not be able to enforce these patents. For a description of these legal proceedings, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

On January 17, 2017, the FDA announced approval of Roxane's ANDA for a generic version of Xyrem. The FDA's letter approving Roxane's ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product. Roxane's approval also includes a waiver that permits Roxane to use a separate REMS program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. On January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal Pharmaceuticals, or Amneal, and one for Ohm Laboratories Inc., formerly known as Ranbaxy, Inc., or Ranbaxy.

The timing of any potential commercial launch of a generic version of Xyrem is uncertain. While the FDA has approved or tentatively approved ANDAs seeking to market generic versions of Xyrem and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs, we do not believe a launch by an ANDA filer is likely to occur prior to either a date agreed in a settlement agreement between us and such ANDA filer or a District Court, or potentially an appellate court, decision in our ongoing patent litigation. We expect that the launch of a generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, would have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects. For further discussion regarding the risks associated with FDA approval of the Roxane ANDA, tentative approval of the Amneal and Ranbaxy ANDAs, potential approval or tentative approval of additional ANDAs and the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, as well as other risks and 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 API for Xyrem is manufactured for us by a single source supplier. The finished product for Xyrem is manufactured both by us in our facility in Ireland, where we commenced manufacturing in the third quarter of 2016, and by our U.S.-based Xyrem supplier. For more information regarding Xyrem supply, see "Business—Manufacturing" in this Part I, Item 1 and the risk factor under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, 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.

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 21 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 22 U.S. patents relating to 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. The American Cancer Society estimates that between 5,000 to 6,000 new cases of ALL will be diagnosed in the U.S. in 2017. Based on data from the U.S. National Cancer Institute and the U.S. Census Bureau available in 2015, we estimate that approximately 50% of ALL patients were diagnosed under age 15 and approximately 20% were diagnosed between 15 and 39 years of age. 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. 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.

In 2016, net product sales of Erwinaze were $200.7 million, which represented 14% of our total net product sales.

We promote Erwinaze in the U.S. through a specialty sales force of approximately 55 sales professionals, who also promote Defitelio in the U.S. 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 28 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 18 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. Our license and manufacturing agreement with PBL expires in December 2020, subject to automatic five-year extensions unless terminated by either party in writing by December 2018. Either party has the right to terminate the agreement in the event of the other party's uncured material breach or insolvency. For more information regarding Erwinaze supply, see "Business—Manufacturing" in this Part I, Item 1 and the risk factor under the heading *"The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, 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, the API 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, also referred to as SOS, a blockage of the small vessels in the liver, that can lead to liver failure and potentially result in significant dysfunction in other organs such as the kidneys and lungs. 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 also the only approved treatment for this potentially life-threatening condition in the EU. We launched Defitelio in certain European countries beginning in 2014 and continue to launch the product in additional European countries on a rolling basis. 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 to eventually 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.

In March 2016, the FDA approved our NDA for Defitelio for the treatment of adult and pediatric patients with VOD with renal or pulmonary dysfunction following HSCT. We launched Defitelio in the U.S. shortly after FDA approval, and our U.S. commercial launch is still at an early stage.

In 2016, Defitelio/defibrotide product sales were $109.0 million, which represented 7% 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 made milestone payments of $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, paid in the fourth quarter of 2015; and (ii) an additional $150.0 million upon FDA approval of defibrotide for VOD, paid in the second quarter of 2016.

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 versus host disease, or GvHD, another potentially fatal complication of HSCT that afflicts up to 50% of all donor transplant patients. We are also developing defibrotide for other potential indications. For more information regarding defibrotide development, see “Business—Research and Development” in this Part I, Item 1.

The drug substance defibrotide was developed and is manufactured in our facility in Italy. 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 “*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers’ failure to comply with manufacturing regulations, 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 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.

Prialt and other products

We also commercialize Prialt, 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 sell the product in the U.S., and we supply Prialt to Eisai, which sells the product in certain countries outside of the U.S.

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 in our sleep and hematology/oncology therapeutic areas.

In the sleep therapeutic area, we have the following ongoing and planned development programs:

- *JZP-110.*

  Phase 3 Clinical Trials. JZP-110 is a late-stage investigational compound being developed for potential treatment of ES in patients with narcolepsy and ES 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 are conducting two Phase 3 clinical trials in patients with ES associated with OSA and one Phase 3 clinical trial in patients with ES associated with narcolepsy. In the third quarter of 2016, we completed enrollment in the two Phase 3 clinical trials in patients with ES associated with OSA. In the fourth quarter of 2016, we completed enrollment in the Phase 3 clinical trial in patients with ES associated with narcolepsy. We enrolled approximately 890 patients in these three trials in the aggregate. We expect preliminary data from the trials in patients with ES associated with OSA by the end of the first quarter of 2017 and from the trial in patients with ES associated with narcolepsy in the second quarter of 2017. Subject to the results of these trials, we are planning to submit an NDA to the FDA in late 2017. In addition, we expect to enroll approximately 600 patients from our Phase 2 and Phase 3 clinical trials in an ongoing open label extension trial evaluating the long-term safety and maintenance of efficacy of JZP-110.

  Phase 2 Clinical Trial. We commenced patient enrollment in a Phase 2 clinical trial of JZP-110 in patients with ES associated with Parkinson's disease in the first quarter of 2017. We expect to enroll approximately 50 adult patients in this trial. There are no FDA-approved therapies for ES in Parkinson's disease in the U.S.

  Other Activities. We are also evaluating future pipeline expansion opportunities for JZP-110 in other disorders and conditions, as well as opportunities for geographic expansion.

- *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 completed enrollment in this trial in the fourth quarter of 2016 and, subject to the results of the trial, anticipate submitting an sNDA and pediatric written request report to the FDA in the fourth quarter of 2017.

- *JZP-507.*

  JZP-507 is an investigational drug candidate that in a pilot study has demonstrated bioequivalence to Xyrem with a 50% reduction in sodium content compared to Xyrem. We are investigating JZP-507 for the potential treatment of both narcolepsy with cataplexy and EDS in narcolepsy. We believe that JZP-507 would offer a clinically meaningful benefit to patients compared to Xyrem. We anticipate submitting an NDA to the FDA by the first quarter of 2018.

- *JZP-258.*

  JZP-258 is an investigational new drug candidate that contains 90% less sodium than Xyrem and is being developed for the potential treatment of both narcolepsy with cataplexy and EDS in narcolepsy. We believe that JZP-258 would offer a clinically meaningful benefit to patients compared to Xyrem. We are planning to initiate a Phase 3 clinical trial of JZP-258 in the EU and U.S. in the first quarter of 2017, and, subject to the results of this trial, we anticipate submitting an NDA to the FDA in 2019.

  Other Activities. We are also pursuing activities related to the potential development of once-nightly dosing options for narcolepsy patients that we believe would provide clinically meaningful improvements to patients compared to Xyrem. We are exploring formulation options, including an evaluation of deuterated oxybate.

In the hematology and oncology therapeutic area, we have the following ongoing and planned development activities:

- *Vyxeos (CPX-351).* Through the acquisition of Celator Pharmaceuticals, Inc., or Celator, in July 2016, or the Celator Acquisition, we acquired worldwide development and commercialization rights to Vyxeos, an investigational

product in development as a treatment for high-risk AML. Vyxeos is currently not approved as a marketed product in any jurisdiction. We initiated a rolling submission of an NDA for Vyxeos to the FDA in the third quarter of 2016. We expect to complete the NDA submission by the end of the first quarter of 2017 and to submit an MAA for Vyxeos to the EMA in the second half of 2017. Our ability to complete the NDA submission on our anticipated timing remains subject to our ability to complete necessary pre-filing activities, including chemistry, manufacturing and controls, or CMC, activities, in order to support our application for marketing approval. We also expect to conduct additional activities, including with respect to CMC, in support of approval of our NDA for Vyxeos after we complete the NDA submission.

FDA Breakthrough Therapy designation has been granted for Vyxeos for the treatment of adults with therapy-related AML or AML with myelodysplasia-related changes. Breakthrough Therapy designation is a process designed to expedite the development and review of a drug that is intended to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies on one or more clinically significant endpoints. In addition, the FDA has granted Fast Track designation to Vyxeos for the treatment of elderly patients with secondary AML. Fast Track is a designation by the FDA of an investigational drug for expedited review to facilitate development of drugs which treat a serious or life-threatening condition and fulfill an unmet medical need.

We are also assessing the potential for approval of Vyxeos in other countries and for development of Vyxeos in indications in addition to the treatment of adults with therapy-related AML or AML with myelodysplasia-related changes.

- *Defibrotide.*

  Phase 3 Clinical Trial. We enrolled the first patient in a Phase 3 clinical trial of defibrotide to evaluate the safety and efficacy of defibrotide for the prevention of VOD in high-risk and very high-risk patients following HSCT in the first quarter of 2017. We expect to enroll approximately 400 patients in this global trial and, depending on the results from the interim analysis, the enrollment could increase to up to approximately 600 patients.

  Planned Phase 2 Clinical Trial. We expect to initiate a Phase 2 proof of concept trial to evaluate defibrotide for the prevention of aGvHD following HSCT in the fourth quarter of 2017.

  Other Activities. We are pursuing regulatory approval of defibrotide in Canada. We are also evaluating the potential of defibrotide in additional post-HSCT complications, as well as investigating defibrotide's potential utility in other serious, life-threatening conditions.

- *Asparaginase Programs*. We are pursuing activities related to the development of improved products for patients with ALL, including an effective, well-tolerated and long-acting recombinant crisantaspase that could offer clinically meaningful benefits compared to Erwinaze. In addition, in July 2016, we entered into an agreement with Pfenex Inc., or Pfenex, under which Pfenex granted us worldwide rights to develop and commercialize multiple early-stage hematology product candidates. The agreement includes an option for us to negotiate a license for a recombinant pegaspargase product candidate with Pfenex.

We recorded research and development expenses of $162.3 million, $135.3 million and $85.2 million in 2016, 2015 and 2014, respectively. We also recorded charges of $23.8 million, $0.0 million and $202.6 million to in-process research and development in 2016, 2015 and 2014, 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, Defitelio and Prialt directly to physicians in specialties appropriate for each product. Outside of the U.S., our hematology and oncology sales force has approximately 28 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 promote Defitelio along with

Erwinaze to many hematology and oncology specialists who operate in the same hospitals, and we believe that we benefit from operational synergies from this overlap. 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.

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 pharmaceutical companies for product and product candidate acquisition and in-licensing opportunities. These competitors include other specialty pharmaceutical companies and established companies that may have a competitive advantage over us due to their size and financial resources.

We also face competition, and may in the future face additional competition, from manufacturers of generic drugs, including in connection with the FDA's recent approval and tentative approvals of generic versions of Xyrem. 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 some 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 products face competition as described below:

- *Xyrem*. Xyrem is the only product approved by the FDA and currently marketed in the U.S. for the treatment of both cataplexy and EDS in patients with narcolepsy. On January 17, 2017, the FDA announced approval of Roxane's ANDA for a generic version of Xyrem. The FDA's letter approving Roxane's ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product. Roxane's approval also includes a waiver that permits Roxane to use a separate REMS program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. On January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal and one for Ranbaxy, and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs. However, the timing of any potential commercial launch of a generic version of Xyrem is uncertain. We do not believe a launch by an ANDA filer is likely to occur prior to either a date agreed in a settlement agreement between us and such ANDA filer or a District Court, or potentially an appellate court, decision in our ongoing patent litigation. For further discussion of ongoing patent litigation and related proceedings, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K and the risk factor under the heading "*The approval and launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem*" in Part I, Item 1A of this Annual Report on Form 10-K. For further discussion regarding the risks associated with FDA approval of the Roxane ANDA, tentative approval of the Amneal and Ranbaxy ANDAs, potential approval or tentative approval of additional ANDAs and the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, as well as other risks and 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.
- 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, even though 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 of SSRIs, while loss of sleep is a commonly reported side effect of SNRIs. These side effects may be problematic for patients with narcolepsy.

The only other products both approved by the FDA and currently marketed 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 wakefulness promoting agents, including Provigil, its generic equivalents and Nuvigil, which are administered during the day.

We are also aware of products being developed by others for use as treatment options in cataplexy and/or EDS in patients with narcolepsy, including a product to treat adult patients with narcolepsy with or without cataplexy that recently received marketing approval in Europe. While this product is currently not approved by the FDA for marketing in the U.S. or, to our knowledge, subject to a pending application for such approval, the receipt of marketing approval and commercialization of this product in the U.S. for the treatment of narcolepsy, or marketing approval and commercialization of other products currently being developed for the treatment of narcolepsy, could, depending on the targeted patient population, negatively impact our ability to maintain and grow sales of Xyrem.

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, Avadel Pharmaceuticals plc, or Avadel, 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 is conducting a Phase 3 pivotal trial pursuant to an FDA-approved special protocol assessment. If Avadel 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 compete directly with Xyrem and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

- *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. Any potential new treatment could reduce the market for Erwinaze. As a biologic product, Erwinaze also faces potential competition from biosimilar products.
- *Defitelio*. Defitelio is the only approved treatment in the U.S. for the treatment of adult and pediatric patients with VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT and the only approved treatment in the EU for severe VOD in adults and children undergoing 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.
- *Vyxeos*. AML, a cancer indication for which we intend to commercialize Vyxeos, has established therapies. A key consideration in the treatment of AML patients is the patient's suitability for chemotherapy. The patient population studied in the Vyxeos Phase 3 clinical trial included AML patients deemed able to tolerate chemotherapy. There are existing options for the treatment of newly-diagnosed AML patients who can tolerate chemotherapy, such as cytarabine in combination with an anthracycline (i.e., daunorubicin), known as 7+3. In addition, we are aware of several other products in development for use as treatment options for AML patients, such as targeted agents (FLT-3, IDH-1, IDH-2, CD-33, CAR T-cell). Some of the patient populations being studied for these products in development overlap with the patient population studied in the Vyxeos Phase 3 clinical trial.

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 to, or uncertainties around, 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.

For more information on the competitive risks we face generally, see the risk factor under the heading "*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"* in Part I, Item 1A of this Annual Report on Form 10-K.

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 and Defitelio are 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 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 in 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 21 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 by product, attributed to U.S. and non-U.S. sources and attributed to customers who represented at least 10% of our total revenues in each of 2016, 2015 and 2014, 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; Ewing, New Jersey; Vancouver, British Columbia; Oxford, United Kingdom; Lyon, France; Villa Guardia (Como), Italy; Athlone, Ireland; and elsewhere in Europe. For a discussion of risks related to our operations, see the risk factors under the headings "Risks Related to Our Business," "Risks Related to Our Industry" and "Risks Related to Our Financial Condition and Results" 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 received FDA approval of our manufacturing and development facility in Ireland in June 2016, and we commenced commercial operations at this facility in the third quarter of 2016. We are using this facility for the manufacture of Xyrem and

plan to also use this facility for the manufacture of development-stage product candidates. However, other than our Ireland facility and our manufacturing plant in Italy where we produce the defibrotide drug substance, we currently do not have our own commercial manufacturing capability for our products, product candidates, or their APIs, or packaging capability. As a result, our ability to develop and supply products in a timely and competitive manner depends primarily on third party suppliers being able to meet our ongoing commercial and clinical trial needs. We have a single source of supply for most of our marketed products, product candidates and their APIs. We and our manufacturers may 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. These difficulties can be heightened when we or our suppliers are required to produce finished product at commercial scale or to produce increased quantities to meet growing demand. In addition, we and our suppliers are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and other equivalent rules and regulations prescribed by non-U.S. regulatory authorities. If we or any of our suppliers encounter these or any other manufacturing, quality or compliance difficulties with respect to any of our products, particularly Xyrem and Erwinaze, because we maintain limited inventories for these products, we may be unable to meet commercial demand for such products.

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 API of Xyrem. Siegfried was approved by the FDA as our supplier in November 2011 and now supplies sodium oxybate to our U.S.-based manufacturer of Xyrem and, through a Siegfried affiliate in Europe, to our Ireland manufacturing facility. 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 2021, 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 establishes the general terms and conditions pursuant to which Patheon will provide manufacturing services for drug products, including Xyrem and Defitelio, as specified by us in product agreements entered into from time to time. Although we have commenced manufacturing of Xyrem in our Ireland facility, we expect to rely on Patheon as our U.S.-based supplier of Xyrem for the foreseeable future. However, 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. Accordingly, we require DEA quotas for Siegfried, our U.S.-based sodium oxybate supplier, to procure sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to obtain the sodium oxybate from Siegfried in order to manufacture and 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. For the last few years, our suppliers were allocated only a portion of the published annual aggregate quota for the API. If one or more ANDA filers were to begin manufacturing a generic sodium oxybate product, generic manufacturers would need to obtain a portion of the annual aggregate API quota, which could decrease the DEA quota allocation obtained on our behalf by Siegfried and Patheon. 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 this Part I, Item 1.

Erwinaze. Erwinaze is exclusively licensed to us, and manufactured for us, by PBL, which is our sole supplier for Erwinaze. Our license and manufacturing agreement with PBL expires in December 2020, subject to automatic five-year extensions unless terminated by either party in writing by December 2018. 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. The Erwinaze BLA includes a number of post-marketing commitments related to the manufacture of Erwinaze by PBL.

In January 2017, the FDA issued a warning letter to PBL citing significant violations of cGMP for finished pharmaceuticals and significant deviations from cGMP for APIs. We cannot predict if or when PBL will correct the violations

and deviations to the satisfaction of the FDA. Any failure to do so could result in the FDA refusing admission of Erwinaze into the U.S., as well as additional enforcement actions by the FDA and other regulatory entities.

Moreover, the current manufacturing capacity for Erwinaze is 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 and to address the production delays, quality challenges and related regulatory scrutiny. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build product inventory levels that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues. We have experienced product quality, manufacturing and inventory challenges that have resulted, and may continue to result, in disruptions in our ability to supply certain markets, including the U.S., from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. Most recently, we experienced supply interruptions of Erwinaze in the U.S. and other countries in the third and fourth quarters of 2016. We cannot predict whether the FDA's required remediation activities in connection with the warning letter will further strain manufacturing capacity and adversely affect Erwinaze supply, particularly in light of our extremely limited product inventory. As capacity constraints and supply disruptions continue, whether as a result of continued quality or other manufacturing issues, regulatory issues or otherwise, we will be unable to build a desired excess level of product inventory, our ability to supply the market may continue to be compromised and physicians' decisions to use Erwinaze have been, and in the future may continue to be, negatively impacted.

Under our agreement with PBL, 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.

For further information regarding the risks we face with respect to the manufacture and supply of Erwinaze, see the risk factor under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, 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.

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 under a specific product agreement entered into under our master agreement with Patheon. Patheon is the sole provider of our commercial and clinical supply of Defitelio; however, we are not required to purchase Defitelio exclusively from Patheon. In 2015, the FDA issued an FDA Form 483 to Patheon Italia that included observations related to the Ferentino, Italy facility that manufactures Defitelio. Although we are advised that Patheon Italia remediated the observations to the FDA's satisfaction, the FDA will continue to inspect and evaluate this facility for ongoing compliance with applicable requirements. If Patheon does not or is not able to supply us with Defitelio 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 anticipated revenues from Defitelio 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.

Product Candidates. Certain of our product candidates and their APIs are supplied to us by third party contract manufacturers. To conduct our ongoing and any future clinical trials of, complete marketing authorization submissions for, and potentially launch our product candidates, we need to have sufficient quantities of product manufactured. In addition, to obtain FDA approval of any product candidate, we or our supplier or suppliers for that product will need to obtain approval by the FDA to manufacture and supply product, in some cases based on qualification data provided to the FDA as part of an NDA submission. Any failure of us or a supplier to obtain FDA approval to manufacture and supply product or any delay in receiving, or failure to receive, adequate supplies of a product on a timely basis or in accordance with applicable specifications could negatively impact our ability to successfully launch and commercialize products and generate sales of products at the levels we expect.

Vyxeos is manufactured using Celator's CombiPlex technology. CombiPlex products represent formulations with increased manufacturing complexities associated with producing drug delivery vehicles encapsulating two or more drugs that are maintained at a fixed ratio and, in the case of Vyxeos, two drugs that are co-encapsulated in a freeze-dried format. Vyxeos is manufactured by Baxter Oncology GmbH, which is a sole source supplier from a single site location.

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 "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, 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 acquire or obtain licenses to 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.* We have 22 patents relating to Xyrem that expire at various times from December 2019 to March 2033, of which 18 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, five are formulation patents expiring between December 2019 and July 2020; seven are REMS patents, 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 three are method of administration patents relating to a drug-drug interaction, or DDI, between Xyrem and divalproex sodium 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. We have received a pediatric written request from the FDA, and we intend to submit the results of a pediatric clinical study in response to this request. If the FDA determines that the submission meets the terms and conditions of the written request, then six months of pediatric exclusivity will be added to the term of each patent listed for Xyrem in the Orange Book. 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 sent us notices that they had filed ANDAs with the FDA seeking approval to market a generic version of Xyrem, and in January 2017, the FDA granted approval of one, and tentative approvals of two, of these ANDAs. We filed patent lawsuits against each of these seven companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents, and we have entered into settlement agreements with two of these companies.

  In July 2016, the PTAB issued final decisions that the claims of six of seven REMS patents are unpatentable. We filed a notice of appeal of these decisions on February 22, 2017. If the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled, and we will not be able to enforce these patents. In March 2016, the PTAB partially instituted an inter partes review on a seventh REMS patent, declining to review 25 of 28 claims. A PTAB decision on the three claims that were tried is expected before the end of the first quarter of 2017.

  In September 2016, Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, submitted a Citizen Petition to the FDA requesting that, for safety reasons, the FDA refuse to approve any sodium oxybate ANDA with a proposed package insert or REMS that omits the portions of the Xyrem package insert and the Xyrem REMS that instruct prescribers on adjusting the dose of the product when it is co-administered with divalproex sodium (also known as valproate or valproic acid). On January 17, 2017, the FDA granted the Citizen Petition with respect to the Xyrem package insert. The FDA concluded that it will not approve any sodium oxybate ANDA referencing Xyrem that does not include in its package insert the portions of the currently approved Xyrem package insert related to the drug-drug interaction with divalproex sodium. The FDA stated that it did not need to reach the question of whether the drug-drug interaction information could have been excluded from the generic sodium oxybate REMS materials because it was approving a REMS in connection with a sodium oxybate ANDA including that information. Our Xyrem patents include three patents relating to the safe and effective use of Xyrem by decreasing the dose of Xyrem when used concomitantly with divalproex sodium, or DDI patents, covering these instructions on the Xyrem package insert and Xyrem REMS. We cannot predict whether or when one or more of the ANDA filers may pursue a challenge to the FDA's response to the Citizen Petition or whether any such challenges would be successful.

  We cannot predict whether we will be able to maintain the validity of any of our patents or will otherwise obtain a judicial determination that a generic sodium oxybate product, its package insert or the generic sodium oxybate REMS

infringes any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem or instead require the ANDA filers to pay damages in the form of lost profits or a reasonable royalty.

For a description of the foregoing matters, see “Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K, “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.

- *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. None of these patents are listed in the Orange Book.
- *Erwinaze*. 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 this Part I, Item 1.

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

- *Vyxeos.* Vyxeos and its related technologies are claimed in multiple U.S. and non-U.S. patents. We acquired rights to Vyxeos, the CombiPlex technology platform and related technologies in the Celator Acquisition. We have a portfolio of U.S. and non-U.S. patents and patent applications relating to Vyxeos, including three U.S. formulation patents expiring between September 2027 and April 2029 and two U.S. patents covering the CombiPlex technology platform expiring in January 2027, subject to any patent term extensions.
- *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 in September 2015. Two U.S. method of use patents covering treatment of sleep-related conditions will expire in June 2026 and August 2027, subject to any patent term extension.
- *JZP-507 and JZP-258.* Certain patents and patent applications relating to Xyrem cover JZP-507 and JZP-258. In addition, JZP-507 and JZP-258 are claimed in formulation patents that will expire in January 2033.

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 trade secrets and 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. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality agreements with our employees, consultants, advisors and partners. Nevertheless, 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. In addition, if our employees, consultants, advisors or partners develop inventions or processes independently, or jointly with us, that may be applicable to our products, 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. Enforcing a claim that a third party illegally obtained, or 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.

Failure to obtain or maintain patent and/or 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, and pending trademark and service mark applications, in the U.S. and elsewhere in the world to further protect the proprietary position of our products.

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 development 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, the drug is typically tested to assess metabolism, pharmacokinetics, pharmacological actions and side effects associated with increasing doses. 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. In addition, Phase 4, or post-approval, clinical trials may be required by the FDA and are used to gain additional safety data or to document a clinical benefit in the case of products approved under Accelerated Approval regulations.

The FDA performs an initial review of 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 current goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or 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. PDUFA was first authorized by the U.S. Congress in 1992, and, among other things, permits the FDA to collect "user fees" from pharmaceutical manufacturers to fund the drug approval process. These user fees have been reauthorized by the U.S. Congress four times since 1992, most recently in 2012 with the authorization of PDUFA V. PDUFA V

expires on September 30, 2017, and we cannot predict whether user fees will be reauthorized or on what terms, or the impact of any failure to reauthorize user fees on the FDA's PDUFA goal dates.

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 under "Business—Government Regulation—*The Hatch-Waxman Act*" below and in the risk factors under the headings "*The 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*" and "Risks Related to Our Intellectual Property" in Part I, Item 1A of this Annual Report on Form 10-K.

During the review of a marketing application, the FDA 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 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 and grants a related authorization. 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 EC decides, following a related opinion from the EMA and 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 is anticipated to enter into force in mid-2018. 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 reference listed drug, or RLD. Under this path, the applicant is permitted to rely to some degree on the FDA’s finding that the RLD 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 RLD 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 RLD (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 RLD the FDA previously found to be safe and effective.

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 approval is sought after patent expiration is called a “Paragraph III Patent Certification.” A certification that the new product will not infringe the RLD’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 RLD 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 RLD. 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 another period of regulatory exclusivity, including an exclusivity held by another ANDA filer, has not expired. 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 for damages if the NDA holder ultimately prevails in the patent litigation.

We intend to vigorously defend any patents for our approved products, including our Orange Book-listed patents. Seven companies sent us notices of Paragraph IV Certification that they had 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 filed patent lawsuits against each of these companies seeking to prevent the introduction of a generic version of Xyrem that would infringe our patents. In the second quarter of 2016, we settled two of these lawsuits, granting the settling ANDA applicants a license to manufacture, market and sell their generic versions of Xyrem on or after December 31, 2025, or earlier depending on the occurrence of certain events. On January 17, 2017, the FDA announced approval of Roxane's ANDA for a generic version of Xyrem. The FDA's letter approving Roxane's ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product.

On January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal and one for Ranbaxy. However, the timing of any potential commercial launch of a generic version of Xyrem is uncertain. While the FDA has approved or tentatively approved ANDAs seeking to market generic versions of Xyrem and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs, we do not believe a launch by an ANDA filer is likely to occur prior to either a date agreed in a settlement agreement between us and such ANDA filer or a District Court, or potentially an appellate court, decision in our ongoing patent litigation. If we prevail at trial or on appeal, we cannot guarantee that the court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem. Instead, the court may order an ANDA filer that is found to infringe to pay damages in the form of lost profits or a reasonable royalty, which could be significant. Additional ANDAs seeking to market a generic version of Xyrem and/or Section 505(b)(2) NDAs seeking approval of a product that is similar, but not identical, to Xyrem, may be filed in the future. For example, Avadel, a company that is using its proprietary technology for delivery of a sodium oxybate formulation that is undergoing clinical trials, has indicated that it intends to seek approval of its product candidate using a 505(b)(2) NDA approval pathway. For a further description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K, 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.

Section 505-1(i)(1) of the FDCA generally provides that (i) an ANDA that references a drug subject to a REMS with ETASU is required to have a REMS with the same elements as the RLD and (ii) the ANDA drug and the RLD shall use a single shared system to assure safe use. However, the FDA may waive this requirement for a single shared system and approve an ANDA with a separate REMS with differing but comparable aspects of ETASU 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 RLD 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 RLD before granting a waiver of the single shared system requirement. The FDCA further states that a REMS shall not be used by the NDA holder to block or delay generic drugs from entering the market.

The FDA approval of the Roxane ANDA on January 17, 2017 includes a waiver of the shared-REMS requirement that permits Roxane to use a separate REMS program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. In connection with the waiver, FDA issued a statement that it considers the generic sodium oxybate REMS to have the same ETASU as the Xyrem REMS and operationalizes those elements in a comparable manner to achieve the same level of safety as the Xyrem REMS. Specifically, the FDA stated that both the Xyrem REMS and the generic sodium oxybate REMS require that (1) healthcare providers who prescribe the drug be specially certified; (2) the drug be dispensed only by pharmacies that are specially certified; and (3) the drug be dispensed and shipped only to patients who are enrolled in the REMS program with documentation of safe use conditions. However, the FDA stated that the generic sodium oxybate REMS, unlike the Xyrem REMS, permits multiple

certified pharmacies and multiple databases that are connected via an electronic “switch” system. The generic sodium oxybate REMS also requires the certified pharmacies in its system to contact the Xyrem REMS program to verify that the patient has no other active prescriptions for Xyrem that overlap with the generic prescription to be filled and to identify any patient and prescriber disenrollments from the Xyrem system for suspected abuse, misuse and diversion. We were not involved in development of the generic sodium oxybate REMS and were not consulted regarding any features of the waiver-granted REMS. We will evaluate whether the FDA’s waiver of the requirement for a single, shared system REMS in connection with approval and tentative approval of the ANDAs meets the conditions for such a waiver under applicable law and, to the extent that we determine that the waiver was not permissible under applicable law, will evaluate potential challenges to the FDA’s waiver decision. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the FDA’s waiver of the single shared system REMS requirement, its approval and tentative approval of generic versions of Xyrem or the consequences of distribution of sodium oxybate through the generic sodium oxybate REMS approved by the FDA. We expect that 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 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.

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 RLD. 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 until March 2023, seven years from its FDA approval.

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. We believe that Erwinaze will 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 for our products 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. We completed enrollment in this trial in the fourth quarter of 2016 and, subject to the results of the trial, anticipate submitting an sNDA and pediatric written request report to the FDA in the fourth quarter of 2017.

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. It has also received orphan designation from the Korean Ministry of Food and Drug Safety for this indication. 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 impose certain post-approval requirements, 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.

A drug product approved by the FDA may also be subject to scheduling as a controlled substance under the CSA, depending on the drug's potential for abuse. Controlled substances that are pharmaceutical products are subject to a high

degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. We expect that JZP-110 will be subject to scheduling under the CSA before it can be commercially launched. At or before the time JZP-110 receives FDA approval, the FDA, the U.S. Department of Health and Human Services, or HHS, and the DEA will undertake the administrative process set out in the CSA to schedule the drug in order for the drug product to be prescribed to patients in the U.S. The CSA requires the DEA to issue an interim final order scheduling the drug within 90 days after the FDA approves the drug and the DEA receives a scientific and medical evaluation and scheduling recommendation from the HHS.

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 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 pharmacovigilance legislation, which includes requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. This legislation provides the EMA and the competent authorities of the EU member states with the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders 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 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, administrative, civil and criminal penalties, among other enforcement remedies both in the U.S. and in non-U.S. countries.

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 cGMP standards when manufacturing medicinal products and APIs, including the manufacture of APIs outside of the EU with the intention to import the APIs 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, which we refer to together as 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 "Pharmaceutical Pricing and Reimbursement" in this Part I, Item 1 and 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 and appear likely in the 115th U.S. Congress and under the Trump Administration. The nature and extent of any legislative changes to the Healthcare Reform Act are uncertain at this time. 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 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 API, 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 manufactured and procured in the U.S. in any given calendar year through a quota system and, as a result, quotas from the DEA are required in order to manufacture and package sodium oxybate and Xyrem in the U.S. Accordingly, we require DEA quotas for Siegfried, our U.S.-based sodium oxybate supplier, to procure sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to obtain the sodium oxybate from Siegfried in order to manufacture and supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, our U.S.-based sodium oxybate and Xyrem suppliers 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 more information, see the risk factor under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, 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.

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. In addition, 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. 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 Act 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. In May and October 2016 and February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to

Medicare patients and documents concerning the provision of financial assistance to Medicare patients taking drugs sold by us. The OIG has established guidelines that permit pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. If we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. For more information regarding applicable 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. In recent years, certain courts have determined that the First Amendment of the U.S. Constitution permits communications regarding off-label uses of drug products, as long as such communications are truthful and not misleading. At the beginning of 2017, the FDA released proposed rule changes and draft guidance on FDA's interpretation on the limitations of such speech. These cases and regulatory actions create additional uncertainty regarding the limits of permissible communication regarding our products.

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 governing privacy and data security. These laws include security breach notification requirements and protection of consumer health information. The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Although there are legal mechanisms to facilitate the transfer of personal data from the European Economic Area, or EEA, and Switzerland to the U.S., the decision of the European Court of Justice that invalidated the safe harbor framework on which we previously relied has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it was no longer 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 February 2016, the EC announced an agreement with the DOC to replace the invalidated safe harbor framework with a new EU-U.S. "Privacy Shield." On July 12, 2016, the EC adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the European Court of Justice in its recent ruling by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and FTC and making commitments on the part of public authorities regarding access to information.

U.S.-based companies may certify compliance with the privacy principles of the Privacy Shield. Certification to the Privacy Shield, however, is not mandatory. If a U.S.-based company does not certify compliance with the Privacy Shield, it may rely on other authorized mechanisms to transfer personal data. In September 2016, we filed for certification for our U.S.-based subsidiaries under the Privacy Shield. This certification was approved in January 2017.

The privacy and data security landscape is still in flux. In September 2016, the Irish privacy advocacy group, Digital Rights Ireland, brought an action for annulment of the EC decision on the adequacy of Privacy Shield, Case T-670/16, which is pending before the European Court of Justice. Should the European Court of Justice invalidate the Privacy Shield, it will no longer be possible to transfer data from the EU to entities in the U.S. under a Privacy Shield certification, in which case other legal mechanisms would need to be put in place.

Healthcare providers who prescribe our products and research institutions that 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, our affiliates or our agents 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.

Failure to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors and/or adverse publicity that negatively affect our business.

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 was officially adopted in April 2016 and will be applicable in May 2018, 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 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. In addition, data protection authorities of 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.

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 in the U.S. to change the healthcare system in ways that could impact our ability to sell our products profitably, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U.S. We expect to continue 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 impacting pharmaceutical product pricing that are intended to curb rising healthcare costs. These cost containment measures may include federal and state 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 through required disclosures; 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.

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.

In addition, drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny, including with respect to companies that have increased the price of products after acquiring those products from other companies. Both the U.S. House of Representatives and the U.S. Senate have conducted several 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 any government investigation with respect to our drug pricing or other business practices, we could incur significant expense and could be distracted from operation of our business and execution of our strategy. Any such investigation could also 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. For more information, see the risk factors under the headings "*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*" and "*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.

Third party payors, including governmental payors such as the Medicare and Medicaid programs, managed care organizations and private health insurers, 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 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. 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. 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 files 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 certain of our drugs to 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. Risks relating to price reporting and payment obligations are further 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. 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 Drug Rebate program also participate in the 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B 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 Drug 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, which became effective in April 2016, to implement the changes to the Medicaid rebate program under the Healthcare Reform Act. The issuance of the final regulation, as well as any other regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program, has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly 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 and grantees, 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, 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.

Similar to what is occurring inside the U.S., political, economic and regulatory developments outside of the U.S. 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. Pursuant to Directive 2011/24/EU, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The EU member states were required to implement the provisions of the Directive into their national legislation by October 2013. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This could lead to harmonization between EU member states of the criteria taken into account in the conduct of HTA and their impact on pricing and reimbursement decisions.

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 EU member states.

Any additional legislation, regulations, policies or reforms relating to the healthcare industry, pharmaceutical pricing or third party coverage and reimbursement that may be enacted in the future in the U.S., the EU or the EU member states, and any negative publicity we may experience with respect to pricing of our products or the pricing of pharmaceutical drugs generally, may negatively impact the prices that we charge for our products, including Xyrem, and our commercial opportunity and/or our revenues from sales of our products. For more information, 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.

Employees

As of February 21, 2017, we had approximately 1,040 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 acquisition of Gentium S.r.l. In July 2016, we completed the Celator 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 75.0% and 72.5% of our net product sales for the years ended December 31, 2016 and 2015. Our future plans assume that sales of Xyrem will increase, although our plans assume a slower rate of increase than in recent years. While Xyrem product sales grew from 2015 to 2016, 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 January 2017, 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 commercialization of a generic version of Xyrem, including in connection with the recent approval by the U.S. Food and Drug Administration, or FDA, of an abbreviated new drug application, or ANDA, for a generic version of Xyrem, as well as tentative approval of two additional ANDAs;
- the potential U.S. introduction of an alternative product to Xyrem for treating cataplexy and/or excessive daytime sleepiness, or EDS, in narcolepsy;
- changes to, increases of or uncertainties around regulatory restrictions, including changes to our Xyrem risk evaluation and mitigation strategy, or REMS, particularly in light of the FDA's waiver of the single shared system REMS requirement for sodium oxybate and approval of a separate generic sodium oxybate REMS;
- any increase in pricing pressure from, or restrictions on reimbursement imposed by, third party payors;
- changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing by government entities;
- operational disruptions at the Xyrem central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA;
- any supply or manufacturing problems, including any problems with our sole source Xyrem API provider;
- 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
- our U.S.-based sodium oxybate and Xyrem suppliers' ability to obtain sufficient quotas from the U.S. Drug Enforcement Administration, or DEA, to satisfy our needs for Xyrem.

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.

The approval and launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem.

Although Xyrem is protected by patents covering its manufacture, formulation, distribution system and method of use, multiple third parties have filed ANDAs seeking FDA approval of generic versions of Xyrem. In addition, we are aware of a third party that has stated that it intends to file a new drug application, or NDA, under section 505(b)(2) to market a once-nightly formulation of sodium oxybate for treatment of cataplexy and/or EDS in narcolepsy. Notwithstanding our patents, it is possible that once its application is approved, an ANDA filer or NDA filer could introduce a competing sodium oxybate product before our patents expire if it is determined that it does not infringe our patents, or 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 being held liable for damages for patent infringement. As discussed below, the FDA has approved the first ANDA for Xyrem and has tentatively approved two additional ANDAs.

Seven companies sent us notices that they had filed ANDAs with the FDA seeking approval to market a generic version of Xyrem, and we filed patent lawsuits against each of these companies in the District Court for New Jersey, or District Court. In the second quarter of 2016, we settled two of these lawsuits, granting the settling ANDA applicants a license to manufacture, market and sell their generic versions of Xyrem on or after December 31, 2025, or earlier depending on the occurrence of certain events. In 2016, the District Court consolidated all of our pending patent litigation against West-Ward Pharmaceuticals Corp., formerly known as Roxane Laboratories, Inc., or Roxane, (with the exception of the case filed against Roxane in August 2016) and set the combined consolidated case for trial in the second quarter of 2017. In the first quarter of 2017, the District Court bifurcated and stayed the part of the combined consolidated case involving the patents on the Xyrem distribution system, or REMS patents. We cannot predict the timing or outcome of this or the other ANDA litigation proceedings against the remaining non-settling ANDA filers, which have been consolidated as one case in the District Court, with no trial date set.

Certain ANDA filers 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. The PTAB instituted IPR trials with respect to patents and patent claims that are the subject of certain of these petitions. In July 2016, the PTAB issued final decisions that the claims of six of seven REMS patents are unpatentable. We filed a notice of appeal of these decisions on February 22, 2017. If the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled, and we will not be able to enforce these patents. In March 2016, the PTAB partially instituted an IPR on a seventh REMS patent, declining to review 25 of 28 claims. A PTAB decision on the three claims that were tried is expected before the end of the first quarter of 2017. For a description of these legal proceedings, 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 pending IPR or other proceeding, the outcome of any appeal of the July 2016 IPR decisions with respect to the six REMS patents or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

On January 17, 2017, the FDA announced approval of Roxane’s ANDA for a generic version of Xyrem. The FDA’s letter approving Roxane’s ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product. Roxane’s approval also includes a waiver that permits Roxane to use a separate REMS program from Xyrem, on the condition that Roxane’s waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. On January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal Pharmaceuticals, or Amneal, and one for Ohm Laboratories Inc., formerly known as Ranbaxy, Inc., or Ranbaxy, and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs.

The timing of any potential commercial launch of a generic version of Xyrem is uncertain. It is possible that Roxane or any other company that receives FDA approval of an ANDA for a generic version of Xyrem or an NDA for another sodium oxybate product could introduce a generic version of Xyrem or other sodium oxybate product before our patents expire if it is determined that any such generic version of Xyrem or sodium oxybate product does not infringe our patents, or 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 being held liable for damages for patent infringement. We cannot predict whether we will be able to maintain the validity of any of our patents or will otherwise obtain a judicial determination that a generic sodium oxybate product, its package insert or the generic sodium oxybate REMS infringes any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem or instead require the ANDA filers to pay damages in the form of lost profits or a reasonable royalty. However, we expect that the launch of a generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, would have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects. For further discussion regarding the risks associated with FDA approval of the Roxane ANDA, tentative approval of the Amneal and Ranbaxy ANDAs, potential approval or tentative approval of additional ANDAs and the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that

compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see "Business-Government Regulation-The Hatch-Waxman Act" in this Part I, Item 1 of this Annual Report on Form 10-K 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 this Part I, Item 1A.

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, Avadel Pharmaceuticals plc, or Avadel, 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 is conducting a Phase 3 pivotal trial pursuant to an FDA-approved special protocol assessment, and has indicated that it intends to seek approval of its product candidate using a 505(b)(2) NDA approval pathway, which allows companies to seek approval of a product that is similar, but not identical, to a previously-approved brand-name product. If Avadel 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 compete with Xyrem and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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 some 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. In addition, the FDA's approval of a separate REMS for generic sodium oxybate products means that such products could be distributed through multiple pharmacies. Such changes in the distribution of Xyrem may lead to negative experiences for patients, prescribers and the public that could impact acceptance of sodium oxybate as a treatment for EDS and cataplexy in narcolepsy. We expect that generic competition for Xyrem would have a material adverse effect on our business, financial condition, results of operations and growth prospects. For more information about potential competition for Xyrem, see the risk factor under the heading "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" in this Part I, Item 1A.

The 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 elements such as 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 Food and Drug Administration Amendments Act, or FDAAA. The FDAAA, which amended the Federal Food, Drug and Cosmetic Act, or FDCA, required that deemed REMS and related documents be updated to comply with the current requirements for REMS documents. In February 2015, the FDA notified Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, of the FDA's approval of the current Xyrem REMS, which includes provisions requiring distribution through a single pharmacy.

The 2015 Xyrem REMS approval letter included statements from the FDA that (i) the approval action should not be construed or understood as agreement with what the FDA stated was our position 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 (particularly now that the FDA has approved a separate REMS for the ANDA filers that contemplates interaction with the Xyrem REMS), 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 sodium oxybate competitors, make it more difficult or expensive for us to distribute Xyrem, make distribution easier for future sodium oxybate competitors, impair the safety profile of Xyrem and/or negatively affect sales of Xyrem. Moreover, a sodium oxybate distribution system that is less restrictive than the Xyrem REMS, such as the generic sodium oxybate REMS approved by the FDA in January 2017, may increase the risks associated

with sodium oxybate distribution, as patients, consumers and others may not differentiate generic sodium oxybate from Xyrem, or differentiate between the different REMS programs. Any negative outcomes, including but not limited to risks to the public, caused by or otherwise related to a separate generic sodium oxybate REMS, could have a significant negative impact in terms of product liability, goodwill, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, any of which could have a material adverse effect on our Xyrem revenues.

In August 2015, we implemented the current Xyrem REMS, and we have submitted and expect to continue to submit ongoing assessments as set forth in the FDA's Xyrem REMS approval letter. However, we cannot guarantee that our implementation and ongoing assessments will be satisfactory to the FDA or that the Xyrem REMS will satisfy the FDA's expectations in its 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; 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 Specialty Distribution Services, Inc., or 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 reference listed drug, or RLD, and (ii) the ANDA drug and the RLD shall use a single shared system to assure safe use. However, the FDA may waive this requirement for a single shared system and approve an ANDA with a separate REMS with differing but comparable aspects of ETASU 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 RLD 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 RLD before granting a waiver of the single shared system requirement. The FDCA further states that a REMS shall not be used by the NDA holder to block or delay generic drugs from entering the market.

In January 2017, the FDA announced approval of the Roxane ANDA and waived the shared REMS requirement. The FDA's waiver of the shared REMS requirement permits Roxane to use a separate REMS program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. In connection with the waiver, FDA issued a statement that it considers the generic sodium oxybate REMS to have the same ETASU as the Xyrem REMS and operationalizes those elements in a comparable manner to achieve the same level of safety as the Xyrem REMS. We were not involved in development of the generic sodium oxybate REMS and were not consulted regarding any features of the waiver-granted REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the FDA's waiver of the single shared system REMS requirement, its approval and tentative approval of generic versions of Xyrem or the consequences of distribution of sodium oxybate through generic sodium oxybate REMS approved by the FDA. We expect that 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.

We may face pressure to modify the Xyrem REMS, or to license or share intellectual property pertinent to the Xyrem REMS, including proprietary data required for safe distribution of sodium oxybate, in connection with the FDA's approval of the generic sodium oxybate REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the approval of the generic sodium oxybate REMS, or licensing or sharing intellectual property pertinent to our Xyrem REMS or elements of the Xyrem REMS.

In September 2016, Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, submitted a Citizen Petition to the FDA requesting that, for safety reasons, the FDA refuse to approve any sodium oxybate ANDA with a proposed package insert or REMS that omits the portions of the Xyrem package insert and the Xyrem REMS that instruct prescribers on adjusting the dose of the product when it is co-administered with divalproex sodium (also known as valproate or valproic acid). On January 17, 2017, the FDA granted the Citizen Petition with respect to the Xyrem package insert. The FDA concluded that it will not approve any sodium oxybate ANDA referencing Xyrem that does not include in its package insert the portions of the currently approved Xyrem package insert related to the drug-drug interaction with divalproex sodium. The FDA stated that it

did not need to reach the question of whether the drug-drug interaction information could have been excluded from the generic sodium oxybate REMS materials because it was approving a REMS in connection with a sodium oxybate ANDA including that information. Our Xyrem patents include three method of administration patents relating to a drug-drug interaction, or DDI patents, covering these instructions on the Xyrem package insert and Xyrem REMS. We cannot predict whether or when one or more of the ANDA filers may pursue a challenge to the FDA's response to the Citizen Petition or whether any such challenges would be successful. Likewise, we cannot predict whether we will be able to maintain the validity of any of our patents or will otherwise obtain a judicial determination that the generic sodium oxybate package insert or the generic sodium oxybate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem or instead require the ANDA filers to pay damages in the form of lost profits or a reasonable royalty.

For a description of the foregoing matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K, "Business-Government Regulation-The Hatch-Waxman Act" in Part I, Item 1 of this Annual Report on Form 10-K, and the risk factors under the headings "*The approval and launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem*" and "Risks Related to Our Intellectual Property" in this Part I, Item 1A.

The Federal Trade Commission, or 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 letter 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 ETASU 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 REMS patents should not have been listed in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or 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 Xyrem labeling 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.

The FDA has required that Xyrem's labeling 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 labeling. Warnings in the Xyrem labeling 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.

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 this Part I, Item 1A.

Risks Related to Our Business

While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products and, in the case of our product candidates, our ability to obtain regulatory approval in the U.S. and Europe and, if approved, to successfully launch and commercialize those product candidates. 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, and we have made a significant investment in Vyxeos and other product candidates, which are currently not approved as marketed products in any jurisdiction.

Erwinaze

Erwinaze (called Erwinase in markets outside the U.S.), a biologic product, is used in conjunction with chemotherapy to treat patients with acute lymphoblastic leukemia, or ALL, with hypersensitivity to *E. coli*-derived asparaginase. Erwinaze was approved by the FDA under a biologics license application, or 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 is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL, which is wholly owned by the U.K. Secretary of State for Health. Our agreement with PBL, including our license, expires in December 2020, subject to five-year extensions unless terminated by either party in writing by December 2018. We cannot predict whether the term of the agreement will be extended or, if extended, the terms of any such extension.

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 European Union's, or 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 current sales levels and to increase sales is our extremely limited inventory of Erwinaze, past supply interruptions and our need to minimize or avoid additional supply interruptions due to capacity constraints, production delays, quality or regulatory challenges and other manufacturing difficulties. See the discussion regarding Erwinaze supply issues in the risk factor under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in this Part I, Item 1A.

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 rights to Erwinaze, including if our agreement terminates at the end of its current term in December 2020, or if we otherwise fail to maintain or grow sales of Erwinaze, our growth prospects could be negatively affected.

Defitelio

We made a significant investment in Defitelio in 2014, adding the product to our portfolio as a result of our acquisition of Gentium S.r.l, or Gentium, which we refer to as the Gentium Acquisition, and then securing worldwide rights to the product by acquiring rights to defibrotide in the Americas in August 2014. We launched Defitelio in certain European countries beginning in 2014 and continue to launch the product in additional European countries on a rolling basis. On March 30, 2016, the FDA approved our NDA for Defitelio for the treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome, or SOS, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT. We launched Defitelio in the U.S. shortly after FDA approval, and our U.S. commercial launch is still at an early stage.

Our ability to realize the anticipated benefits from this investment is subject to risks and uncertainties, including:

- the continued acceptance of Defitelio in the U.S. by hospital pharmacy and therapeutics committees and the continued availability of adequate coverage and reimbursement by government programs and third party payors;
- the lack of experience of U.S. physicians in diagnosing and treating VOD, particularly in adults, and the possibility that physicians may delay initiation of treatment or terminate treatment before the end of the recommended dosing schedule;
- our ability to successfully maintain or grow sales of Defitelio in Europe;
- delays or problems in the supply or manufacture of the product;
- the limited size of the population of VOD patients who are indicated for treatment with Defitelio (particularly if changes in HSCT treatment protocols reduce the incidence of VOD diagnosis);
- our ability to meet the post-marketing commitments and requirements imposed by the FDA in connection with its approval of our NDA for Defitelio; and
- our ability to obtain marketing approval in other countries and to develop the product for additional indications.

We are in the process of making pricing and reimbursement submissions with respect to Defitelio in certain 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 European 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 European countries will 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 the EU. Many European countries periodically review their reimbursement classes, which could have an adverse impact on the reimbursement status of Defitelio. We have developed estimates of anticipated pricing in the EU, 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 the EU, 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 in the EU would be negatively affected. If we are unable to obtain and maintain favorable pricing and reimbursement approvals in European countries that represent significant markets, especially where a country's reimbursed price influences other countries, our anticipated revenue from and growth prospects for Defitelio in the EU could be negatively affected. In addition, our ability to commercialize Defitelio successfully in the U.S. will depend on, among other things, the continued availability of adequate coverage or reimbursement by U.S. government programs and third party payors.

The European Commission, or EC, granted marketing authorization to Defitelio 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 European Medicines Agency, or EMA. As a result, if we fail to meet the approval condition for Defitelio established by the EC, 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. In addition, the FDA imposed several post-marketing commitments and requirements in connection with its approval of our NDA for Defitelio in March 2016, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. We may be unable to comply with these or other post-marketing obligations imposed as part of the marketing approvals for Defitelio. If we fail to meet any of these post-marketing obligations, our sales of and revenues from Defitelio could be materially adversely affected, and our potential future maintenance and growth of the market for this product may be limited.

The size of the population of VOD patients who are indicated for treatment with Defitelio is limited, and changes in HSCT treatment protocols could reduce the incidence of VOD diagnosis. Changes in treatment protocols that reduce the incidence of VOD diagnosis could adversely affect our anticipated revenues from Defitelio and our business, financial condition, results of operations and growth prospects.

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, or if any future approvals we receive are for narrower indications than we expect, our anticipated revenue from defibrotide and our growth prospects would be negatively affected.

Due to the limited amount of historical sales data from commercialization of Defitelio, our Defitelio sales will be difficult to predict from period to period. As a result, Defitelio sales results or trends in any period are not necessarily indicative of future performance. 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.

If we fail to maintain or increase prescriptions and revenue from sales of Xyrem, Erwinaze and Defitelio, our business, financial condition, results of operations and growth prospects could be materially adversely affected. We may choose to increase the price of our products, and price adjustments may negatively affect our sales volumes. Also, sales of each of our products 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 marketed 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.

Product Candidates

In furtherance of our growth strategy, we have made significant investments in a number of product candidates. In particular, we have made a significant investment in Vyxeos through the acquisition of Celator Pharmaceuticals, Inc., or Celator, which we refer to as the Celator Acquisition. Vyxeos is currently not approved as a marketed product in any jurisdiction and is the first injectable fixed ratio, drug delivery combination oncology product based on the CombiPlex technology platform that the FDA and EMA would potentially be considering for approval. We initiated a rolling submission of an NDA for Vyxeos to the FDA in the third quarter of 2016. We expect to complete the NDA submission by the end of the first quarter of 2017 and to make a regulatory submission for Vyxeos in Europe in the second half of 2017. Our ability to complete the NDA submission on our anticipated timing remains subject to our ability to complete necessary pre-filing activities, including chemistry, manufacturing and controls, or CMC, activities, in order to support our application for marketing approval. We also expect to conduct additional activities, including with respect to CMC, in support of approval of our NDA for Vyxeos after we complete the NDA submission. In addition, although the FDA has granted Fast Track designation to Vyxeos for the treatment of elderly patients with secondary acute myeloid leukemia, or AML, and Breakthrough Therapy for the treatment of adults with therapy-related AML or AML with myelodysplasia-related changes, these designations do not guarantee that we will be able to take advantage of the expedited review procedures and do not increase the likelihood that Vyxeos will receive marketing approval. We cannot predict whether our NDA for Vyxeos will be approved in a timely manner, if at all.

Our ability to realize the anticipated benefits from our investment in Vyxeos is subject to a number of additional risks and uncertainties, including:

- our ability to differentiate Vyxeos from other liposomal chemotherapies and generically available chemotherapy combinations with which physicians and treatment centers are more familiar;
- the need to establish pricing and reimbursement support for Vyxeos in the event we are able to obtain marketing approval for Vyxeos in the U.S. or in other countries;
- the acceptance of Vyxeos in the U.S. and other countries by hospital pharmacy and therapeutics committees and the availability of adequate coverage and reimbursement by government programs and third party payors;
- delays or problems in the supply or manufacture of the product, including with respect to the requirement of the third parties upon which we rely to manufacture Vyxeos and its active pharmaceutical ingredients, or APIs, obtain the approval of the FDA and/or other regulatory authorities to manufacture Vyxeos and to manufacture sufficient quantities of Vyxeos in accordance with applicable specifications; and
- the limited size of the population of high-risk AML patients who may potentially be indicated for treatment with Vyxeos, particularly given the ongoing clinical trials by other companies with the same patient population.

In addition, subject to the results of ongoing clinical trials for JZP-110, we plan to submit an NDA to the FDA for JZP-110 in late 2017. We also expect to submit an NDA to the FDA for JZP-507 by the first quarter of 2018. Any failure or delay in completing necessary clinical trials and conducting other activities, including CMC activities, that are required to complete our planned NDA submissions and obtain regulatory approval could materially and adversely affect our business, financial condition, results of operations and growth prospects. See the discussion under the heading "*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*" in this Part I, Item 1A for a discussion of risks related to our clinical trials of JZP-110. With respect to JZP-507, while we believe that we have a path to obtain the data necessary to complete our planned NDA submission for JZP-507 by the first quarter of 2018, we may not be able to generate sufficient data on our anticipated timing, or at all, or may be required to conduct more extensive studies than we currently anticipate, either of which could delay or prevent submission of an NDA.

See also the discussions under the headings "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects"* and "*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" in this Part I, Item 1A.

If we are unable to obtain regulatory approval for our product candidates, including Vyxeos in the U.S. or in Europe, in a timely manner, or at all, or if sales of an approved product do not reach the levels we expect, our anticipated revenue from our product candidates would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, 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 API and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. We and our manufacturers may 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. These difficulties can be heightened when we or our suppliers are required to produce finished product at commercial scale or to produce increased quantities to meet growing demand. In addition, we and our suppliers are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and other equivalent rules and regulations prescribed by non-U.S. regulatory authorities. If we or any of our suppliers encounter these or any other manufacturing, quality or compliance difficulties with respect to any of our products, particularly Xyrem and Erwinaze, because 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 received FDA approval of our manufacturing and development facility in Ireland in June 2016, and we commenced commercial operations at this facility in the third quarter of 2016. We are using this facility for the manufacture of Xyrem and plan to also use this facility for the manufacture of development-stage products. However, other than our Ireland facility and our manufacturing plant in Italy where we produce the defibrotide drug substance, we currently do not have our own commercial manufacturing capability for our products, product candidates or their APIs, or packaging capability. As a result, our ability to develop and supply products in a timely and competitive manner depends primarily on third party suppliers being able to meet our ongoing commercial and clinical trial needs for API, other raw materials, packaging materials and finished products. In part due to the limited market size for our products and product candidates, we have a single source of supply for most of our marketed products, product candidates and their APIs. These single source arrangements put us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties at our suppliers.

Siegfried (USA) Inc., subsequently renamed Siegfried USA, LLC, or Siegfried, has been our sole supplier of sodium oxybate since 2012. Siegfried supplies sodium oxybate to our U.S.-based manufacturer of Xyrem and now supplies sodium oxybate, through a Siegfried affiliate in Europe, to our Ireland manufacturing facility. 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 API to enable the manufacture of the quantities of Xyrem that we need. Patheon Pharmaceuticals Inc., which we refer to together with its affiliates as Patheon, is our sole manufacturer and supplier of Xyrem in the U.S. Although we have commenced manufacturing of Xyrem in our Ireland facility, we expect to rely on Patheon as our U.S.-based supplier of Xyrem for the foreseeable future, and we cannot assure you that Patheon can or will continue to supply on a timely basis, or at all, the quantities of Xyrem that we need from Patheon.

The API of Xyrem, sodium oxybate, is a Schedule I controlled substance in the U.S. The DEA limits the quantity of certain Schedule I controlled substances that may be manufactured and procured in the U.S. in any given calendar year through a quota system and, as a result, quotas from the DEA are required in order to manufacture and package sodium oxybate and Xyrem in the U.S. Accordingly, we require DEA quotas for Siegfried, our U.S.-based sodium oxybate supplier, to procure sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to obtain the sodium oxybate from Siegfried in order to manufacture and supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, Siegfried and Patheon 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 API. If one or more ANDA filers were to begin manufacturing a generic sodium oxybate product, generic manufacturers would need to obtain a portion of the annual aggregate API quota, which could decrease the DEA quota allocation obtained on our behalf by Siegfried and Patheon. 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. The need for quotas has prevented us in the past, and may prevent us in the future, from building significant inventories. For 2017, both Siegfried and Patheon 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.

Erwinaze is licensed from and manufactured for us by a single source, 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 by PBL. We cannot predict if or when PBL will comply with its manufacturing-related post-marketing commitments that are part of the BLA approval. In March 2016, the FDA conducted an inspection of the PBL manufacturing facility and issued an FDA Form 483 to PBL that included observations related to a range of operational systems and processes. On April 2016 and September 2016, PBL responded to the FDA Form 483 with its plan, including required remediation activities, to address the observations, and subsequently provided additional information in response to another FDA request. In January 2017, the FDA issued a warning letter to PBL citing significant violations of cGMP for finished pharmaceuticals and significant deviations from cGMP for APIs. We cannot predict if or when PBL will correct the violations and deviations to the satisfaction of the FDA. Any failure to do so to the satisfaction of the FDA could result in the FDA refusing admission of Erwinaze into the U.S., as well as additional enforcement actions by the FDA and other regulatory entities.

In the United Kingdom, or UK, where PBL's manufacturing facilities are located, PBL is subject to similar inspections conducted by the UK Medicines and Healthcare Products Regulatory Agency, or MHRA. Inability to comply with regulatory requirements of the FDA, the MHRA or other competent authorities in the EU member states in which Erwinaze is subject to marketing authorization could adversely affect Erwinaze supply, particularly in light of our extremely limited product inventory, and could result in: enforcement actions by the FDA, MHRA or other EU member states' competent authorities (including the issuance of the local equivalents of FDA Form 483s or warning letters); the approval of the FDA or these competent authorities being suspended, varied, or revoked; product release being delayed, or suspended; or product being seized or recalled. Any of these actions 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 or a delay in supply and may decrease any profit we would otherwise achieve with Erwinaze.

Moreover, the current manufacturing capacity for Erwinaze is completely absorbed by demand for the product. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build product inventory levels that can be used to absorb supply disruptions resulting from quality, regulatory or other issues. We have experienced product quality, manufacturing and inventory challenges that have resulted, and may continue to result, in disruptions in our ability to supply certain markets, including the U.S., and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. Most recently, we experienced supply interruptions of Erwinaze in the U.S. and other countries in the third and fourth quarters of 2016. We cannot predict whether the required remediation activities in connection with the January 2017 warning letter will further strain manufacturing capacity and adversely affect Erwinaze supply, particularly in light of our extremely limited product inventory. As capacity constraints and supply disruptions continue, whether as a result of continued quality or other manufacturing issues, regulatory issues or otherwise, we will be unable to build a desired excess level of product inventory, our ability to supply the market may continue to be compromised and physicians' decisions to use Erwinaze have been, and may continue to be, negatively impacted.

If quality or other manufacturing issues or regulatory difficulties persist and result in a disruption to supply or capacity constraints, under our agreement with PBL, 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 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 and clinical supply of Defitelio. In 2015, the FDA issued an FDA Form 483 to Patheon Italia that included observations related to the Ferentino, Italy facility that manufactures Defitelio. Although we are advised that Patheon Italia remediated the observations to the FDA's satisfaction, the FDA will continue to inspect and evaluate this facility for ongoing compliance with applicable requirements. If Patheon does not or is not able to supply us with Defitelio 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 anticipated revenues from Defitelio 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, the API in Defitelio is derived from porcine DNA. If our porcine DNA 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 Defitelio.

Vyxeos is manufactured using Celator's CombiPlex technology. CombiPlex products represent formulations with increased manufacturing complexities associated with producing drug delivery vehicles encapsulating two or more drugs that are maintained at a fixed ratio and, in the case of Vyxeos, two drugs that are co-encapsulated in a freeze-dried format. Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. Baxter successfully manufactured batches that were used in Celator's completed Phase 3 clinical trial for Vyxeos, but Baxter has experienced batch failures due to mechanical, component and other issues. While other contract manufacturers may be able to produce Vyxeos, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. Consequently, engaging an alternate manufacturer may be difficult, costly and time-consuming. If Baxter does not deliver sufficient quantities of Vyxeos in accordance with applicable specifications on a timely basis, whether due to batch failures or other delays, or if Baxter is unable to receive FDA approval to manufacture Vyxeos, our ability to obtain FDA approval and successfully launch and commercialize an approved Vyxeos product and generate sales of this product at the level we expect could be materially and adversely affected.

In addition, while the APIs in Vyxeos, cytarabine and daunorubicin, are available from a number of suppliers, certain suppliers have received warning letters from the FDA. As a result, we have qualified other suppliers for each API, and we will provide the qualification data to the FDA as part of our NDA submission. If the FDA does not approve either API supplier or restricts importation of API from either supplier, and we are unable to qualify API from additional suppliers in a timely manner, or at all, our ability to obtain FDA approval and successfully launch and commercialize an approved Vyxeos product and generate sales of this product at the level we expect could be materially and adversely affected.

To conduct our ongoing and any future clinical trials of, complete marketing authorization submissions for, and potentially launch our other product candidates, we need to have sufficient quantities of product manufactured. There can be no assurance that we or our suppliers will be able to produce sufficient supplies of our product candidates in a timely manner or in accordance with applicable specifications. In addition, to obtain FDA approval of any product candidate, we or our supplier or suppliers for that product must obtain approval by the FDA to manufacture and supply product, in some cases based on qualification data provided to the FDA as part of our NDA submission. Any delay in generating, or failure to generate, data required in connection with submission of the CMC portions of any NDA could negatively impact our ability to meet our anticipated submission dates, and therefore our anticipated timing for obtaining FDA approval, or our ability to obtain FDA approval at all. In addition, any failure of us or a supplier to obtain approval by the FDA to manufacture and supply product or any delay in receiving, or failure to receive, adequate supplies of a product on a timely basis or in accordance with applicable specifications could negatively impact our ability to successfully launch and commercialize products and generate sales of products at the levels we expect.

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 cGMP, requirements. DEA regulations also govern facilities where controlled substances such as sodium oxybate 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 API 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 APIs 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 APIs 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 1,040 in February 2017. 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.

In addition, on June 23, 2016, eligible members of the electorate in the United Kingdom decided by referendum to leave the EU, or Brexit. We have a significant office in Oxford, England, which focuses on commercialization of our products outside of the U.S., among other activities. We do not know to what extent, or when, Brexit or any other future changes to

membership in the EU will impact our business, if at all. In particular, our ability to conduct international business out of the United Kingdom may be materially and adversely affected.

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

If physicians do not prescribe our products, we cannot 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 its diagnosis, and the severity of side effects;
- acceptance by physicians and patients of each product as a safe and effective treatment;
- availability of sufficient product inventory to meet demand, particularly with respect to Erwinaze;
- physicians' decisions relating to treatment practices based on availability of product inventory;
- 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;
- the conditions for reimbursement required by, and appropriate pricing and availability of reimbursement from, third party payors; and
- the availability of financial or other assistance for patients who are uninsured or underinsured.

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 gamma-hydroxybutyrate, or GHB, and its effects, including with respect to illegal use, overdoses, serious injury and death. Because sodium oxybate, the API 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. Moreover, a sodium oxybate distribution system that is less restrictive than the Xyrem REMS, such as the generic sodium oxybate REMS approved by the FDA in January 2017, may increase the risks associated with sodium oxybate distribution, as patients, consumers and others may not differentiate generic sodium oxybate from Xyrem, or differentiate between the different REMS programs. Any negative outcomes, including but not limited to risks to the public, caused by or otherwise related to the separate generic sodium oxybate REMS could have a significant negative impact in terms of product liability, goodwill, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, any of which could have a material adverse effect on our Xyrem revenues.

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 this Part I, Item 1A.

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.

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. We may not be able to realize the anticipated benefits of any acquisition or in-licensing for a variety of reasons, including if:

- we are unable to obtain and maintain adequate funding to complete the development of, obtain regulatory approval for and commercialize an acquired product candidate;
- 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;
- we experience 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.

For example, in July 2016 we made a substantial investment in Celator through the Celator Acquisition. The aggregate consideration for the Celator Acquisition was $1.5 billion. The Celator Acquisition broadened our hematology/oncology portfolio with the acquisition of worldwide development and commercialization rights to Vyxeos. Vyxeos is currently not approved as a marketed product in any jurisdiction. While we have commenced a rolling submission for Vyxeos in the U.S. and plan to make a regulatory submission in Europe as well, there can be no guarantee that we will obtain approval in any jurisdiction in a timely manner, or at all. If we are unable to obtain regulatory approval for Vyxeos in the U.S. or Europe in a timely manner, or at all, or if sales of Vyxeos following regulatory approvals 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. See also the discussion under the heading "*While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products and, in the case of our product candidates, our ability to obtain regulatory approval in the U.S. and Europe and, if approved, to successfully launch and commercialize those product candidates. Our inability to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in this Part I, Item 1A.

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, such as the Celator Acquisition. 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 the 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. If a product candidate fails at any stage of development and does not receive regulatory approval, we will not be able to commercialize it and receive any return on our investment in that product candidate.

For example, we are conducting three Phase 3 clinical trials and an open label extension trial for JZP-110, a late-stage investigational compound being developed for potential treatment of excessive sleepiness, or ES, in patients with narcolepsy and ES in patients with obstructive sleep apnea, or OSA. We expect preliminary data from the two Phase 3 clinical trials in patients with ES associated with OSA by the end of the first quarter of 2017 and from the Phase 3 clinical trial in patients with ES associated with narcolepsy in the second quarter of 2017. Results from earlier Phase 2 clinical trials may not be predictive of the results from the Phase 3 clinical trials for JZP-110, and in addition, for ES in patients with OSA, there were no studies conducted for JZP-110 prior to our Phase 3 clinical trials. One or more of the Phase 3 clinical trials may fail to demonstrate the desired safety or efficacy for this product candidate. If the preliminary results, or the final results, of one or more of the Phase 3 clinical trials for JZP-110 fail to demonstrate the desired safety or efficacy of this product candidate, we may be required to conduct additional clinical trials before submitting for regulatory approval in either or both indications, which would be costly and time-consuming and could prevent us from submitting an NDA to the FDA on our anticipated timeline, or at all. Moreover, if we submit an NDA to the FDA for approval and the FDA determines that our safety or efficacy data do not warrant marketing approval, we will not be able to commercialize JZP-110, and we will not receive any return on our investment.

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 a non-U.S. regulatory agency, which may restrict our ability to sell, or adversely affect 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;
- difficulty identifying or enrolling eligible patients, in some cases based on the number of clinical trials with enrollment criteria targeting the same patient population;
- 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 Xyrem is the only product approved by the FDA and currently marketed in the U.S. for the treatment of both cataplexy and EDS in patients with narcolepsy, cataplexy is often treated with tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors, even though these products are not approved by the FDA for the treatment of cataplexy. Other treatments for EDS in patients with narcolepsy include stimulants and wakefulness promoting agents, such as Provigil® (modafinil) and Nuvigil® (armodafinil), as well as generic versions of Provigil, the only other products both approved by the FDA and currently marketed for the treatment of EDS in patients with narcolepsy. Provigil, its generic equivalents and Nuvigil are also approved for improving wakefulness in patients with EDS associated with treated OSA or shift work disorder.

We are also aware of products being developed by others for use as treatment options in cataplexy and/or EDS in patients with narcolepsy, including a product to treat adult patients with narcolepsy with or without cataplexy that recently received marketing approval in Europe. While this product is currently not approved by the FDA for marketing in the U.S. or, to our knowledge, subject to a pending application for such approval, the receipt of marketing approval and commercialization of this product in the U.S. for the treatment of narcolepsy could, depending on the targeted patient population, negatively impact our ability to maintain and grow sales of Xyrem.

The FDA has approved or tentatively approved ANDAs seeking to market generic versions of Xyrem and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs. 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, Avadel has stated that it is conducting a Phase 3 pivotal trial pursuant to an FDA-approved special protocol assessment. If Avadel 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 compete directly with Xyrem and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We expect that the launch of a generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, would have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects. For further discussion regarding the risks associated with FDA approval and tentative approval of ANDAs, potential approval or tentative approval of additional ANDAs and the potential launch of a generic version of Xyrem, or the approval of other sodium oxybate products that compete with Xyrem, as well as other risks and 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 this Part I, Item 1A.

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. 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 regimen is not well established.

With respect to Vyxeos, AML, a cancer indication for which we intend to commercialize Vyxeos, has established therapies. A key consideration in the treatment of AML patients is the patient's suitability for chemotherapy. The patient population studied in the Vyxeos Phase 3 clinical trial included AML patients deemed able to tolerate chemotherapy. There are existing options for the treatment of newly-diagnosed AML patients who can tolerate chemotherapy, such as cytarabine in combination with an anthracycline (i.e., daunorubicin), known as 7+3. In addition, we are aware of several other products in development for use as treatment options for AML patients, such as targeted agents (FLT-3, IDH-1, IDH-2, CD-33, CAR T-cell). Some of the patient populations being studied for these products in development overlap with the patient population studied in the Vyxeos Phase 3 clinical trial. The existence of established treatment options and the development of competing products for the treatment of patients in the patient population studied in the Vyxeos Phase 3 clinical trial or similar patient

populations could negatively impact our ability to successfully launch and commercialize an approved Vyxeos product and achieve the level of sales we expect, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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, including in connection with the FDA's recent approval and tentative approvals of generic versions of Xyrem. 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 some 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 *"The approval and launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem"* in this Part I, Item 1A.

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.

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 Defitelio 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 Defitelio 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.

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 and often changing 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, Defitelio and Vyxeos. 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.

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. It is possible that Roxane or any other company that receives FDA approval of an ANDA for a generic version of Xyrem or an NDA for another sodium oxybate product could introduce a generic version of Xyrem or other sodium oxybate product before our patents expire if it is determined that any such generic version of Xyrem or sodium oxybate product does not infringe our patents, or 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 being held liable for damages for patent infringement. For a description of our ongoing patent proceedings in the District Court and the PTAB and related regulatory matters and further discussion regarding the risks associated with the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K, "Business-Government Regulation-*The Hatch-Waxman Act*" in Part I, Item 1 of this Annual Report on Form 10-K and the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" and "*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 this Part I, Item 1A.

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 independently develop similar or alternative products without infringing our intellectual property rights, such as products that are not covered by the claims of our patents, or for which we do not have adequate exclusive rights 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;
- 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 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 rely on trade secrets and 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. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality agreements with our employees, consultants, advisors and partners. Nevertheless, 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. In addition, if our employees, consultants, advisors and partners develop inventions or processes independently, or jointly with us, that may be applicable to our products, 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. Enforcing a claim that a third party illegally obtained or 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. Failure to obtain or maintain patent and/or trade secret protection, for any reason, could have a material adverse effect on our business.

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 U.S. Biologics Price Competition and Innovation Act, or 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. However, the BPCIA may evolve over time based on 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. In addition, the IPR process under the Leahy-Smith 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 as well as ANDA litigants have challenged valuable pharmaceutical patents through the IPR process. There is a risk that a court will decide that our 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. For a description of our ongoing patent proceedings in the District Court and the PTAB and further discussion regarding the risks associated with the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K, "Business-Government Regulation-*The Hatch-Waxman Act*" in Part I, Item 1 of this Annual Report on Form 10-K and the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" and "*It is difficult and costly to*

protect our proprietary rights, and we may not be able to ensure their protection" in this Part I, Item 1A. 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.

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.

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.

In September 2016, Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, submitted a Citizen Petition to the FDA requesting that, for safety reasons, the FDA refuse to approve any sodium oxybate ANDA with a proposed package insert or REMS that omits the portions of the Xyrem package insert and the Xyrem REMS that instruct prescribers on adjusting the dose of the product when it is co-administered with divalproex sodium (also known as valproate or valproic acid). Our Xyrem patents include three DDI patents covering these instructions on the Xyrem package insert and Xyrem REMS. Our lawsuits against each of the Xyrem ANDA filers allege infringement of multiple patents, including the DDI patents, and seek a permanent injunction to prevent these Xyrem ANDA filers from introducing a generic version of Xyrem that would infringe our patents. On January 17, 2017, the FDA granted the Citizen Petition with respect to the Xyrem package insert. The FDA concluded that it will not approve any sodium oxybate ANDA referencing Xyrem that does not include in its package insert the portions of the currently approved Xyrem package insert related to the drug-drug interaction with divalproex sodium. The FDA stated that it did not need to reach the question of whether the drug-drug interaction information could have been excluded from the generic sodium oxybate REMS materials because it was approving a REMS in connection with a sodium oxybate ANDA including that information. We cannot predict whether or when one or more of the ANDA filers may pursue a challenge

to the FDA's response to the Citizen Petition or whether any such challenges would be successful. Likewise, we cannot predict whether we will be able to maintain the validity of any of our patents or will otherwise obtain a judicial determination that the generic sodium oxybate package insert or the generic sodium oxybate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem. For a description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K, "Business-Government Regulation-*The Hatch-Waxman Act*" in Part I, Item 1 of this Annual Report on Form 10-K, 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 this Part I, Item 1A.

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. In July 2016, the PTAB issued final decisions that the claims of six of seven REMS patents are unpatentable; if the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled, and we will not be able to enforce these patents. In March 2016, the PTAB partially instituted an IPR on a seventh REMS patent, declining to review 25 of 28 claims. A PTAB decision on the three claims that were tried is expected before the end of the first quarter of 2017. For a description of these matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K. The Xyrem REMS approval letter 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 (particularly now that the FDA has approved a separate REMS for the ANDA filers that contemplates interaction with the Xyrem REMS), 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 sodium oxybate 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 and other intellectual property to protect our Xyrem distribution system from sodium oxybate competitors may be reduced. In addition, the extent of protection provided by our patents and other intellectual property related to the distribution of Xyrem depends on the nature of the distribution system that may be used by any sodium oxybate competitor. If the generic sodium oxybate REMS that has been approved by the FDA in connection with its approval of Roxane's ANDA does not fall within the scope of any of the claims of our patents, those patents will not be a barrier to the generic version's entry into the market. We cannot be certain whether our existing patents, patents that may be granted in the future or other intellectual property will be construed to cover the generic sodium oxybate REMS. 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 DEA, 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 API, 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.

An approved drug product or drug candidate that has not yet been approved by the FDA may be subject to scheduling as a controlled substance under the U.S. Controlled Substances Act, or CSA, depending on the drug's potential for abuse.

Controlled substances that are pharmaceutical products are subject to a high degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The CSA requires the DEA to issue an interim final order scheduling the drug within 90 days after the FDA approves the drug and the DEA receives a scientific and medical evaluation and scheduling recommendation from the U.S. Department of Health and Human Services, or HHS. We expect that JZP-110 will be subject to scheduling under the CSA before it can be commercially launched. Moreover, depending on its scheduling, the manufacture, importation, exportation, domestic distribution, storage, sale and legitimate use of JZP-110 may be subject to a significant degree of regulation by the DEA. For a description of the DEA scheduling process, see "Business-Government Regulation-Post-Approval Regulation" in Part I, Item 1 of this Annual Report on Form 10-K.

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. In non-EU countries, 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 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 this Part I, Item 1A, 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.

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, particularly in light of our extremely limited product inventory, and could result in FDA approval being revoked, product release being delayed resulting in product shortage or product recalls, any 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. See also the discussion under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects.*" in this Part I, Item 1A.

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, and the FDA imposed several post-marketing commitments and requirements in connection with its approval of our NDA for Defitelio in March 2016, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. If we fail to meet any of these post-marketing obligations, the ongoing validity of the marketing authorization may be called into question, our sales of and revenues from Defitelio could be materially adversely affected and our potential future maintenance and growth of the market for this product may be limited.

In addition, since a significant proportion of the regulatory framework in the U.K. is derived from EU directives and regulations, Brexit could materially change the regulatory regime applicable to our operations, including with respect to the approval of our product candidates. Any such changes to the regulatory regime could have a material adverse effect on the pharmaceutical industry generally and on our ability to obtain approval for our product candidates or, if approved, to successfully commercialize our product candidates.

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 Patient Protection and Affordable Care Act, as amended by the Healthcare 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 program, or the 340B 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 this Part I, Item 1A. 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 increased 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 and appear likely in the 115th U.S. Congress and under the Trump Administration. The nature and extent of any legislative changes to the Healthcare Reform Act are uncertain at this time. 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, the Centers for Medicare and Medicaid Services, or 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. CMS subsequently issued a rule requiring individual market qualified health plans to accept third-party premium and cost-sharing payments from certain government-related entities. In September 2014, the Office of Inspector General, or 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. 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.

Patient assistance programs that receive partial financial support from companies have become the subject of enhanced government and regulatory scrutiny. For example, the OIG has established guidelines that permit pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. If we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. In May and October 2016 and February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients and documents concerning the provision of financial assistance to Medicare patients taking drugs sold by us. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management and increase our expenses. 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 this Part I, Item 1A.

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 central pharmacy for Xyrem, 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 competent authorities of the EU Member States on behalf of the EMA also periodically inspect our records related to safety reporting. Following such inspections, the FDA may issue notices on FDA Form 483 and warning letters that could cause us to modify certain activities. The EMA's Pharmacovigilance Risk Assessment Committee, or the PRAC, may propose to the Committee for 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. An FDA Form 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 an FDA Form 483 at the conclusion of a pharmacovigilance inspection conducted by the FDA. The FDA Form 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 FDA Form 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 FDA Form 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 studies or trials. 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.

EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders 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, all 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, 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, and the FDA imposed several post-marketing requirements and commitments in connection with its March 2016 approval of our NDA for Defitelio, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. We may be unable to comply with these or other post-marketing obligations. If we fail to meet any of these post-marketing obligations, the ongoing validity of the marketing authorization may be called into question, our sales of and revenues from Defitelio could be materially adversely affected and our potential future maintenance and growth of the market for this product may be limited.

Erwinase and defibrotide are available on a named patient basis in many countries where they are not commercially available. 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 laws 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. In recent years, certain courts have determined that the First Amendment of the U.S. Constitution permits communications regarding off-label uses of drug products, as long as such communications are truthful and not misleading. At the beginning of 2017, the FDA released proposed rule changes and draft guidance on the FDA's interpretation on the limitations of such speech. These cases and regulatory actions create additional uncertainty regarding the limits of permissible communication regarding our products.

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 U.S. Department of Justice, or DOJ, the FTC, the United States Department of Commerce, or 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, a controlled substance under the CSA, are also subject to DEA and state regulations relating to manufacturing, storage, distribution and physician prescription procedures, including limitations on prescription refills and 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, relevant state authorities or any comparable international requirements could lead to a variety of sanctions, including revocation or denial of renewal of DEA registrations, fines, injunctions, or civil or criminal penalties, could result in, among other things, additional operating costs to us or delays in shipments outside or into the U.S. and could have an adverse effect on our business and financial condition.

In addition, the DEA limits the quantity of certain Schedule I controlled substances that may be produced or procured in the U.S. in any given calendar year through a quota system. Accordingly, we require DEA quotas for Siegfried, our U.S.-based sodium oxybate supplier, to procure sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to obtain the sodium oxybate from Siegfried in order to manufacture and supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, Siegfried and Patheon 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 API. If one or more ANDA filers were to begin manufacturing a generic sodium oxybate product, generic manufacturers would need to obtain a portion of the annual aggregate API quota, which could decrease the DEA quota allocation obtained on our behalf by Siegfried and Patheon. 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 2017, both Siegfried and Patheon have been allocated most, but not all, of their respective requested quotas. If, in the future, 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.

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 Medicare patients, 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. 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 Physician Payment Sunshine Act, or Sunshine provisions, requires extensive tracking of payments and transfers of value to physicians and teaching hospitals and public reporting of the data collected. By March 31 of each calendar year, 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. Public reporting under the Sunshine provisions has resulted 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, or if we otherwise fail to comply with the Sunshine provisions, 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 May 2016, we received a subpoena from the U.S. Attorney’s Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients, and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. In October 2016, we received a second subpoena updating and further specifying document requests regarding support to 501(c)(3) organizations that provide financial assistance to Medicare patients and the provision of financial assistance for Medicare patients taking drugs sold by us. In February 2017, we received a third subpoena requesting documents regarding our support to a specific 501(c)(3) organization that established a fund for narcolepsy patients in January 2017. Other companies have disclosed similar subpoenas and continuing inquiries. We are cooperating with this investigation. We are unable to predict how long this investigation will continue, whether we will receive additional subpoenas in connection with this investigation, or its outcome, but we expect that we will continue to incur significant costs in connection with the investigation, regardless of the outcome. We may also become subject to similar investigations by other state or federal governmental agencies or offices. The investigation by the U.S. Attorney’s Office and any additional investigations of our patient assistance programs or other business practices may result in damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions against us or 501(c)(3) organizations that we support (including organizations that provide assistance to narcolepsy and chronic pain patients), negative publicity or other negative actions as to us or 501(c)(3) organizations that we support that could

harm our reputation, impact our business practices, reduce demand for, or patient access to, Xyrem and Prialt and/or reduce coverage of Xyrem and Prialt, including by federal health care programs and state health care programs. Any voluntary settlement with the U.S. Attorney's Office could result in substantial payments, and entry into a Corporate Integrity Agreement, which would impose costs and burdens on our operation of the business. If any or all of these events occur, our business and stock price could be materially and adversely affected. For more information, see the risk factors 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 this Part I, Item 1A.

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 U.S. Foreign Corrupt Practices Act, or 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 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. 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 governing privacy and data security. These laws include security breach notification requirements and protection of consumer health information. The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Although there are legal mechanisms to facilitate the transfer of personal data from the European Economic Area, or EEA, and Switzerland to the U.S., the decision of the European Court of Justice that invalidated the safe harbor framework on which we previously relied has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it was no longer 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 February 2016, the EC announced an agreement with the DOC to replace the invalidated safe harbor framework with a new EU-U.S. "Privacy Shield." On July 12, 2016, the EC adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the European Court of Justice in its recent ruling by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and FTC and making commitments on the part of public authorities regarding access to information.

U.S.-based companies may certify compliance with the privacy principles of the Privacy Shield. Certification to the Privacy Shield, however, is not mandatory. If a U.S.-based company does not certify compliance with the Privacy Shield, it may rely on other authorized mechanisms to transfer personal data. In September 2016, we filed for certification for our U.S.-based subsidiaries under the Privacy Shield. This certification was approved in January 2017.

The privacy and data security landscape is still in flux. In September 2016, the Irish privacy advocacy group, Digital Rights Ireland, brought an action for annulment of the EC decision on the adequacy of Privacy Shield, Case T-670/16, which is pending before the European Court of Justice. Should the European Court of Justice invalidate the Privacy Shield, it will no longer be possible to transfer data from the EU to entities in the U.S. under a Privacy Shield certification, in which case other legal mechanisms would need to be put in place.

Healthcare providers who prescribe our products and research institutions that 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, our affiliates or our agents 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.

Failure to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors and/or adverse publicity that negatively affect our business.

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 was officially adopted in April 2016 and will be applicable in May 2018, 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 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. In addition, data protection authorities of 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.

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 letter 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 REMS patents should not have been listed in the Orange Book, and that the Xyrem REMS is blocking competition. In January 2017, the FDA announced approval of the Roxane ANDA and waived the shared REMS requirement. For more information, see the risk factor under the heading "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" in this Part I, Item 1A. Any claim 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 APIs, 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 APIs and drug products, including the defibrotide drug substance and its finished form. These facilities are also subject to inspection and regulation by the EMA. Following initial approval in a jurisdiction, the competent 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. Our failure to comply with these price reporting and rebate payment obligations could 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 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. 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. As noted above, CMS recently issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the Healthcare Reform Act. The issuance of the final regulation, as well as any other regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program, has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final regulation.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B 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, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. 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 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. The Health Resources and Services Administration, or HRSA, recently initiated the process of updating the agreement with participating manufacturers. The Healthcare Reform Act also obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340B program. In 2015, HRSA issued proposed omnibus guidance that addresses many aspects of the 340B program, and in August 2016, HRSA issued a proposed regulation regarding an administrative dispute resolution process for the 340B program. It is unclear when or whether the guidance or regulation will be released in final form under the Trump Administration. On January 5, 2017, HRSA issued a final regulation regarding the calculation of 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. The Trump Administration has directed that this regulation, which was slated to become effective March 6, 2017, be temporarily delayed until March 21, 2017, and the regulation could be subject to further delay or other modification by the Trump Administration. Implementation of this final rule and the issuance of any other 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 an 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 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 U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or 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 Federal Ceiling Price, or FCP, to four federal agencies (VA, U.S. Department of Defense, or DOD, Public Health Service, and U.S. Coast Guard). 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. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to penalties of $178,156 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 drug costs in the U.S. These cost containment measures may include federal and state 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 through required disclosures; 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, in March 2016, CMS proposed to conduct a demonstration project that would reduce the Medicare payment rates for most Part B drugs from average sales price plus 6% to average sales price plus 2.5% for approximately half of the country. However, in December 2016, CMS announced that it would not move forward with the demonstration project.

Additionally, drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny, including with respect to companies that have increased the price of products after acquiring those products from other companies. Both the U.S. House of Representatives and the U.S. Senate have conducted several 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 any government investigation with respect to our drug pricing or other business practices, we could incur significant expense and could be distracted from operation of our business and execution of our strategy. Any such investigation could also 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. In May and October 2016 and February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients and documents concerning the provision of financial assistance to Medicare patients taking drugs sold by us. For more information, see the risk factors under the headings "*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*" and "*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 this Part I, Item 1A. 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 and Defitelio, 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 beginning in 2014 and continue to launch the product in additional European countries on a rolling basis. 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. In addition, on March 30, 2016, the FDA approved our NDA for defibrotide for the treatment of adult and pediatric patients with VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT. We launched Defitelio in the U.S. shortly after FDA approval, and our U.S. commercial launch is still at an early stage. Our ability to commercialize Defitelio successfully in the U.S. will depend on, among other things, the continued availability of adequate coverage or reimbursement by U.S. government programs and third party payors. For more information, see the risk factor under the heading "*While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products and, in the case of our product candidates, our ability to obtain regulatory approval in the U.S. and Europe and, if approved, to successfully launch and commercialize those product candidates. Our inability to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in this Part I, Item 1A.

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 inpatient hospital services provided under Medicare, which some states also use for Medicaid. The MS-DRG system entitles a hospital 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 hospital 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 in the form of National Average Drug Acquisition Cost files 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 the commercial opportunities for our products 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 January 2017, 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 (particularly in the event a generic version with a lower price than Xyrem is introduced) will not negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our products, which could negatively impact our sales volumes and revenue.

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 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. Pursuant to Directive 2011/24/EU, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The EU member states were required to implement the provisions of the Directive into their national legislation by October 25, 2013. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This could lead to harmonization between EU member states of the criteria taken into account in the conduct of HTA and their impact on pricing and reimbursement decisions.

The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product, however, still 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 EC 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. Even if 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 and Results

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

As of December 31, 2016, we had total indebtedness of approximately $2.1 billion, which included $0.9 billion in outstanding borrowings under our revolving credit facility, $712.9 million of outstanding secured indebtedness under a credit agreement that we entered into in June 2015 and subsequently amended in July 2016, which we refer to as the amended 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 amended 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.

The amended credit agreement provides for a $750.0 million principal amount term loan due in July 2021 and a $1.25 billion revolving credit facility, with loans under such revolving credit facility due in July 2021, subject to early mandatory repayments under certain circumstances. The amended 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.

The amended 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 the amended 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 amended 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 the amended credit agreement could also lead to a default under other debt agreements or obligations, 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 other debt agreements or obligations, including the amended 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 the amended credit agreement, the lenders under the amended 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. The amended 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 the amended 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 business combination between Jazz Pharmaceuticals, Inc. and Azur Pharma, which we refer to as the Azur Merger, our acquisition of EUSA Pharma Inc., or EUSA Pharma, which we refer to as the EUSA Acquisition, the Gentium Acquisition and the Celator 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 or other competition for Xyrem or our other 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, including as a result of the potential for Brexit to contribute to sustained instability in the global financial markets, 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 $40.3 million, including interest and penalties, through the date of the assessment translated at the foreign exchange rate at December 31, 2016. 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 our 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. Any of these actions 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. after the Azur Merger (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 has issued several sets of final and temporary regulations under Section 7874 since 2012. Most recently, in April 2016, the IRS

issued temporary regulations under Section 7874 reflecting guidance that the IRS previously announced in notices dated September 2014 and November 2015, as well as additional rules, and in January 2017, the IRS issued final and temporary regulations under Section 7874 making further revisions to prior guidance. 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 to other tax laws relating to multinational corporations could adversely affect us*," in this Part I, Item 1A.

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 $281.2 million, before tax effect, for 2017, $142.0 million, before tax effect, for 2018 and a combined total of $341.9 million, before tax effect, for 2019 to 2032.

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 to 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. 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 Trump Administration and many members of the U.S. Congress have called for comprehensive tax reform and have stated that U.S. tax reform should be a priority for the incoming Congress. Although it is not possible to determine the impact of any tax reform on us, tax reform, if enacted, could adversely affect our effective tax rate and our results of operations and financial condition.

The U.S. Congress, the EU, the Organization for Economic Co-operation and Development and other government agencies in jurisdictions where we and our affiliates do business have also 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 Ireland, 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, 2016, we had recorded $3.9 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 currently conduct only limited hedging activities, involving the use of foreign exchange forward contracts, to manage currency risk related to certain intercompany loans denominated in non-functional currencies. These foreign exchange forward contracts are not designated as hedges; gains and losses on these derivative instruments are designed to offset gains and losses on the underlying balance sheet exposures. 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 $157.16 on April 22, 2016 and a low of $96.74 on November 3, 2016 during the period from December 31, 2015 through December 31, 2016. 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. Our ability to meet analysts' forecasts, investors'

expectations and our financial guidance is substantially dependent on our ability to maintain or increase sales of Xyrem and Defitelio and to successfully launch Vyxeos commercially in the U.S. In addition, we will need to minimize future supply interruptions of Erwinaze in order to meet revenue expectations for Erwinaze. The risks and uncertainties associated with our ability to maintain or increase sales of Xyrem, Erwinaze and Defitelio and to successfully launch Vyxeos include those discussed elsewhere in these risk factors. 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 transactions, including the Gentium Acquisition, the Celator 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 21, 2017, we had 59,742,232 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. 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.

We are subject to Irish law, which 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 liability 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 are generally 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, and the shareholder approval requirements for certain types of transactions differ from those in the U.S., and in some cases are greater, under Irish law. 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 2016, 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 the amended 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 the amended 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 from 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 or to 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 2016 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, Philadelphia, Pennsylvania and Ewing, New Jersey.

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 exercised our option to terminate the Dublin Lease effective in May 2017, and have an option to terminate the second lease in January 2019, with no less than six months' prior written notice. In August 2016, we entered into an operating lease agreement for approximately 44,000 square feet of office space in Dublin, Ireland for a term of 20 years, with an option to terminate at the end of eight years with no less than one year's prior written notice and the payment of a termination fee, and a further option to terminate at the end of 15 years with no less than one year's prior written notice. We have constructed 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 2019; 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. 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 30,000 square feet of office space in Philadelphia, Pennsylvania of which 19,000 square feet is occupied under a lease that expires in April 2019 and 11,000 square feet is occupied under a sublease that expires in December 2017. In addition, we have offices in Canada, Oxford, United Kingdom, Villa Guardia (Como), Italy, Lyon, France, 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 own a manufacturing facility in Villa Guardia (Como), Italy, which is primarily used for the manufacture of Defitelio. 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 Patent Certification, or Paragraph IV Certification, from West-Ward Pharmaceuticals Corp., formerly known as Roxane Laboratories, Inc., or Roxane, that it had submitted an abbreviated new drug application, or ANDA, to the U.S. Food and Drug Administration, or 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. 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 were consolidated by the District Court into a single case, which we refer to as the first Roxane consolidated case. In the first Roxane consolidated case, we allege that 10 of our patents covering Xyrem are or will be infringed by Roxane's ANDA, which was approved by the FDA in January 2017, and seek 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, we filed three actions against Roxane in the District Court on February 20, 2015, June 1, 2015 and January 27, 2016 that were consolidated by the District Court into a second case, which we refer to as the second Roxane consolidated case. In the second Roxane consolidated case, we allege that five of our patents covering Xyrem are or will be infringed by Roxane's ANDA and seek a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe those patents.

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, or the risk evaluation and mitigation strategy, or REMS, patents.

In July 2016, the District Court determined that it would try all of the patents at issue in the first and second Roxane consolidated cases together, including the REMS patents that were previously bifurcated and stayed, and set trial in this combined consolidated case for the second quarter of 2017. In the first quarter of 2017, the District Court bifurcated and stayed the part of the combined consolidated case involving the REMS patents. Also in the first quarter of 2017, the FDA approved Roxane's ANDA with a REMS that is separate from the Xyrem REMS.

On August 12, 2016, we filed a lawsuit against Roxane in the District Court alleging that an additional later-issued REMS patent 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 September 2016, Roxane moved to dismiss the lawsuit. This motion is pending.

The actual timing of events in our litigation with Roxane may be 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 extended Amneal's 30-month stay period to coincide with the date of Par's 30-month stay period. The stay expired on May 20, 2016.

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. In March 2016, Par moved to dismiss claims involving our patents 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), or our method of administration patents relating to a drug-drug interaction, or DDI patents. In August 2016, we and Par stipulated to dismiss claims relating to our patents covering the formulation of Xyrem on the grounds that Par had notified FDA that it had converted its Paragraph IV Certifications to a Paragraph III Certification.

On June 4, 2014, we received a notice of Paragraph IV Certification from Ohm Laboratories Inc., formerly known as Ranbaxy, Inc., 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. In May 2016, the Ranbaxy litigation was settled as described below. In the first quarter of 2017, the FDA tentatively approved the ANDAs of Amneal and Ranbaxy.

On October 30, 2014, we received a notice of Paragraph IV Certification from Teva Pharmaceutical Industries Ltd., formerly known as 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. In March 2015, Watson moved to dismiss the portion of the case based on our Orange Book-listed REMS patents on the grounds that these patents do not cover patentable subject matter. In November 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of inter partes review, or IPR, proceedings before the Patent Trial and Appeal Board, or 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 had 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 were or would 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. On November 26, 2015, we received an additional notice of Paragraph IV Certification from Wockhardt regarding newly issued patents listed in the Orange Book, and we filed an additional lawsuit against Wockhardt in the District Court alleging that our patents covering Xyrem were or would 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. In April 2016, the Wockhardt litigation was settled as set forth below.

On July 23, 2015, we received a Paragraph IV Certification from Lupin Inc., or Lupin, that it had 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.

In January, April and June 2016, the District Court issued orders consolidating all of the cases then pending against Amneal, Par, Ranbaxy, Watson, Wockhardt and Lupin into a single case for all purposes. No trial date has been set in that consolidated case.

We entered into settlement agreements with Wockhardt and Ranbaxy on April 18, 2016 and May 9, 2016, respectively, that resolved our patent litigation against Wockhardt and Ranbaxy. Under the settlement agreements, we granted each of Wockhardt and Ranbaxy a license to manufacture, market, and sell its generic version of Xyrem on or after December 31, 2025, or earlier depending on the occurrence of certain events. The specific terms of the settlement agreements are confidential.

The settlements with Wockhardt and Ranbaxy do not resolve the litigation against Amneal, Par, Watson and Lupin, which is ongoing. We cannot predict the specific timing or outcome of events in this matter with respect to the remaining defendants 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 the six REMS patents. In July 2016, the PTAB issued final decisions that the claims of these six patents are unpatentable; as a result, if the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled. We have filed notices of appeal with respect to these IPR decisions to the United States Court of Appeals for the Federal Circuit. In September 2015, certain of the ANDA filers filed a petition for IPR with respect to the validity of an additional REMS patent. In March 2016, the PTAB partially instituted an IPR on a seventh REMS patent, declining to review 25 of 28 claims. A PTAB decision on the three claims that were tried is expected before the end of the first quarter of 2017.

In October 2015, Ranbaxy and Par filed petitions for IPR with respect to the validity of one of our DDI patents, and Amneal filed an IPR petition on the same patent in February 2016. In April 2016, the PTAB denied Par's petition in its entirety and issued a decision on Ranbaxy's petition, instituting an IPR trial with respect to 16 of the claims under the patent subject to this petition and denying the petition with respect to the other 18 claims. In July 2016, the PTAB denied Amneal's petition in its entirety. In March 2016, Ranbaxy filed a petition for IPR with respect to the validity of the second of our DDI patents. In connection with settlement of our litigation with Ranbaxy, both of the IPR petitions filed by Ranbaxy were terminated.

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 connection with settlement of our patent litigation with Wockhardt, this IPR petition was terminated.

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 pending IPR or other proceeding, the outcome of any appeal of the July 2016 IPR decisions with respect to the six REMS patents or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

Shareholder Litigation Matters Relating to Celator Acquisition. On June 21, 2016, a putative class-action lawsuit challenging our acquisition of Celator Pharmaceuticals, Inc., or Celator, captioned *Dunbar v. Celator Pharmaceuticals, Inc.*, or the Dunbar action, was filed in the Superior Court of New Jersey. We refer to our acquisition of Celator in this report as the Celator Acquisition. The complaint was filed against Celator, each member of the Celator board of directors, Jazz Pharmaceuticals plc and our wholly owned subsidiary Plex Merger Sub, Inc., or Plex. The complaint generally alleges that the Celator directors breached their fiduciary duties in connection with the Celator Acquisition, and that Jazz Pharmaceuticals plc and Plex aided and abetted these alleged breaches of fiduciary duty. The complaint also generally asserts that the Celator directors breached their fiduciary duties to Celator's public stockholders by, among other things, (i) agreeing to sell Celator to us at an inadequate price, (ii) implementing an unfair process, (iii) agreeing to certain provisions of the merger agreement for the Celator Acquisition that allegedly favored us and deterred alternative bids, and (iv) failing to disclose purportedly material information in Celator's Schedule 14D-9 filing with the U.S. Securities and Exchange Commission, or SEC. The plaintiff sought, among other things, an injunction against the consummation of the Celator Acquisition and an award of costs and expenses, including a reasonable allowance for attorneys' and experts' fees.

Between June 27, 2016 and June 29, 2016, two putative class-action lawsuits challenging the Celator Acquisition, captioned *Palmisciano v. Celator Pharmaceuticals, Inc.*, or the Palmisciano action, and *Barreto v. Celator Pharmaceuticals, Inc.*, or the Barreto action, were filed in the District Court. The complaints were filed against Celator and each member of the Celator board of directors. The complaints assert causes of action under sections 14 and 20 of the Securities Exchange Act of 1934, as amended, predicated on Celator's and the Celator directors' alleged failure to disclose purportedly material information in Celator's Schedule 14D-9 filing with the SEC. The plaintiffs sought, among other things, an injunction against the consummation of the Celator Acquisition and an award of costs and expenses, including a reasonable allowance for attorneys' and experts' fees. Neither Jazz Pharmaceuticals plc nor Plex were named defendants in these actions.

On July 6, 2016, the defendants to the Dunbar action, the Palmisciano action and the Barreto action entered into a memorandum of understanding regarding settlement of these actions with the plaintiffs. The memorandum of understanding outlines the terms of the parties' agreement in principle to settle and release all claims which were or could have been asserted in these actions. In consideration for such settlement and release, the parties to these actions agreed, among other things, that Celator would amend its Schedule 14D-9 to include certain supplemental disclosures. The Schedule 14D-9 was amended by Celator on July 6, 2016, and the Celator Acquisition was completed on July 12, 2016. The settlement remains subject to, among other items, confirmatory discovery, the execution of a stipulation of settlement by the parties, final approval of the settlement by the District Court in the Barreto action and dismissal with prejudice of the Dunbar action and the Palmisciano action.

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—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
Calendar Quarter—2016		
First Quarter	$ 139.55	$ 108.50
Second Quarter	$ 160.00	$ 129.00
Third Quarter	$ 153.98	$ 117.34
Fourth Quarter	$ 126.36	$ 95.80

On February 21, 2017, the last reported sales price per share of our ordinary shares was $135.93 per share.

Holders of Ordinary Shares

As of February 21, 2017, there were two 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 2016 and 2015, 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 to 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, 2016, there were no unregistered sales of equity securities by us during the year ended December 31, 2016.

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, 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.

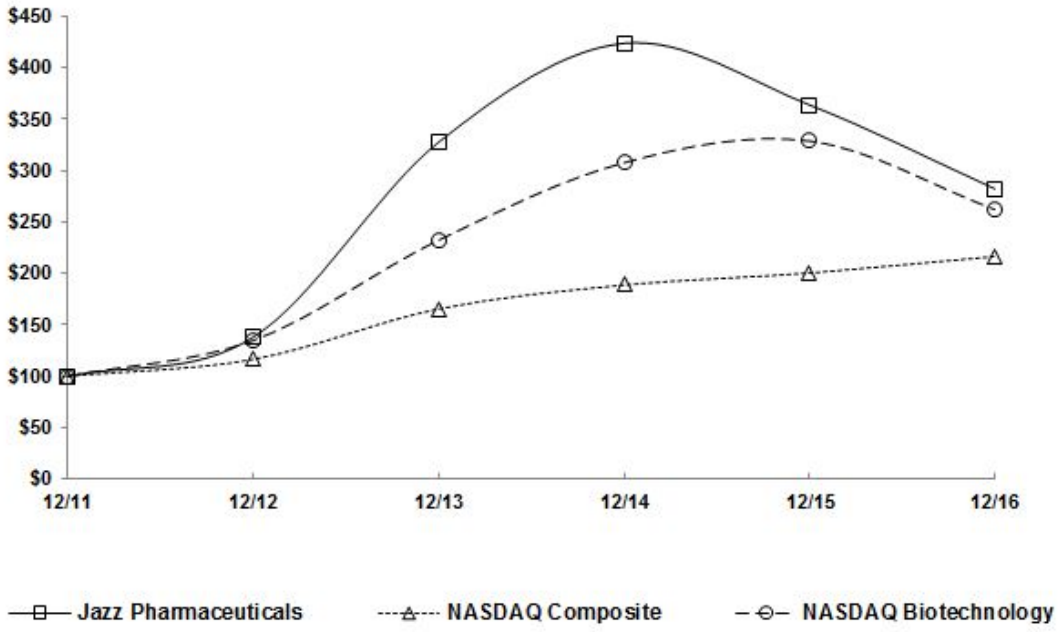
Stamp Duty. Irish stamp duty (if any) may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. A transfer of our ordinary 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, 2011 in (i) our ordinary shares; (ii) the NASDAQ Composite Index; and (iii) the NASDAQ Biotechnology Index through December 31, 2016. Information set forth in the graph below represents the performance of the Jazz Pharmaceuticals, Inc. common stock from December 31, 2011 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, 2016. 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, 2016:

	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, 2016	—	$ —	—	$ —
November 1 - November 30, 2016	22,500	$ 110.40	22,500	$ 297,516,445
December 1 - December 31, 2016	152,300	$ 105.02	152,300	$ 281,524,820
Total	174,800	$ 105.71	174,800	

(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 2016, 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, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015 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, 2013 and 2012, and the selected consolidated balance sheet data as of December 31, 2014, 2013 and 2012 are derived from audited consolidated financial statements not included in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2016(1)	2015	2014(2)	2013	2012(3)
	(In thousands, except per share amounts)				
Consolidated Statements of Income Data:					
Revenues:					
Product sales, net	$ 1,477,261	$ 1,316,819	$ 1,162,716	$ 865,398	$ 580,527
Royalties and contract revenues	10,712	7,984	10,159	7,025	5,452
Total revenues	1,487,973	1,324,803	1,172,875	872,423	585,979
Operating expenses:					
Cost of product sales (excluding amortization and impairment of intangible assets)	105,386	102,526	117,418	102,146	78,425
Selling, general and administrative	502,892	449,119	406,114	304,303	223,882
Research and development	162,297	135,253	85,181	41,632	20,477
Acquired in-process research and development	23,750	—	202,626	4,988	—
Intangible asset amortization	101,994	98,162	126,584	79,042	65,351
Impairment charges	—	31,523	39,365	—	—
Total operating expenses	896,319	816,583	977,288	532,111	388,135
Income from operations	591,654	508,220	195,587	340,312	197,844
Interest expense, net	(61,942)	(56,917)	(52,713)	(26,916)	(16,869)
Foreign currency gain (loss)	3,372	1,445	8,683	(1,697)	(3,620)
Loss on extinguishment and modification of debt	(638)	(16,815)	—	(3,749)	—
Income before income tax provision (benefit) and equity in loss of investee	532,446	435,933	151,557	307,950	177,355
Income tax provision (benefit)	135,236	106,399	94,231	91,638	(83,794)
Equity in loss of investee	379	—	—	—	—
Income from continuing operations	396,831	329,534	57,326	216,312	261,149
Income from discontinued operations, net of taxes	—	—	—	—	27,437
Net income	396,831	329,534	57,326	216,312	288,586
Net loss attributable to noncontrolling interests	—	(1)	(1,061)	—	—
Net income attributable to Jazz Pharmaceuticals plc	$ 396,831	$ 329,535	$ 58,387	$ 216,312	$ 288,586
Net income attributable to Jazz Pharmaceuticals plc per ordinary share:					
Basic:					
Income from continuing operations	$ 6.56	$ 5.38	$ 0.98	$ 3.71	$ 4.61
Income from discontinued operations	—	—	—	—	0.48
Net income attributable to Jazz Pharmaceuticals plc	$ 6.56	$ 5.38	$ 0.98	$ 3.71	$ 5.09
Diluted:					
Income from continuing operations	$ 6.41	$ 5.23	$ 0.93	$ 3.51	$ 4.34
Income from discontinued operations	—	—	—	—	0.45
Net income attributable to Jazz Pharmaceuticals plc	$ 6.41	$ 5.23	$ 0.93	$ 3.51	$ 4.79
Weighted-average ordinary shares used in per share calculations - basic	60,500	61,232	59,746	58,298	56,643
Weighted-average ordinary shares used in per share calculations - diluted	61,870	63,036	62,614	61,569	60,195

	As of December 31,				
	2016(1)	2015	2014(2)	2013	2012(3)
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investments	$ 425,963	$ 988,785	$ 684,042	$ 636,504	$ 387,196
Working capital	490,663	1,031,025	799,044	660,589	360,034
Total assets (4)(5)	4,800,227	3,332,612	3,308,617	2,225,900	1,952,014
Long-term debt, current and non-current (4)	2,029,625	1,188,444	1,313,161	539,436	443,298
Retained earnings (accumulated deficit)	528,907	302,686	34,704	18,532	(61,296)
Total Jazz Pharmaceuticals plc shareholders' equity	1,877,339	1,598,646	1,371,144	1,295,534	1,121,292

(1) On May 27, 2016, we entered into a definitive merger agreement with Celator Pharmaceuticals, Inc., or Celator, pursuant to which we made a cash tender offer of $30.25 per share for all of the outstanding shares of Celator's common stock. On July 12, 2016, we completed the acquisition of Celator, which acquisition we refer to in this report as the Celator Acquisition, under the terms of the merger agreement. Celator became an indirect wholly-owned subsidiary of Jazz Pharmaceuticals plc, and each share of Celator common stock then outstanding (other than shares owned by us or Celator) was converted into the right to receive $30.25, the same price per share offered in the tender offer. The aggregate cash consideration for the Celator Acquisition was $1.5 billion. The results of operations of the acquired Celator business, along with the estimated fair values of the assets acquired and liabilities assumed in the Celator Acquisition, have been included in our consolidated financial statements since the closing of the Celator Acquisition on July 12, 2016. On July 12, 2016, we entered into an amendment to our 2015 credit agreement, which amended agreement we refer to in this report as our amended credit agreement, that provides for a revolving credit facility of $1.25 billion, which replaced our prior revolving credit facility of $750.0 million, and a $750.0 million term loan facility. We used the proceeds of $1.0 billion of loans under the revolving credit facility, together with cash on hand, to fund the Celator Acquisition. The maturity date of both our revolving credit facility and term loan facility was extended from June 2020 to July 2021 pursuant to the amended credit facility.

(2) 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 in this report as the Gentium Acquisition. 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.

(3) 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.

(4) Effective January 1, 2016, we adopted Accounting Standards Update, or ASU, No. 2015-03 “Interest - Imputation of Interest” which 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. The standard requires retrospective application. Prior period amounts for all years presented above were reclassified to conform to the current period presentation. Total assets and total long-term debt, current and non-current at December 31, 2015, 2014, 2013 and 2012 have been reduced by $16.1 million, $29.3 million, $10.5 million and $13.5 million, respectively, to reflect the adoption of ASU No. 2015-03.

(5) The indirect effects of certain unrecognized tax benefits, previously classified within other non-current assets for all years presented above, have been reclassified to deferred tax assets, net, non-current and deferred tax liability, net, non-current to conform to current period presentation.

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, and marketed in the U.S. 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 sodium)**, a product approved in the U.S. for the treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome, or SOS, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT, and in Europe (where it is marketed as Defitelio® (defibrotide)) for the treatment of severe VOD in adults and children undergoing 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 and new geographic markets;
- Acquiring or licensing rights to 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 total net product sales increased by 12% in 2016 compared to 2015, primarily due to an increase in Xyrem and Defitelio product sales. We expect total net product sales to increase in 2017 over 2016, primarily due to expected growth in sales of our lead marketed products, as well as sales from the anticipated U.S. commercial launch of Vyxeos™, an

investigational product in development as a treatment for high-risk acute myeloid leukemia, or AML. Our ability to increase net product sales is subject to a number of risks and uncertainties as set forth below and under "Risk Factors" in Item I, Part 1A of this Annual Report on Form 10-K, including completion of submission of our new drug application, or NDA, for Vyxeos and its approval by the FDA.

Significant Developments Affecting Our Business

Approval of Generic Versions of Xyrem

On January 17, 2017, the FDA announced approval of an abbreviated new drug application, or ANDA, for a generic version of Xyrem, held by West-Ward Pharmaceuticals Corp., formerly known as Roxane Laboratories, Inc., or Roxane. The FDA's letter approving Roxane's ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product. Roxane's approval also includes a waiver that permits Roxane to use a separate risk evaluation and mitigation strategy, or REMS, program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. On January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal Pharmaceuticals, or Amneal, and one for Ohm Laboratories Inc., formerly known as Ranbaxy, Inc., or Ranbaxy. For further discussion, see "-Challenges, Risks and Trends Related to Our Lead Marketed Products" below.

2016 Developments

On March 30, 2016, the FDA granted marketing approval for Defitelio for the treatment of adult and pediatric patients with VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT. We launched Defitelio in the U.S. shortly after FDA approval.

On July 12, 2016, we completed the acquisition of Celator Pharmaceuticals, Inc., or Celator, which we refer to as the Celator Acquisition. The Celator Acquisition broadened our hematology/oncology portfolio with the acquisition of worldwide development and commercialization rights to Vyxeos. In the third quarter of 2016, we initiated a rolling submission of an NDA to the FDA for Vyxeos. We expect to complete the NDA submission by the end of the first quarter of 2017. Our ability to complete the NDA submission for Vyxeos and to obtain FDA approval of the NDA is subject to a number of risks and uncertainties, including those set forth under the heading "*While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products and, in the case of our product candidates, our ability to obtain regulatory approval in the U.S. and Europe and, if approved, to successfully launch and commercialize those product candidates. Our inability to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K.

In connection with the Celator Acquisition, on July 12, 2016, we entered into our amended credit agreement providing for a revolving credit facility of $1.25 billion, which replaced our prior revolving credit facility of $750.0 million, and a $750.0 million term loan facility, of which $712.9 million principal amount remained outstanding as of December 31, 2016.

In the third quarter of 2016, we commenced commercial operations at our new manufacturing facility in Ireland after receiving FDA approval of the facility in June 2016. In September 2016, we manufactured and shipped our first commercial batch of Xyrem from this facility, reducing our dependence on our third-party Xyrem supplier.

In November 2016, 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.

Continued Emphasis on Research and Development

We have continued our focus on research and development activities, and, in 2016, we achieved meaningful milestones in our 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	Excessive sleepiness, or ES, in obstructive sleep apnea, or OSA	Patient enrollment in two Phase 3 trials completed in third quarter of 2016; expect preliminary data by end of first quarter of 2017; subject to results of trials, plan to submit an NDA, to the FDA in late 2017
JZP-110	ES in narcolepsy	Patient enrollment in Phase 3 trial completed in fourth quarter of 2016; expect preliminary data in second quarter of 2017; subject to results of trial, plan to submit an NDA to the FDA in late 2017
JZP-110	ES in Parkinson's disease	First patient enrolled in Phase 2 trial in first quarter of 2017
Xyrem	EDS and cataplexy in pediatric narcolepsy patients with cataplexy	Patient enrollment in Phase 3 trial completed in fourth quarter of 2016; subject to results of trial, expect to submit a supplemental NDA, or sNDA, and pediatric written request report to the FDA in fourth quarter of 2017
JZP-507	EDS and cataplexy in narcolepsy	Expect to submit an NDA to the FDA by first quarter of 2018
JZP-258	EDS and cataplexy in narcolepsy	Expect to initiate Phase 3 trial in the European Union, or EU, and U.S. in first quarter of 2017; subject to results of trial, expect to submit an NDA to the FDA in 2019
Oxybate once-nightly dosing	Narcolepsy	Program progressing; evaluation of deuterated oxybate and other formulation options continues as part of once-nightly development process
Hematology/Oncology		
Vyxeos (CPX-351)	High-risk acute myeloid leukemia, or AML	Initiated a rolling submission of an NDA to the FDA in third quarter of 2016; expect to complete the NDA submission by end of first quarter of 2017; expect to submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, in second half of 2017
Defibrotide	Prevention of VOD in high-risk patients following HSCT	First patient enrolled in Phase 3 trial in first quarter of 2017
Defibrotide	Prevention of acute Graft versus Host Disease, or aGvHD, following HSCT	Expect to initiate Phase 2 proof of concept trial in fourth quarter of 2017
Asparaginase	ALL and other hematologic disorders	Evaluation of early-stage product candidates

For further details regarding these development activities, see "Business - Research and Development" in Item 1 of Part I, Business, of this Annual Report on Form 10-K.

For 2017 and beyond, we expect that our research and development expenses will increase from historical levels, particularly as we initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates. Our ability to continue to undertake our planned development activities, as well as the success of these activities, are subject to a number of risks and uncertainties, including those set forth under the headings "Risks Related to Our Business" and "Risks Related to Our Industry" in Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K.

Challenges, Risks and Trends Related to Our Lead Marketed Products

Xyrem. Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which accounted for 75% of our net product sales for the year ended December 31, 2016 and 73% of our net product sales for the year ended December 31, 2015. 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 product development efforts relating to Xyrem, including seeking to enhance and enforce our intellectual property rights and to develop product, service and safety improvements for patients.

Our future plans assume that sales of Xyrem will increase, although our plans assume a slower rate of increase than in recent years. While Xyrem product sales grew from 2015 to 2016 and 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 January 2017, and we cannot assure you that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes.

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, including those related to:

- the potential commercialization of a generic version of Xyrem, including in connection with the recent approval by the FDA of ANDA for a generic version of Xyrem, as well as tentative approval of two additional ANDAs, as further described below;
- the potential U.S. introduction of an alternative product to Xyrem for treating cataplexy and/or EDS in narcolepsy;
- changes to, increases of or uncertainties around regulatory restrictions, including changes to our Xyrem REMS, particularly in light of the FDA's waiver of the single shared systems REMS requirement for sodium oxybate and approval of a separate generic sodium oxybate REMS, as further described below;
- any increase in pricing pressure from, or restrictions on reimbursement imposed by, third party payors;
- changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing by government entities;
- operational disruptions at the Xyrem central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA;
- any supply or manufacturing problems, including any problems with our sole source Xyrem API provider;
- 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
- our U.S.-based sodium oxybate and Xyrem suppliers' ability to obtain sufficient quotas from the U.S. Drug Enforcement Administration, or DEA, to satisfy our needs for Xyrem.

Seven companies sent us notices that they had filed ANDAs with the FDA seeking approval to market a generic version of Xyrem, and we filed patent lawsuits against each of these companies in the District Court for New Jersey, or District Court. In the second quarter of 2016, we settled two of these lawsuits, granting the settling ANDA applicants a license to manufacture, market and sell their generic versions of Xyrem on or after December 31, 2025, or earlier depending on the occurrence of certain events. In 2016, the District Court consolidated all of our pending patent litigation (other than our lawsuit filed in August 2016) and set the consolidated case for trial in the second quarter of 2017. In the first quarter of 2017, the District Court bifurcated and stayed the part of the consolidated case involving the patents on the Xyrem distribution system, or REMS patents. We cannot predict the timing or outcome of this or the other ANDA litigation proceedings against the remaining non-settling ANDA filers, which have been consolidated as one case in the District Court, with no trial date set. In July 2016, the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office issued final decisions that the claims of six of seven REMS patents are unpatentable. We filed a notice of appeal of these decisions on February 22, 2017. If the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled, and we will not be able to enforce these patents. In March 2016, the PTAB partially instituted an IPR on a seventh REMS patent, declining to review 25 of 28 claims. A PTAB decision on the three claims that were tried is expected before the end of the first quarter of 2017. For a description of these legal proceedings, 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 pending IPR or other proceeding or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

In September 2016, Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, submitted a Citizen Petition to the FDA requesting that, for safety reasons, the FDA refuse to approve any sodium oxybate ANDA with a proposed package insert or REMS that omits the portions of the Xyrem package insert and the Xyrem REMS that instruct prescribers on adjusting the dose of the product when it is co-administered with divalproex sodium (also known as valproate or valproic acid). On January 17, 2017, the FDA granted the Citizen Petition with respect to the Xyrem package insert. The FDA concluded that it will not approve any sodium oxybate ANDA referencing Xyrem that does not include in its package insert the portions of the currently approved Xyrem package insert related to the drug-drug interaction with divalproex sodium. The FDA stated that it did not need to reach the question of whether the drug-drug interaction information could have been excluded from the generic sodium oxybate REMS materials because it was approving a REMS in connection with a sodium oxybate ANDA including that information. Our Xyrem patents include three method of administration patents relating to a drug-drug interaction, or DDI patents, covering these instructions on the Xyrem package insert and Xyrem REMS. We cannot predict whether or when one or more of the ANDA filers may pursue a challenge to the FDA's response to the Citizen Petition or whether any such challenges would be successful. Likewise, we cannot predict whether we will be able to maintain the validity of any of our patents or will

otherwise obtain a judicial determination that the generic sodium oxybate package insert or the generic sodium oxybate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem. For a description of these matters, including risks and uncertainties related to our REMS, our REMS patents and our DDI patents, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K, "Business-Government Regulation-*The Hatch-Waxman Act*" in Part I, Item 1 of this Annual Report on Form 10-K, 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.

On January 17, 2017, the FDA announced approval of the Roxane ANDA, and on January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal and one for Ranbaxy. The FDA's letter approving Roxane's ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product. Roxane's approval also includes a waiver of the single shared REMS requirement and permits Roxane to use a separate REMS program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. We were not involved in the development of the generic sodium oxybate REMS. We will evaluate whether the FDA's waiver of the requirement for a single, shared system REMS in connection with approval of the ANDAs meets the conditions for such a waiver under applicable law and, to the extent that we determine that the waiver was not permissible under applicable law, will evaluate potential challenges to the FDA's waiver decision. We cannot predict whether or when we may pursue any such challenges or whether any such challenges would be successful.

While the FDA has approved or tentatively approved ANDAs seeking to market generic versions of Xyrem and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs, the timing of any potential commercial launch of a generic version of Xyrem is uncertain. We do not believe a launch by an ANDA filer is likely to occur prior to either a date agreed in a settlement agreement between us and such ANDA filer or a District Court, or potentially an appellate court, decision in our ongoing patent litigation. If we prevail at trial or on appeal, we cannot guarantee that the court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem. Instead, the court may order an ANDA filer that is found to infringe to pay damages in the form of lost profits or a reasonable royalty, which could be significant. We expect that the launch of a generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, would have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects. For further discussion regarding the risks associated with FDA approval of the Roxane ANDA, tentative approval of the Amneal and Ranbaxy ANDAs, potential approval or tentative approval of additional ANDAs and the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see "Business-Government Regulation-The Hatch-Waxman Act" in Part I, Item 1 of this Annual Report on Form 10-K 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.

In connection with FDA approval of the current Xyrem REMS in February 2015, the FDA indicated that it 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 request, seek to require or ultimately require modifications to the Xyrem REMS in connection with approval of the generic sodium oxybate REMS (or otherwise) 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 make it more difficult or expensive for us to distribute Xyrem, make distribution easier for sodium oxybate competitors, impair the safety profile of Xyrem and/or negatively affect sales of Xyrem. We also may face pressure to license or share intellectual property pertinent to the Xyrem REMS, including proprietary data required for safe distribution of sodium oxybate, in connection with the FDA's approval of the generic sodium oxybate REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the approval of the generic sodium oxybate REMS, or licensing or sharing intellectual property pertinent to our Xyrem REMS or elements of the Xyrem REMS.

For a further discussion of other risks relating to Xyrem, see the risk factors under the heading "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" in Part I, Item 1A of this Annual Report on Form 10-K.

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 14% of our net product sales in 2016 and 15% of our net product sales in 2015. 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, a significant challenge to our ability to maintain current sales levels and to increase sales is our extremely limited inventory of Erwinaze, past and continuing supply interruptions and our need to minimize or avoid additional supply interruptions due to capacity constraints, production delays, quality or regulatory challenges and other manufacturing difficulties. Erwinaze is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL.

In January 2017, the FDA issued a warning letter to PBL indicating that it was not satisfied with PBL's responses to the FDA Form 483 issued to PBL in March 2016, citing significant violations of the FDA's current Good Manufacturing Practices, or cGMP, for finished pharmaceuticals and significant deviations from cGMP for active pharmaceutical ingredients, or APIs. We cannot predict whether the FDA's required remediation activities will further strain manufacturing capacity and adversely affect Erwinaze supply, particularly in light of our extremely limited product inventory. We also cannot predict if or when PBL will correct the violations and deviations to the satisfaction of the FDA. Any failure to do so could result in the FDA refusing admission of Erwinaze in the U.S., as well as additional enforcement actions by the FDA and other regulatory entities. Any of these actions 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.

Moreover, the current manufacturing capacity for Erwinaze is 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 and to address the production delays, quality challenges and related regulatory scrutiny. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build product inventory levels that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues. We have experienced product quality, manufacturing and inventory challenges that have resulted, and may continue to result, in disruptions in our ability to supply certain markets, including the U.S., from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. Most recently, we experienced supply interruptions of Erwinaze in the U.S. and other countries in the third and fourth quarters of 2016. As capacity constraints and supply disruptions continue, whether as a result of continued quality or other manufacturing issues, regulatory issues or otherwise, we will be unable to build a desired excess level of product inventory, our ability to supply the market may continue to be compromised and physicians' decisions to use Erwinaze have been, and in the future may continue to be, negatively impacted. 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, as further discussed in "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K.

Defitelio/defibrotide. Sales of Defitelio/defibrotide were 7% of our net product sales for the year ended December 31, 2016 and 5% of our net product sales for the year ended December 31, 2015. We launched Defitelio in certain European countries beginning in 2014 and continue to launch the product in additional European countries on a rolling basis. On March 30, 2016, the FDA approved our NDA for Defitelio for the treatment of adult and pediatric patients with VOD with renal or pulmonary dysfunction following HSCT. We launched Defitelio in the U.S. shortly after FDA approval, and our U.S. commercial launch is still at an early stage.

Our ability to realize the anticipated benefits from our investment in Defitelio is subject to risks and uncertainties, including those risk factors set forth under the heading "Risks Related to Our Business" in Item 1, Part 1A of this Annual Report on Form 10-K. If sales of Defitelio do not reach the levels we expect, our anticipated revenue from the product will be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Other Challenges and Risks

We anticipate that we will continue to face a number of other challenges and risks to our business and our ability to execute our strategy in 2017 and beyond. 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 2016, we made a significant investment in Vyxeos through the Celator Acquisition. Our ability to realize the anticipated benefits from this investment is subject to a number of risks and uncertainties, including the risk factors set forth under "Risks Relating to Our Business" in Part I, Item 1A of this Annual Report on Form 10-K.

In addition, drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny, including with respect to companies that have increased the price of products after acquiring those products from other companies. Both the U.S. House of Representatives and the U.S. Senate have conducted several 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 any government investigation with respect to our drug pricing or other business practices, we could incur significant expense and could be distracted from operation of our business and execution of our strategy.

In May and October 2016 and February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients and documents concerning the provision of financial assistance to Medicare patients taking drugs sold by us. The Office of the Inspector General has established guidelines that permit pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a

first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. For more information, see the risk factors under the headings "*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*" and "*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.

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 and product candidates, particularly with respect to certain products as to which we maintain limited inventories, our dependence on single source suppliers for most of our products, product candidates and APIs, and the requirement that we and our product suppliers be qualified by the FDA to manufacture product and comply with applicable manufacturing regulations;
- 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 and pharmaceutical pricing 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 government programs and 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 comparable non-U.S. regulatory agencies, including with respect to product labeling, requirements for distribution, obtaining sufficient DEA quotas where needed, marketing and promotional activities, patient assistance programs, 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 increase investment in our product pipeline development projects and undertake multiple planned NDA submissions for our product candidates;
- the risks associated with business combination or product or product candidate acquisition transactions, including risks associated with the Celator Acquisition, such as the challenges inherent in the integration of acquired businesses with our historical 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, as a result of, among other things, the Celator Acquisition.

Any of these risks and uncertainties could have a material adverse effect on our business, financial condition, results of operations and growth prospects. 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, 2016, 2015 and 2014 (in thousands except percentages):

	2016 (1)	Change	2015	Change	2014 (2)
Product sales, net	$ 1,477,261	12%	$ 1,316,819	13%	$ 1,162,716
Royalties and contract revenues	10,712	34%	7,984	(21)%	10,159
Cost of product sales (excluding amortization and impairment of intangible assets)	105,386	3%	102,526	(13)%	117,418
Selling, general and administrative	502,892	12%	449,119	11%	406,114
Research and development	162,297	20%	135,253	59%	85,181
Acquired in-process research and development	23,750	N/A(3)	—	N/A(3)	202,626
Intangible asset amortization	101,994	4%	98,162	(22)%	126,584
Impairment charges	—	N/A(3)	31,523	(20)%	39,365
Interest expense, net	61,942	9%	56,917	8%	52,713
Foreign currency gain	(3,372)	133%	(1,445)	(83)%	(8,683)
Loss on extinguishment and modification of debt	638	(96)%	16,815	N/A(3)	—
Income tax provision	135,236	27%	106,399	13%	94,231
Equity in net loss of investee	379	N/A(3)	—	N/A(3)	—
Net loss attributable to noncontrolling interests	—	N/A(3)	(1)	N/A(3)	(1,061)

(1) Our financial results include the financial results of the historical Celator business since the closing of the Celator Acquisition on July 12, 2016.
(2) Our financial results include the financial results of the historical Gentium business since the closing of the Gentium Acquisition on January 23, 2014.
(3) 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, 2016, 2015 and 2014 (in thousands except percentages):

	2016	Change	2015	Change	2014
Xyrem	$ 1,107,616	16%	$ 955,187	23%	$ 778,584
Erwinaze/Erwinase	200,678	(1)%	203,261	2%	199,665
Defitelio/defibrotide	108,952	54%	70,731	—%	70,537
Prialt® (ziconotide) intrathecal infusion	29,120	10%	26,440	—%	26,421
Psychiatry	17,653	(52)%	37,135	(9)%	40,879
Other	13,242	(45)%	24,065	(48)%	46,630
Product sales, net	1,477,261	12%	1,316,819	13%	1,162,716
Royalties and contract revenues	10,712	34%	7,984	(21)%	10,159
Total revenues	$ 1,487,973	12%	$ 1,324,803	13%	$ 1,172,875

Product Sales, Net

Xyrem product sales increased by 16% in 2016 and by 23% in 2015 compared to the immediately preceding years, primarily due to higher average net selling prices in 2016 and 2015 and, to a lesser extent, increases in sales volume. Price increases were instituted in February 2016 and February 2015. Xyrem product sales volumes increased by 6% in both 2016 and 2015 compared to the immediately preceding years. The sales volume increase in both years was 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 and pharmacy operations were satisfactory during 2016. Erwinaze product sales decreased slightly in 2016 compared to 2015, primarily due to a decrease in sales volume, partially offset by price increases instituted in January 2016 and July 2015. In 2016, the company continued to experience supply challenges, which resulted in fluctuations in inventory levels and temporary disruptions to the company's ability to supply certain markets. 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. The Erwinaze sales volume increase in 2015 was 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 increased in 2016 compared to 2015, primarily due to the launch of Defitelio in the U.S. in April 2016 and higher net sales outside the U.S primarily due to higher sales volume. Defitelio/defibrotide product sales in 2015 were consistent with sales in 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%. Prialt product sales increased in 2016 compared to 2015, primarily due to an increase in sales volume. Prialt product sales in 2015 were consistent with sales in 2014. Psychiatry product sales decreased in 2016 and 2015 compared to the immediately preceding years, primarily due to the impact of generic competition. Other product sales decreased in 2016 and 2015 compared to the immediately preceding years, primarily due to our disposition, in March 2015, of certain products and the related business that we originally acquired in the EUSA Acquisition. We expect total product sales will increase in 2017 over 2016, primarily due to anticipated growth in sales of our lead marketed products, as well as sales from the anticipated U.S commercial launch of Vyxeos, partially offset by decreases in sales of certain other products.

Royalties and Contract Revenues

Royalties and contract revenues increased by $2.7 million in 2016 compared to 2015, primarily due to sales-based milestone revenue of $1.0 million recognized in 2016 and higher sales of out-licensed products. Royalties and contract revenues decreased in 2015 compared to 2014, primarily due to a $2.0 million sales-based milestone payment we received in 2014. We expect royalties and contract revenues in 2017 to decrease slightly compared to 2016, primarily due to the sales-based milestone revenue we recognized in 2016.

Cost of Product Sales

Cost of product sales increased in 2016 compared to 2015 primarily due to a change in product mix and an increase in net 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 net product sales. Gross margins as a percentage of net product sales were 92.9%, 92.2% and 89.9% in 2016, 2015 and 2014, respectively. The increase in our gross margin percentage in 2016 compared to 2015 was primarily due to a change in product mix. 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. We expect that our gross margin as a percentage of net product sales will not change materially in 2017 compared to 2016.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased in 2016 compared to 2015, primarily due to an increase of $22.7 million in compensation-related expenses driven by higher headcount, an increase of transaction and integration expenses related to the Celator Acquisition of $13.1 million, a one-time contract termination fee of $11.6 million to eliminate future royalty payments related to Vyxeos, an increase of $8.5 million in legal fees and expenses related to certain legal proceedings and restructuring, and an increase in other expenses related to the expansion and support of our business, including expenses related to the launch of Defitelio in the U.S., partially offset by a one-time charge of $18.0 million in 2015 for settlement of a contract claim liability. 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. We expect selling, general and administrative expenses in 2017 to increase compared to 2016, primarily due to an increase in compensation-related expenses driven by higher headcount and increases in expenses related to the preparation for the potential U.S. commercial launch of Vyxeos, higher promotion costs and patient access and support services for Xyrem, and other expenses related to the expansion and support of our business.

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,		
	2016	2015	2014
Clinical studies and outside services	$ 100,165	$ 63,079	41,769
Personnel expenses	47,969	39,515	38,228
Milestone	750	25,000	—
Other	13,413	7,659	5,184
Total	$ 162,297	$ 135,253	$ 85,181

Research and development expenses increased by $27.0 million in 2016 compared to 2015, primarily due to increased clinical studies and outside services costs related to three Phase 3 clinical trials for JZP-110 and development of other sleep product candidates and expenses related to initiation of a rolling submission of an NDA for Vyxeos. Personnel expenses increased by $8.5 million in 2016 compared to 2015, primarily due to salary and benefit-related expenses (including share-based compensation) primarily driven by increased headcount in support of our development programs and, to a lesser extent, increased headcount due to the Celator Acquisition. 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. Personnel expenses did not change materially in 2015 compared to 2014.

For 2017 and beyond, we expect that our research and development expenses will continue to increase from historical levels particularly as we prepare for a number of anticipated regulatory submissions, 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 2016, acquired in-process research and development, or IPR&D, expense was related to upfront and option payments. In March 2016 we obtained intellectual property and know-how related to recombinant crisantaspase for a payment of $8.8 million. In July 2016 we made a payment of $15.0 million to Pfenex Inc., or Pfenex, under an agreement whereby Pfenex granted us worldwide rights to develop and commercialize multiple early-stage hematology product candidates and an option for us to negotiate a license for a recombinant pegaspargase product candidate.

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 Biopharmaceuticals Co., Ltd, or SK, retained rights, for an upfront payment of $125.0 million to Aerial. We also paid a $2.0 million milestone to SK, which was triggered on assignment of the JZP-110 rights from Aerial to us, and $0.6 million in license fees in connection with JZP-416.

Intangible Asset Amortization

Intangible asset amortization increased in 2016 compared to 2015, primarily due to the commencement of amortization of the Defitelio U.S. intangible asset upon FDA approval in March 2016, partially offset by the cessation of amortization of certain intangible assets that were fully amortized in 2015 and the impact of foreign exchange rates on euro-denominated assets. 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. Intangible asset amortization is expected to increase in 2017 compared to 2016, subject to FDA approval of Vyxeos and commencement of amortization of the related intangible asset.

Impairment Charges

In the fourth quarter of 2015, we recorded an impairment charge of $31.5 million related 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.

Interest Expense, Net

On July 12, 2016, we entered into the amended credit agreement, which provides for a revolving credit facility of $1.25 billion, of which $1.0 billion was drawn to partially fund the Celator Acquisition and $850.0 million remained outstanding as of December 31, 2016, and a $750.0 million term loan facility, of which $712.9 million principal amount remained outstanding as of December 31, 2016. Interest expense, net increased by $5.0 million in 2016 compared to 2015, primarily due to the increase in our average debt balance and increased interest rates on borrowings under the amended credit agreement as compared to the 2015 credit agreement. Interest expense, net increased by $4.2 million 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 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, 2016. 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. We expect interest expense will be higher in 2017 compared to 2016 primarily due to the increase in our average debt balance.

Foreign Currency Gain

Foreign currency gain is primarily related to the translation of euro denominated net monetary liabilities, including intercompany balances, held by subsidiaries with a U.S. dollar functional currency.

Loss on Extinguishment and Modification of Debt

In 2016, we recorded a loss of $0.6 million in connection with our entry into the amended credit agreement in July 2016, which was primarily comprised of new third party fees associated with the modified 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.

Income Tax Provision

Our income tax provision was $135.2 million, $106.4 million and $94.2 million in 2016, 2015 and 2014, respectively. The effective tax rates for 2016, 2015 and 2014 were 25.4%, 24.4% and 62.2%, 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 rates for 2016 and 2015 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 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 rate for 2014 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, 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 and benefits from certain originating income tax credits. The increase in the effective tax rate in 2016 compared to 2015 was primarily due to a decrease in the impact of reductions in tax rates in certain jurisdictions and a decrease in originating tax credits, partially offset by changes in income mix among the various jurisdictions in which we operate. 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.

Equity in Net Loss of Investee

Equity in net loss of investee relates to our share in the net loss of a company in which we have made an investment accounted for under the equity method of accounting.

Net Loss Attributable to Noncontrolling Interests

Net loss attributable to noncontrolling interests 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.

Liquidity and Capital Resources

As of December 31, 2016, we had cash, cash equivalents and investments of $426.0 million, borrowing availability under our revolving credit facility of $399.5 million and long-term debt principal amount of $2.1 billion. Our long-term debt included $850.0 million in outstanding borrowings under our revolving credit facility, $712.9 million aggregate principal amount term loan and $575.0 million principal amount of the 2021 Notes. During 2016, 2015 and 2014, we generated cash flows from operations of $590.5 million, $531.9 million and $407.6 million, respectively, and we expect to continue to generate positive cash flow from operations.

On July 12, 2016, we completed the Celator Acquisition. The aggregate cost to us of the Celator Acquisition was $1.5 billion. On July 12, 2016, we entered into the amended credit agreement, which provides for a revolving credit facility of $1.25 billion replacing our prior revolving credit facility of $750.0 million, and a $750.0 million term loan facility, of which $712.9 million principal amount was outstanding as of December 31, 2016. We used the proceeds of $1.0 billion of loans under the revolving credit facility, together with cash on hand, to fund the Celator Acquisition and expect to use the proceeds from future loans under the revolving credit facility, if any, for general corporate purposes, including corporate development activities. In the fourth quarter of 2016 we made a $150.0 million repayment of borrowings under our revolving credit facility.

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. 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” in Part I, Item 1A of this Annual Report on Form 10-K 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.”* 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 amended 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 million, exclusive of any brokerage commissions. In August 2015, we completed repurchases under the May 2013 share repurchase program. In November 2015, our board of directors authorized another share repurchase program pursuant to which we were authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300 million, exclusive of any brokerage commissions. In September 2016, we completed repurchases under the November 2015 share repurchase program. In November 2016, 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 this 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 depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the amended credit agreement, corporate and regulatory requirements and market conditions. The new share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2016, under the November 2015 and November 2016 repurchase programs, we spent a total of $278.3 million to repurchase 2.2 million of our ordinary shares at an average total purchase price, including brokerage commissions, of $124.09 per share. All ordinary shares repurchased were canceled. As of December 31, 2016, the remaining amount authorized under the November 2016 share repurchase program was $281.5 million.

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

	Year Ended December 31,		
	2016	2015	2014
Net cash provided by operating activities	$ 590,536	$ 531,943	$ 407,606
Net cash used in investing activities	(1,749,300)	(2,255)	(1,067,649)
Net cash provided by (used in) financing activities	540,987	(214,323)	711,034
Effect of exchange rates on cash and cash equivalents	(5,045)	(10,622)	(3,453)
Net increase (decrease) in cash and cash equivalents	$ (622,822)	$ 304,743	$ 47,538

Net cash provided by operating activities of $590.5 million in 2016 related to net income of $396.8 million, adjusted for upfront and option payments totaling $23.8 million in connection with our acquisition of IPR&D assets and non-cash items of $192.7 million primarily related to intangible asset amortization, share-based compensation and amortization of debt discount, deferred financing costs and deferred income taxes. This was partially offset by $22.7 million of net cash outflow related to changes in operating assets and liabilities. Net cash provided by operating activities in 2015 related to net income of $329.5 million, adjusted for non-cash items of $201.4 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. 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 $208.2 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 $60.5 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.

Net cash used in investing activities in 2016 primarily related to the Celator Acquisition for $1.5 billion, a $150.0 million milestone payment to Sigma-Tau that was triggered by the FDA approval of Defitelio on March 30, 2016, purchase of investments of $65.3 million and upfront and option payments of $23.8 million to acquire IPR&D assets. 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 provided by financing activities in 2016 primarily related to net proceeds from issuance of debt of $994.6 million and proceeds of $24.2 million from employee equity incentive and purchase plans, partially offset by $278.3 million used to repurchase our ordinary shares under our share repurchase program, $150.0 million and $28.3 million repayments of borrowings under our revolving credit facility and long-term debt, respectively, and payment of employee withholding taxes of $21.2 million related to share-based awards. 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 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 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.

Credit Agreement

On June 18, 2015, Jazz Pharmaceuticals plc, as guarantor, and certain of our wholly owned subsidiaries, as borrowers, entered into the 2015 credit agreement that provided 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 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 outstanding thereunder.

On July 12, 2016, Jazz Pharmaceuticals plc, as guarantor, and certain of our wholly owned subsidiaries, as borrowers, entered into Amendment No. 1 to our 2015 credit agreement. The amended credit agreement provides for a revolving credit facility of $1.25 billion, which replaces the revolving credit facility of $750.0 million provided for under the 2015 credit agreement, and a $750.0 million term loan facility, of which $712.9 million principal amount was outstanding as of December 31, 2016. We used the proceeds of $1.0 billion of loans under the revolving credit facility, of which $850.0 million was outstanding as of December 31, 2016, together with cash on hand, to fund the Celator Acquisition, and we expect to use the proceeds from future loans under the revolving credit facility, if any, for general corporate purposes, including corporate development activities.

Under the amended credit agreement, the term loan matures on July 12, 2021 and the revolving credit facility terminates, and any loans outstanding thereunder become due and payable, on July 12, 2021.

Borrowings under the amended 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.

Jazz Pharmaceuticals plc and certain of our wholly owned subsidiaries are borrowers under the amended credit agreement. The borrowers' obligations under the amended 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 our 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 2016 and are equal to 5.0% per annum of the principal amount outstanding on July 12, 2016 of $721.9 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 amended credit agreement contains financial covenants that require Jazz Pharmaceuticals plc and our 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, 2016, and are currently, in compliance with these financial covenants.

Exchangeable Senior Notes

In August 2014, Jazz Pharmaceuticals plc, through our 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, 2016 (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 loan - principal	$ 712,852	$ 36,094	$ 99,258	$ 577,500	$ —
Term loan - interest (2)	78,274	19,638	35,916	22,720	—
2021 Notes - principal	575,000	—	—	575,000	—
2021 Notes - interest (3)	53,906	10,780	21,563	21,563	—
Revolving credit facility - principal	850,000	—	—	850,000	—
Revolving credit facility - interest (2)	106,381	24,432	46,446	35,503	—
Revolving credit facility - commitment fee (4)	6,420	1,418	2,835	2,167	—
Commitment to investee (5)	20,000	5,000	10,000	5,000	—
Purchase obligations (6)	28,434	27,074	410	452	498
Operating and facility lease obligations (7)	125,872	15,442	23,136	19,380	67,914
Total	$ 2,557,139	$ 139,878	$ 239,564	$ 2,109,285	$ 68,412

(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 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 July 2016, we entered into an agreement with Pfenex under which Pfenex granted us worldwide rights to develop and commercialize multiple early-stage hematology product candidates. The agreement also includes an option for us to negotiate a license for a recombinant pegaspargase product candidate with Pfenex. Under the agreement, Pfenex received upfront, option and development milestone payments totaling $15.8 million and may be eligible to receive additional payments of up to $165 million based on the achievement of development, regulatory and sales milestones. Potential future milestone payments to other third parties under other agreements could be up to an aggregate of $256 million, of which up to $120 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 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, 2016. The interest rates for our term loan and revolving credit facility borrowings were 2.77% and 2.69%, respectively, at December 31, 2016.

(3) We used the fixed interest rate of 1.875% to estimate interest owed on the 2021 Notes as of December 31, 2016 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 0.35% and assumed undrawn amounts of $399.5 million as of December 31, 2016 to estimate commitment fees owed. Undrawn borrowing capacity as of December 31, 2016 does not include an amount of $0.5 million committed under an outstanding letter of credit.

(5) We committed to invest $25.0 million in Arrivo Bioventures, LLC which can be called on an annual basis over a five-year period. The first capital call of $5.0 million was made during the second quarter of 2016. Our equity method investment is included within other non-current assets on the consolidated balance sheet as of December 31, 2016.
(6) Consists primarily of non-cancelable commitments to third party manufacturers.
(7) Consists primarily of the minimum lease payments for our office buildings and automobile lease payments for our sales force, 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.

We do not provide for Irish income taxes on undistributed earnings of our foreign operations that are intended to be indefinitely reinvested in our foreign subsidiaries. Cumulative unremitted earnings of our foreign subsidiaries totaled approximately $1.2 billion at December 31, 2016. 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, 2016, it is not practicable to determine the amount of the income tax liability related to these undistributed earnings due to a variety of factors.

In addition, our liability for unrecognized tax benefits has been excluded from the above contractual obligations table as the nature and timing of future payments, if any, cannot be reasonably estimated. As of December 31, 2016, our liability for unrecognized tax benefits amounted to $90.9 million (excluding interest and penalties). We do not anticipate that the amount of our existing liability for unrecognized tax benefits will significantly change in the next twelve months.

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 2016, sales of Xyrem to Express Scripts accounted for 74.8% 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, product returns to Express Scripts from patients are rare; during 2016, 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, 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
Provision, net	129,608	(537)	40,430	40,057	209,558
Payments/credits	(123,383)	(1,207)	(40,577)	(39,582)	(204,749)
Balance at December 31, 2016	$ 68,263	$ 4,366	$ 4,749	$ 4,199	$ 81,577

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

Total items deducted from gross product sales were $209.6 million, $205.8 million and $192.5 million, or 12.4%, 13.5% and 14.2% as a percentage of gross product sales, in 2016, 2015 and 2014, 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, 2016, 2015 and 2014.

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 $129.6 million, $124.6 million and $88.7 million, or 7.7%, 8.2% and 6.5% as a percentage of gross product sales, in 2016, 2015 and 2014, respectively. Rebates as a percentage of gross product sales decreased in 2016 compared to 2015 primarily due to decreased Medicaid expense for certain products with generic competition as a result of lower net product sales from those products in 2016, partially offset by increased Tricare per unit rebate amounts. 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. 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 2017 compared to 2016.

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 $0.5 million and $4.4 million in 2016 and 2015, respectively, and a charge of $3.1 million in 2014, or 0%, (0.3%) and 0.3% as a percentage of gross product sales in 2016, 2015 and 2014, respectively. Sales

returns as a percentage of gross product sales did not change materially in 2016 compared to 2015. 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 are not expected to change materially in 2017 compared to 2016.

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 $40.4 million, $39.1 million and $28.7 million, or 2.4%, 2.6% and 2.1% as a percentage of gross product sales in 2016, 2015 and 2014, respectively. Chargebacks as a percentage of gross product sales did not change materially in 2016 compared to 2015. 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. 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 not expected to change materially in 2017 compared to 2016.

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 $40.1 million, $46.5 million and $71.9 million, or 2.4%, 3.1% and 5.3% as a percentage of gross product sales in 2016, 2015 and 2014, respectively. Discounts and distributor fees as a percentage of gross product sales decreased in 2016 compared to 2015 primarily due to decreased distributor fees payable to partner distributors in international markets driven by a change in the distribution model for certain products. 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. 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 2017 compared to 2016.

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 2016 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, 2016, we had $893.8 million of goodwill primarily resulting from the Azur Merger on January 18, 2012, the EUSA Acquisition on June 12, 2012, the Gentium Acquisition on January 23, 2014 and the Celator Acquisition on July 12, 2016.

Intangible Assets

In connection with the Azur Merger, the EUSA Acquisition, the Gentium Acquisition and the Celator 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, 2016, we had $1.1 billion of finite-lived intangible assets and $1.9 billion of IPR&D assets related to the marketed products and the IPR&D projects that we acquired in the Azur Merger, the EUSA Acquisition, the Gentium Acquisition and the Celator Acquisition. We did not recognize an impairment charge related to our intangible assets during 2016. 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.

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, 2016.

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 U.S., 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,		
	2016	2015	2014
Volatility	39%	39%	45%
Expected term (years)	4.2	4.2	4.3
Range of risk-free rates	0.8-1.6%	1.1-1.5%	1.1-1.4%
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 January 2017, the Financial Accounting Standards Board, or the FASB, issued ASU No. 2017-04, “Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment” which simplifies the accounting for goodwill impairment by eliminating Step 2 of the current goodwill impairment test. Goodwill impairment will now be the amount by which the reporting unit’s carrying value exceeds its fair value, limited to the carrying value of the goodwill. The standard is effective for us beginning January 1, 2020. Early adoption is permitted for any impairment tests performed after January 1, 2017. The new guidance is not expected to have a material impact on our results of operations and financial position.

In January 2017, the FASB issued ASU No. 2017-01, “Business Combinations (Topic 805): Clarifying the Definition of a Business” which provides clarification on the definition of a business and adds guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The standard is effective for us beginning January 1, 2018. Early adoption is permitted. The future impact of ASU No. 2017-01 will be dependent upon the nature of our future acquisition or disposition transactions, if any.

In October 2016, the FASB issued ASU No. 2016-16, “Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory” which requires an entity to recognize the income tax consequences of an intra-entity asset transfer, other than an intra-entity asset transfer of inventory, when the transfer occurs. The standard is effective for us beginning January 1, 2018. Early adoption is permitted. We are currently assessing our approach to the adoption of this standard and the impact on our results of operations and financial position.

In August 2016, the FASB issued ASU No. 2016-15, “Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments”. ASU 2016-15 addresses how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for us beginning January 1, 2018. Early adoption is permitted. We do not expect the adoption of this guidance to have a material impact on our consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, “Leases (Topic 842)”. Under the new guidance, lessees will be required to recognize a right-of-use asset, which represents the lessee’s right to use, or control the use of, a specified asset for the lease term, and a corresponding lease liability, which represents the lessee’s obligation to make lease payments under a lease, measured on a discounted basis. ASU No. 2016-02 is effective beginning January 1, 2019 and early application is permitted. ASU No. 2016-02 must be adopted on a modified retrospective transition basis for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the consolidated financial statements. While we are continuing to assess all potential impacts of the standard, we currently believe the most significant impact relates to our accounting for the lease agreement we entered into in January 2015 to lease office space located in Palo Alto, California in a building to be constructed by the landlord, which is accounted for as a build-to-suit arrangement under existing accounting standards, and the lease agreement we entered into in August 2016 for office space in Dublin, Ireland.

In May 2014, the FASB issued ASU No. 2014-09, “Revenue from Contracts with Customers”. The standard 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 the effective date of ASU No. 2014-09. ASU No. 2014-09 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. In March 2016, the FASB issued ASU No. 2016-08, “Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations”, which clarifies the implementation guidance on principal versus agent considerations. In April 2016, the FASB issued ASU No. 2016-10, “Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing”, which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU No. 2016-12, “Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients” related to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. Presently, we plan to adopt ASU No. 2014-09 at its effective date, but we have not yet determined which transition method we will choose. We have substantially completed our review of existing revenue contracts and do not anticipate that the implementation of ASU No. 2014-09 will have a material impact on our results of operations and financial position. We are continuing to review the impact that the new standard will have on our financial statement disclosures.

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 and investments as of December 31, 2016 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. On July 12, 2016, we entered into the amended credit agreement, which provides for a revolving credit facility of $1.25 billion replacing our prior revolving credit facility of $750.0 million, of which $850.0 million was outstanding as of December 31, 2016, and a $750.0 million term loan facility, of which $712.9 million principal amount was outstanding as of December 31, 2016. We used the proceeds of $1.0 billion of loans under the revolving credit facility, together with cash on hand, to fund the Celator Acquisition. Based on indebtedness under our term loan and revolving credit facilities of $1.6 billion as of December 31, 2016, a 1.0% increase in interest rates would increase net interest expense in 2017 by approximately $16 million.

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, 2016, the fair value of the 2021 Notes was estimated to be $553 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, 2016 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, 2016, our primary exposure to transaction risk related to euro net monetary liabilities, including intercompany loans, held by subsidiaries with a U.S. dollar functional currency. As of December 31, 2016, a 10% strengthening/(weakening) in the euro against the U.S. dollar would have (decreased)/increased net income by approximately $6 million. In 2017, to mitigate this risk, we entered into foreign exchange forward contracts to manage currency risk related to certain intercompany loans denominated in non-functional currencies. These foreign exchange forward contracts are not designated as hedges; gains and losses on these derivative instruments are designed to offset gains and losses on the underlying balance sheet exposures.

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-47.

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, 2016.

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, 2016, 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, 2016 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, 2016, 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, 2016, 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, 2016, 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, 2016 and 2015, 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, 2016, and the related financial statement schedule, and our report dated February 28, 2017 expressed an unqualified opinion on those consolidated financial statements and the related financial statement schedule.

/s/ KPMG

Dublin, Ireland
February 28, 2017

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 2017 annual general meeting of shareholders, or our 2017 Proxy Statement, to be filed pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, or Exchange Act. If our 2017 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 2017 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 2017 Proxy Statement, provided that if the 2017 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 2017 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 2017 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 2017 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 2017 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 2017 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 2017 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 2017 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 2017 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-46 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).
2.9	Agreement and Plan of Merger, dated as of May 27, 2016, by and among Jazz Pharmaceuticals plc, Plex Merger Sub, Inc., and Celator Pharmaceuticals, 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 May 31, 2016).
3.1	Amended and Restated Memorandum and Articles of Association of Jazz Pharmaceuticals plc, as amended on August 4, 2016 (incorporated herein by reference to Exhibit 3.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
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 Licence 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. (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 2016).
10.6A	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. 001-33500), as filed with the SEC on June 18, 2015).
10.6B	Amendment No. 1, dated as of July 12, 2016, to 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 Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
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).
10.13C+	Amended and Restated Schedule 3 to Employment Agreement by and between Jazz Pharmaceuticals UK Ltd and Iain McGill (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 June 30, 2016, as filed with the SEC on August 9, 2016).
10.13D+	Change in Control Stock Award Acceleration Agreement by and between Jazz Pharmaceuticals plc and Iain McGill (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 June 30, 2016, as filed with the SEC on August 9, 2016).

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 10.17B 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).
10.15C+	Amended and Restated Schedule 3 to Employment Agreement by and between Jazz Pharmaceuticals Ireland Ltd. 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 June 30, 2016, as filed with the SEC on August 9, 2016).
10.15D+	Change in Control Stock Award Acceleration Agreement by and between Jazz Pharmaceuticals plc and Paul Treacy (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 June 30, 2016, as filed with the SEC on August 9, 2016).
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) for the period ended December 31, 2012, 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).
10.18M+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (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 March 31, 2016, as filed with the SEC on May 10, 2016).
10.18N+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (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 March 31, 2016, as filed with the SEC on May 10, 2016).
10.18O+	Amended and Restated 2011 Equity Incentive Plan (approved August 4, 2016) (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, 2016, as filed with the SEC on August 9, 2016).

10.18P+	Amended and Restated 2011 Equity Incentive Plan (approved November 3, 2016) (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, 2016, as filed with the SEC on November 8, 2016).
10.18Q+	Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (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, 2016, as filed with the SEC on November 8, 2016).
10.18R+	Form of U.S. Option Grant Notice and Form of U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 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 September 30, 2016, as filed with the SEC on November 8, 2016).
10.18S+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 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 September 30, 2016, as filed with the SEC on November 8, 2016).
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).
10.20D+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved August 4, 2016) (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, 2016, as filed with the SEC on August 9, 2016).
10.20E+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved November 3, 2016) (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, 2016, as filed with the SEC on November 8, 2016).
10.20F+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (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, 2016, as filed with the SEC on November 8, 2016).
10.20G+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated Non-Employee Directors 2007 Stock Award Plan (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, 2016, as filed with the SEC on November 8, 2016).
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 (approved November 4, 2015) (incorporated herein by reference to Exhibit 10.22B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 2016).
10.22B+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved November 3, 2016).
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) (incorporated herein by reference to Exhibit 10.22D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 2016).
10.22E+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2017).
10.23+	Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (approved February 10, 2016) (incorporated herein by reference to Exhibit 10.23 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 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 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).
10.25B+	Amended and Restated Non-Employee Director Compensation Policy (approved May 5, 2016) (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, 2016, as filed with the SEC on August 9, 2016).
10.27	Tender and Support Agreement, dated as of May 27, 2016, by and among Jazz Pharmaceuticals plc, Plex Merger Sub, Inc. and each of the persons set forth on Schedule A attached thereto (incorporated herein by reference to Exhibit 99.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on May 31, 2016).
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.

* 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.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Date: February 28, 2017

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 28, 2017
/s/ MATTHEW P. YOUNG **Matthew P. Young**	Executive Vice President and Chief Financial Officer *(Principal Financial Officer)*	February 28, 2017
/s/ KAREN J. WILSON **Karen J. Wilson**	Senior Vice President, Finance *(Principal Accounting Officer)*	February 28, 2017
/s/ PAUL L. BERNS **Paul L. Berns**	Director	February 28, 2017
/s/ PATRICK G. ENRIGHT **Patrick G. Enright**	Director	February 28, 2017
/s/ PETER GRAY **Peter Gray**	Director	February 28, 2017
/s/ HEATHER ANN MCSHARRY **Heather Ann McSharry**	Director	February 28, 2017
/s/ SEAMUS C. MULLIGAN **Seamus C. Mulligan**	Director	February 28, 2017
/s/ KENNETH W. O'KEEFE **Kenneth W. O'Keefe**	Director	February 28, 2017
/s/ NORBERT G. RIEDEL, PH.D. **Norbert G. Riedel, Ph.D.**	Director	February 28, 2017
/s/ ELMAR SCHNEE **Elmar Schnee**	Director	February 28, 2017
/s/ CATHERINE A. SOHN, PHARM.D. **Catherine A. Sohn, Pharm.D.**	Director	February 28, 2017
/s/ RICK E WINNINGHAM **Rick E Winningham**	Director	February 28, 2017

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, 2016 and 2015, 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, 2016. In connection with our audits of the consolidated financial statements, we also have audited the financial statement schedule at Item 15(a)2 for the years ended December 31, 2016, 2015 and 2014. 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, 2016 and 2015, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule for the years ended December 31, 2016, 2015 and 2014, 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, 2016, 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 28, 2017 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

/s/ KPMG

Dublin, Ireland
February 28, 2017

JAZZ PHARMACEUTICALS PLC

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

	December 31,	
	2016	2015
ASSETS		
Current assets:		
Cash and cash equivalents	$ 365,963	$ 988,785
Investments	60,000	—
Accounts receivable, net of allowances of $5,154 and $3,693 at December 31, 2016 and 2015, respectively	234,244	209,685
Inventories	34,051	19,451
Prepaid expenses	24,501	20,699
Other current assets	29,310	19,047
Total current assets	748,069	1,257,667
Property and equipment, net	107,490	85,572
Intangible assets, net	3,012,001	1,185,606
Goodwill	893,810	657,139
Deferred tax assets, net, non-current	15,060	130,148
Deferred financing costs	9,737	7,209
Other non-current assets	14,060	9,271
Total assets	$ 4,800,227	$ 3,332,612
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 22,415	$ 21,807
Accrued liabilities	193,268	164,070
Current portion of long-term debt	36,094	37,587
Income taxes payable	4,506	1,808
Deferred revenue	1,123	1,370
Total current liabilities	257,406	226,642
Deferred revenue, non-current	2,601	3,721
Long-term debt, less current portion	1,993,531	1,150,857
Deferred tax liability, net, non-current	556,733	283,493
Other non-current liabilities	112,617	69,253
Commitments and contingencies (Note 11)		
Shareholders' equity:		
Ordinary shares, nominal value $0.0001 per share; 300,000 shares authorized; 59,820 and 61,305 shares issued and outstanding at December 31, 2016 and 2015, 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, 2016 and 2015	55	55
Capital redemption reserve	472	471
Additional paid-in capital	1,665,232	1,562,900
Accumulated other comprehensive loss	(317,333)	(267,472)
Retained earnings	528,907	302,686
Total shareholders' equity	1,877,339	1,598,646
Total liabilities and shareholders' equity	$ 4,800,227	$ 3,332,612

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,		
	2016	**2015**	**2014**
Revenues:			
Product sales, net	$ 1,477,261	$ 1,316,819	$ 1,162,716
Royalties and contract revenues	10,712	7,984	10,159
Total revenues	1,487,973	1,324,803	1,172,875
Operating expenses:			
Cost of product sales (excluding amortization and impairment of intangible assets)	105,386	102,526	117,418
Selling, general and administrative	502,892	449,119	406,114
Research and development	162,297	135,253	85,181
Acquired in-process research and development	23,750	—	202,626
Intangible asset amortization	101,994	98,162	126,584
Impairment charges	—	31,523	39,365
Total operating expenses	896,319	816,583	977,288
Income from operations	591,654	508,220	195,587
Interest expense, net	(61,942)	(56,917)	(52,713)
Foreign currency gain	3,372	1,445	8,683
Loss on extinguishment and modification of debt	(638)	(16,815)	—
Income before income tax provision and equity in loss of investee	532,446	435,933	151,557
Income tax provision	135,236	106,399	94,231
Equity in loss of investee	379	—	—
Net income	396,831	329,534	57,326
Net loss attributable to noncontrolling interests	—	(1)	(1,061)
Net income attributable to Jazz Pharmaceuticals plc	$ 396,831	$ 329,535	$ 58,387
Net income attributable to Jazz Pharmaceuticals plc per ordinary share:			
Basic	$ 6.56	$ 5.38	$ 0.98
Diluted	$ 6.41	$ 5.23	$ 0.93
Weighted-average ordinary shares used in per share calculations - basic	60,500	61,232	59,746
Weighted-average ordinary shares used in per share calculations - diluted	61,870	63,036	62,614

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,		
	2016	2015	2014
Net income	$ 396,831	$ 329,534	$ 57,326
Other comprehensive loss:			
Foreign currency translation adjustments	(49,861)	(145,375)	(178,264)
Other comprehensive loss	(49,861)	(145,375)	(178,264)
Total comprehensive income (loss)	346,970	184,159	(120,938)
Comprehensive loss attributable to noncontrolling interests	—	(1)	(1,075)
Comprehensive income (loss) attributable to Jazz Pharmaceuticals plc	$ 346,970	$ 184,160	$ (119,863)

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	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

JAZZ PHARMACEUTICALS PLC

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

	Ordinary Shares		Non-voting Euro Deferred						
	Shares	Amount	Shares	Amount	Capital Redemp-tion Reserve	Additional Paid-in Capital	Accumu-lated Other Compre-hensive Income (Loss)	Retained Earnings	Total Equity
Balance at December 31, 2015	61,305	$ 6	4,000	$ 55	$ 471	$ 1,562,900	$ (267,472)	$ 302,686	$ 1,598,646
Cumulative effect adjustment from adoption of ASU No. 2016-09 (Note 2)	—	—	—	—	—	—	—	107,687	107,687
Issuance of ordinary shares in conjunction with exercise of share options	399	—	—	—	—	16,880	—	—	16,880
Issuance of ordinary shares under employee stock purchase plan	70	—	—	—	—	7,294	—	—	7,294
Issuance of ordinary shares in conjunction with vesting of restricted stock units	289	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(21,234)	—	—	(21,234)
Share-based compensation	—	—	—	—	—	99,392	—	—	99,392
Shares repurchased	(2,243)	—	—	—	1	—	—	(278,297)	(278,296)
Other comprehensive loss	—	—	—	—	—	—	(49,861)	—	(49,861)
Net income	—	—	—	—	—	—	—	396,831	396,831
Balance at December 31, 2016	59,820	$ 6	4,000	$ 55	$ 472	$ 1,665,232	$ (317,333)	$ 528,907	$ 1,877,339

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,		
	2016	**2015**	**2014**
Operating activities			
Net income	$ 396,831	$ 329,534	$ 57,326
Adjustments to reconcile net income to net cash provided by operating activities:			
Intangible asset amortization	101,994	98,162	126,584
Share-based compensation	98,771	91,550	69,638
Impairment charges	—	31,523	39,365
Depreciation	11,786	9,894	7,097
Acquired in-process research and development	23,750	—	202,626
Loss on disposal of property and equipment	47	172	24
Acquisition accounting inventory fair value step-up adjustments	—	—	10,477
Deferred income taxes	(41,163)	(68,358)	(49,254)
Provision for losses on accounts receivable and inventory	2,209	4,062	2,493
Loss on extinguishment and modification of debt	638	16,815	—
Amortization of debt discount and deferred financing costs	22,133	22,738	13,725
Other non-cash transactions	(3,741)	(5,187)	(11,986)
Changes in assets and liabilities:			
Accounts receivable	(25,603)	(24,841)	(55,041)
Inventories	(17,024)	6,271	(7,630)
Prepaid expenses and other current assets	(15,700)	3,720	11,936
Other long-term assets	267	(4,573)	(3,060)
Accounts payable	361	(2,280)	(37,966)
Accrued liabilities	10,134	2,986	20,997
Income taxes payable	2,962	(6,271)	8,634
Deferred revenue	(1,315)	(536)	(1,203)
Contingent consideration	—	—	(14,900)
Other non-current liabilities	23,199	26,562	17,724
Net cash provided by operating activities	590,536	531,943	407,606
Investing activities			
Acquisitions, net of cash acquired	(1,502,443)	—	(828,676)
Acquisition of intangible assets	(150,000)	—	—
Acquisition of investments	(65,275)	—	—
Acquisition of in-process research and development	(23,750)	—	(202,626)
Purchases of property and equipment	(7,832)	(35,958)	(36,347)
Net proceeds from sale of business	—	33,703	—
Net cash used in investing activities	(1,749,300)	(2,255)	(1,067,649)
Financing activities			
Net proceeds from issuance of debt	994,647	898,642	1,194,385
Proceeds from employee equity incentive and purchase plans and exercise of warrants	24,174	40,523	58,487
Share repurchases	(278,296)	(61,553)	(42,215)
Acquisition of noncontrolling interests	—	(73)	(136,969)
Payment of contingent consideration	—	—	(35,100)
Payment of employee withholding taxes related to share-based awards	(21,234)	(26,102)	(18,030)
Repayments of long-term debt	(28,304)	(905,760)	(9,524)
Repayments under revolving credit facility	(150,000)	(160,000)	(300,000)
Net cash provided by (used in) financing activities	540,987	(214,323)	711,034
Effect of exchange rates on cash and cash equivalents	(5,045)	(10,622)	(3,453)
Net increase (decrease) in cash and cash equivalents	(622,822)	304,743	47,538
Cash and cash equivalents, at beginning of period	988,785	684,042	636,504
Cash and cash equivalents, at end of period	$ 365,963	$ 988,785	$ 684,042

JAZZ PHARMACEUTICALS PLC

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

	Year Ended December 31,		
	2016	2015	2014
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 39,898	$ 40,099	$ 31,978
Cash paid for income taxes	160,306	145,597	108,189
Non-cash investing activities:			
Construction-in-progress related to facility lease obligation	23,799	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, and currently marketed 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 sodium)**, a product approved in the U.S. for the treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome, or SOS, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT, and in Europe (where it is marketed as Defitelio® (defibrotide)) for the treatment of severe VOD in adults and children undergoing 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 and new geographic markets;
- Acquiring or licensing rights to 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 U.S. 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.

Reclassifications

Certain prior period amounts presented in these consolidated financial statements and the accompanying footnotes have been reclassified to conform to the current period presentation. The indirect effects of certain unrecognized tax benefits, previously classified within other non-current assets as of December 31, 2015, have been reclassified to deferred tax assets, net, non-current and deferred tax liability, net, non-current in the consolidated balance sheet and Note 18.

Adoption of New Accounting Standards

Effective January 1, 2016, we adopted Accounting Standards Update, or 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. The standard requires retrospective application. The adoption of ASU No. 2015-03 resulted in a $16.1 million reduction of both deferred financing costs and long-term debt, less current portion in our consolidated balance sheet as of December 31, 2015.

In March 2016, the Financial Accounting Standards Board, or the FASB issued ASU No. 2016-09, "Improvements to Employee Share-Based Payment Accounting". The standard simplifies several areas of accounting for share-based compensation arrangements. ASU No. 2016-09 is effective for us beginning January 1, 2017. We elected to early adopt ASU No. 2016-09 in the fourth quarter of 2016 which required us to reflect any adjustments as of January 1, 2016, the beginning of the annual period that includes the interim period of adoption.

ASU No. 2016-09 requires that all excess tax benefits and tax deficiencies be recognized as income tax benefit or expense in the income statement and no longer delays recognition of a tax benefit until the tax benefit is realized through a reduction to taxes payable. On adoption of ASU No. 2016-09, we recorded a $107.7 million cumulative-effect adjustment to opening retained earnings and deferred tax assets, net, non-current as of January 1, 2016 for previously unrecognized excess tax benefits and recognized excess tax benefits of $7.7 million in our income tax provision for the year ended December 31, 2016.

Adoption of the changes to the accounting for statutory withholding tax requirements had no impact on our consolidated financial statements. We elected to continue to estimate forfeitures expected to occur in determining the amount of compensation cost to be recognized in each period.

We elected to apply the presentation requirements for cash flows related to excess tax benefits retrospectively to all periods presented which resulted in an increase in net cash provided by operating activities and a reduction in net cash provided by financing activities of $1.8 million for the year ended December 31, 2014. There was no impact on our consolidated statement of cash flows for the year ended December 31, 2015. The presentation requirements for cash flows related to employee taxes paid for withheld shares had no impact on any of the periods presented in our consolidated statements of cash flows since such cash flows have historically been presented as a financing activity.

Significant Risks and Uncertainties

Our financial results remain significantly influenced by sales of Xyrem. In 2016, net product sales of Xyrem were $1,107.6 million, which represented 75% 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 commercialization of a generic version of Xyrem, including in connection with the recent approval by the FDA of an abbreviated new drug application, or ANDA, for a generic version of Xyrem, as well as tentative approval of two additional ANDAs; the potential U.S. introduction of an alternative product to Xyrem for treating cataplexy and/or EDS, in narcolepsy; changes to, increases of or uncertainties around regulatory restrictions, including changes to our Xyrem risk evaluation and mitigation strategy, or REMS, particularly in light of the FDA's waiver of the single shared system REMS requirement for sodium oxybate and approval of a separate generic sodium oxybate REMS; any increase in pricing pressure from, or restrictions on reimbursement imposed by, third party payors; changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing by government entities; operational disruptions at the Xyrem central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA; any supply or manufacturing problems, including our sole source Xyrem API provider; 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 our U.S.-based sodium oxybate and Xyrem suppliers' ability to obtain sufficient quotas from the U.S. Drug Enforcement Administration, or DEA, to satisfy our needs for Xyrem.

Seven companies sent us notices that they had filed ANDAs with the FDA seeking approval to market a generic version of Xyrem, and we filed patent lawsuits against each of these companies in the District Court for New Jersey, or District Court. In the second quarter of 2016, we settled two of these lawsuits, granting the settling ANDA applicants a license to manufacture, market and sell their generic versions of Xyrem on or after December 31, 2025, or earlier depending on the occurrence of certain events. In 2016, the District Court consolidated all of our pending patent litigation (other than our lawsuit filed in August 2016) against West-Ward Pharmaceuticals Corp., formerly known as Roxane Laboratories, Inc., or Roxane, and set the case for trial in the second quarter of 2017. In the first quarter of 2017, the District Court bifurcated and stayed the part of the consolidated case involving the patents on the Xyrem distribution system, or REMS patents. We cannot predict the timing or outcome of this or the other ANDA litigation proceedings. In July 2016, the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO, issued final decisions that the claims of six of seven REMS patents are unpatentable; if the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled, and we will not be able to enforce these patents. For a description of these legal proceedings, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

On January 17, 2017, the FDA announced approval of Roxane's ANDA for a generic version of Xyrem. The FDA's letter approving Roxane's ANDA notes that Roxane was the first ANDA applicant and is eligible for 180 days of generic drug exclusivity for its generic product. Roxane's approval also includes a waiver that permits Roxane to use a separate REMS

program from Xyrem, on the condition that Roxane's waiver-granted REMS system be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. On January 19, 2017, the FDA tentatively approved two additional ANDAs for generic versions of Xyrem, one for Amneal Pharmaceuticals, or Amneal, and one for Ohm Laboratories Inc., formerly known as Ranbaxy, Inc., or Ranbaxy.

While the FDA has approved or tentatively approved ANDAs seeking to market generic versions of Xyrem and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs, the timing of any potential commercial launch of a generic version of Xyrem is uncertain. We do not believe a launch by an ANDA filer is likely to occur prior to either a date agreed in a settlement agreement between us and such ANDA filer or a District Court, or potentially an appellate court, decision in our ongoing patent litigation. If we prevail at trial or on appeal, we cannot guarantee that the court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem. Instead, the court may order an ANDA filer that is found to infringe to pay damages in the form of lost profits or a reasonable royalty, which could be significant. We expect that the launch of a generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, would have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects. For further discussion regarding the risks associated with FDA approval of the Roxane ANDA, tentative approval of the Amneal and Ranbaxy ANDAs, potential approval or tentative approval of additional ANDAs and the potential launch of a generic version of Xyrem, or the approval and launch of other sodium oxybate products that compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see "Business-Government Regulation-The Hatch-Waxman Act" in 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.

In August 2015, we implemented the current Xyrem REMS, and we have submitted and expect to continue to submit ongoing assessments as set forth in the FDA's Xyrem REMS approval letter. However, we cannot guarantee that our implementation and ongoing assessments will be satisfactory to the FDA or that the Xyrem REMS will satisfy the FDA's expectations in its 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; 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 (particularly now that the FDA has approved a separate REMS for the ANDA filers that contemplates interaction with the Xyrem REMS), 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 sodium oxybate competitors, make it more difficult or expensive for us to distribute Xyrem, make distribution easier for future sodium oxybate competitors, impair the safety profile of Xyrem and/or negatively affect sales of Xyrem.

We may face pressure to modify the Xyrem REMS, or to license or share intellectual property pertinent to the Xyrem REMS, including proprietary data required for safe distribution of sodium oxybate, in connection with the FDA's approval of the generic sodium oxybate REMS. We cannot predict the outcome or impact on our business of any future action that we may take with respect to the approval of the generic sodium oxybate REMS, or licensing or sharing intellectual property pertinent to our Xyrem REMS or elements of the Xyrem REMS. For more information, see the risk factors under the headings "*The approval and launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem*" and "*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.

In September 2016, Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, submitted a Citizen Petition to the FDA requesting that, for safety reasons, the FDA refuse to approve any sodium oxybate ANDA with a proposed package insert or REMS that omits the portions of the Xyrem package insert and the Xyrem REMS that instruct prescribers on adjusting the dose of the product when it is co-administered with divalproex sodium (also known as valproate or valproic acid). On January 17, 2017, the FDA granted the Citizen Petition with respect to the Xyrem package insert. The FDA concluded that it will not approve any sodium oxybate ANDA referencing Xyrem that does not include in its package insert the portions of the currently approved Xyrem package insert related to the drug-drug interaction with divalproex sodium. The FDA stated that it did not need to reach the question of whether the drug-drug interaction, or DDI, information could have been excluded from the generic sodium oxybate REMS materials because it was approving a REMS in connection with a sodium oxybate ANDA including that information. Our Xyrem patents include three DDI patents covering these instructions on the Xyrem package insert and Xyrem REMS. We cannot predict whether or when one or more of the ANDA filers may pursue a challenge to the FDA's response to the Citizen Petition or whether any such challenges would be successful. Likewise, we cannot predict

whether we will be able to maintain the validity of any of our patents or will otherwise obtain a judicial determination that the generic sodium oxybate package insert or the generic sodium oxybate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents the ANDA filers from marketing their generic versions of Xyrem or instead require the ANDA filers to pay damages in the form of lost profits or a reasonable royalty. For a description of these matters, see “Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K, “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.

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 2016, 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 $200.7 million, which represented 14% 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.

Erwinaze is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL. Erwinaze was approved by the FDA under a biologics license application, or BLA, and was launched in the U.S. in November 2011. The Erwinaze BLA includes a number of post-marketing commitments related to the manufacture of Erwinaze by PBL. We cannot predict if or when PBL will comply with its manufacturing-related post-marketing commitments that are part of the BLA approval. In January 2017, the FDA issued a warning letter to PBL, citing significant violations of FDA’s current Good Manufacturing Practices, or cGMP, for finished pharmaceuticals and significant deviations from cGMP for active pharmaceutical ingredients, or APIs. We cannot predict if or when PBL will correct the violations and deviations to the satisfaction of the FDA. Any failure to do so could result in the FDA refusing admission of Erwinaze into the U.S., as well as additional enforcement actions by the FDA and other regulatory entities.

In addition, 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. The current manufacturing capacity for Erwinaze is 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 and to address the production delays, quality challenges and related regulatory scrutiny. As a consequence of constrained manufacturing capacity, we have had an extremely limited or no ability to build product inventory levels that can be used to absorb disruptions to supply resulting from quality, regulatory or other issues. We have experienced product quality, manufacturing and inventory challenges that have resulted, and may continue to result, in disruptions in our ability to supply certain markets, including the U.S., from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. Most recently, we experienced supply interruptions of Erwinaze in the U.S. and other countries in the third and fourth quarters of 2016. We cannot predict whether the FDA’s required remediation activities in connection with the warning letter will further strain manufacturing capacity and adversely affect Erwinaze supply, particularly in light of our extremely limited product inventory. As capacity constraints and supply disruptions continue, whether as a result of continued quality or other manufacturing issues, regulatory issues or otherwise, we will be unable to build a desired excess level of product inventory, our ability to supply the market may continue to be compromised and physicians’ decisions to use Erwinaze have been, and in the future may continue to be, negatively impacted.

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 7% of our net product sales in 2016. 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 2016. 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 March 2016, the FDA approved our NDA for Defitelio for the treatment of adult and pediatric patients with VOD with renal or pulmonary dysfunction following HSCT. 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. We launched Defitelio in the U.S. shortly after FDA approval, and our U.S. commercial launch is still at an early stage. Our ability to realize the anticipated benefits from our investment in Defitelio is subject to risks and uncertainties, including the continued acceptance of Defitelio in the U.S. by hospital pharmacy and therapeutics committees and the continued availability of adequate coverage and reimbursement by government programs and third party payors; the lack of experience of U.S. physicians in diagnosing and treating VOD, particularly in adults, and the possibility that physicians may delay initiation of treatment or terminate treatment before the end of the recommended dosing schedule; our ability to successfully maintain or grow sales of Defitelio in Europe; delays or problems in the supply or manufacture of the product; the limited size of the population of VOD patients who are indicated for treatment with Defitelio (particularly if changes in HSCT treatment protocols reduce the incidence of VOD diagnosis); our ability to meet the post-marketing commitments and requirements imposed by the FDA in connection with its approval of our NDA for Defitelio; and our ability to obtain marketing approval in other countries and to develop the product for additional indications, 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. If sales of Defitelio do not reach the levels we expect, our anticipated revenue from the product will be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, in 2016, we made a significant investment in Vyxeos through the Celator Acquisition. Our ability to realize the anticipated benefits from this investment is subject to a number of risks and uncertainties discussed in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K. If we are unable to obtain regulatory approval for Vyxeos in the U.S. or in Europe in a timely manner, or at all, or if sales of an approved Vyxeos product do not reach the levels we expect, our anticipated revenue from Vyxeos 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, Defitelio/defibrotide and Vyxeos, 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 and product candidates, particularly with respect to certain products as to which we maintain limited inventories, our dependence on single source suppliers for most of our products, product candidates and APIs, and the requirement that we and our product suppliers be qualified by the FDA to manufacture product and comply with applicable manufacturing regulations;
- 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 and pharmaceutical pricing 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 government programs and 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 comparable non-U.S. regulatory agencies, including with respect to product labeling, requirements for distribution, obtaining sufficient DEA quotas where needed, marketing and promotional activities, patient assistance programs, 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 increase investment in our product pipeline development projects and undertake multiple planned NDA submissions for our product candidates;
- the risks associated with business combination or product or product candidate acquisition transactions, including risks associated with the Celator Acquisition, such as the challenges inherent in the integration of acquired businesses with our historical 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, as a result of, among other things, the Celator Acquisition.

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 investments. 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 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 U.S., 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, 2016, 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 73% of gross accounts

receivable, and McKesson Corporation and affiliates, which accounted for 13% of gross accounts receivable. As of December 31, 2015, five customers accounted for 90% of gross accounts receivable including Express Scripts, which accounted for 69% of gross accounts receivable, and IDIS Limited, which accounted for 11% of gross accounts receivable.

We depend on single source suppliers for most of our products, product candidates and their APIs. We commenced manufacturing of Xyrem in our Ireland facility in the third quarter of 2016.

Cash Equivalents and Investments

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.

Investments consist of time deposits with initial maturities of greater than three months. Collectively, cash equivalents and investments 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 investments 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 API 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. Estimated useful lives are as follows:

Buildings	40 years
Manufacturing equipment and machinery	5-10 years
Computer software and equipment	3 years
Furniture and fixtures	5 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 of inventory costs associated with the fair value step-up in acquired inventory in 2014. Excluded from cost of product sales shown on the consolidated statements of income is amortization of acquired developed technology of $99.0 million, $93.0 million and $122.6 million in 2016, 2015 and 2014, 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 $29.5 million, $27.9 million and $25.7 million in 2016, 2015 and 2014, 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.

Deferred Financing Costs

Deferred financing costs are reported at cost, less accumulated amortization and are presented in the consolidated balance sheets as a direct deduction from the carrying value of the associated debt, with the exception of deferred financing costs associated with revolving-debt arrangements which are presented as assets. The related amortization expense is included in interest expense, net in our consolidated statements of income.

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 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,		
	2016	2015	2014
Numerator:			
Net income attributable to Jazz Pharmaceuticals plc	$ 396,831	$ 329,535	$ 58,387
Denominator:			
Weighted-average ordinary shares used in per share calculation - basic	60,500	61,232	59,746
Dilutive effect of employee equity incentive and purchase plans	1,370	1,804	2,402
Dilutive effect of warrants	—	—	466
Weighted-average ordinary shares used in per share calculation - diluted	61,870	63,036	62,614
Net income per ordinary share :			
Basic	$ 6.56	$ 5.38	$ 0.98
Diluted	$ 6.41	$ 5.23	$ 0.93

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, 2016 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 years presented because including them would have an anti-dilutive effect (in thousands):

	Year Ended December 31,		
	2016	2015	2014
1.875% exchangeable senior notes due 2021	2,878	2,878	1,112
Options to purchase ordinary shares and RSUs	3,010	1,609	819
Ordinary shares under ESPP	93	—	—

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 January 2017, the FASB, issued ASU No. 2017-04, "Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment" which simplifies the accounting for goodwill impairment by eliminating Step 2 of the current goodwill impairment test. Goodwill impairment will now be the amount by which the reporting unit's carrying value exceeds its fair value, limited to the carrying value of the goodwill. The standard is effective for us beginning January 1, 2020. Early adoption is permitted for any impairment tests performed after January 1, 2017. The new guidance is not expected to have a material impact on our results of operations and financial position.

In January 2017, the FASB issued ASU No. 2017-01, "Business Combinations (Topic 805): Clarifying the Definition of a Business" which provides clarification on the definition of a business and adds guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The standard is effective for us beginning January 1, 2018. Early adoption is permitted. The future impact of ASU No. 2017-01 will be dependent upon the nature of our future acquisition or disposition transactions, if any.

In October 2016, the FASB issued ASU No. 2016-16, "Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory" which requires an entity to recognize the income tax consequences of an intra-entity asset transfer, other than an intra-entity asset transfer of inventory, when the transfer occurs. The standard is effective for us beginning January 1, 2018. Early adoption is permitted. We are currently assessing our approach to the adoption of this standard and the impact on our results of operations and financial position.

In August 2016, the FASB issued ASU No. 2016-15, "Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments". ASU 2016-15 addresses how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for us beginning January 1, 2018. Early adoption is permitted. We do not expect the adoption of this guidance to have a material impact on our consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, "Leases (Topic 842)". Under the new guidance, lessees will be required to recognize a right-of-use asset, which represents the lessee's right to use, or control the use of, a specified asset for the lease term, and a corresponding lease liability, which represents the lessee's obligation to make lease payments under a lease, measured on a discounted basis. ASU No. 2016-02 is effective beginning January 1, 2019 and early application is permitted. ASU No. 2016-02 must be adopted on a modified retrospective transition basis for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the consolidated financial statements. While we are continuing to assess all potential impacts of the standard, we currently believe the most significant impact relates to our accounting for the lease agreement we entered into in January 2015 to lease office space located in Palo Alto, California in a building to be constructed by the landlord, which is accounted for as a build-to-suit arrangement under existing accounting standards, and the lease agreement we entered into in August 2016 for office space in Dublin, Ireland.

In May 2014, the FASB issued ASU No. 2014-09, "Revenue from Contracts with Customers". The standard 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 the effective date of ASU No. 2014-09. ASU No. 2014-09 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. In March 2016, the FASB issued ASU No. 2016-08, "Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations", which clarifies the implementation guidance on principal versus agent considerations. In April 2016, the FASB issued ASU No. 2016-10, "Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing", which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU No. 2016-12, "Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients" related to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. Presently, we plan to adopt ASU No. 2014-09 at its effective date, however we have not yet determined which transition method we will choose. We have substantially completed our review of existing revenue contracts and currently do not anticipate that the implementation of ASU No. 2014-09 will have a material impact on our results of operations and financial position. We are continuing to review the impact that the new standard will have on our financial statement disclosures.

3. Business Combination, Asset Acquisitions, Equity Method Investment and Disposition

Celator Acquisition

On May 27, 2016, we entered into a definitive merger agreement with Celator pursuant to which we made a cash tender offer of $30.25 per share for all of the outstanding shares of Celator's common stock. As of the expiration of the offer period on July 12, 2016, 36,516,173 shares, which represented approximately 81% of Celator's then outstanding common stock, were properly tendered and not withdrawn in the tender offer. The condition to the tender offer that more than 50% of Celator's outstanding common stock be validly tendered and not withdrawn prior to the expiration of the tender offer was satisfied. In addition, notices of guaranteed delivery were delivered with respect to 2,016,237 additional shares, representing approximately 4% of Celator's outstanding common stock as of the expiration of the tender offer. On July 12, 2016, we completed the Celator Acquisition under the terms of the merger agreement, pursuant to which Celator became an indirect wholly owned subsidiary of Jazz Pharmaceuticals plc and each share of Celator common stock then outstanding (other than shares owned by us or Celator) was converted into the right to receive $30.25, the same price per share offered in the tender offer. The aggregate cash consideration for the Celator Acquisition was $1.5 billion.

On July 12, 2016, we entered into the amended credit agreement that provides for a revolving credit facility of $1.25 billion, which replaced our prior revolving credit facility of $750.0 million, and a $750.0 million term loan facility, of which $712.9 million remained outstanding as of December 31, 2016. Please see Note 9 for further information regarding the 2015 credit agreement and the amended credit agreement. We used the proceeds of $1.0 billion of loans under the revolving credit facility, together with cash on hand, to fund the Celator Acquisition.

Celator was an oncology-focused biopharmaceutical company seeking to transform the science of combination therapy and develop products to improve patient outcomes in cancer. The Celator Acquisition broadened our hematology/oncology portfolio with the acquisition of worldwide development and commercialization rights to Vyxeos, an investigational product in development as a treatment for high-risk acute myeloid leukemia. In addition, the Celator Acquisition provided us with Celator's proprietary technology platform, CombiPlex, which has the potential to enable the rational design and rapid evaluation of optimized combinations of additional anti-cancer drugs.

The Celator Acquisition was accounted for as a business combination using the acquisition method under which assets and liabilities of Celator were recorded at their respective estimated fair values as of the closing date of the Celator Acquisition and added to the assets and liabilities of Jazz Pharmaceuticals plc, including an amount for goodwill representing the difference between the acquisition consideration and the estimated fair value of the identifiable net assets. The results of operations of Celator and the estimated fair values of the assets acquired and liabilities assumed have been included in our consolidated financial statements since the closing date of the Celator Acquisition.

In 2016, we incurred $10.0 million in acquisition-related costs related to the Celator Acquisition, which primarily consisted of banking, legal, accounting and valuation-related expenses. These expenses were recorded in selling, general and administrative expense in the accompanying consolidated statements of income. We did not recognize any revenues from the acquired Celator business in 2016. The portion of total expenses and net loss associated with the acquired Celator business was not separately identifiable due to the integration with our operations.

The preliminary fair values of assets acquired and liabilities assumed at the closing date of the Celator Acquisition are summarized below (in thousands):

Cash and cash equivalents	$	26,137
Other receivables		386
Prepaid expenses and deposits		151
Property and equipment		767
Intangible assets		1,811,250
Goodwill		252,825
Other non-current assets		43
Accrued liabilities		(19,076)
Deferred tax liability, net, non-current		(542,901)
Other non-current liabilities		(1,002)
Total acquisition consideration - cash paid	$	1,528,580

The fair value estimates for the assets acquired and liabilities assumed were based upon preliminary calculations, and our estimates and assumptions are subject to change as we obtain additional information for our estimates during the measurement period (up to one year from the acquisition date). The areas of these preliminary estimates that are not yet finalized relate primarily to tax-related items. During the three months ended December 31, 2016, we recorded a measurement period adjustment which reduced deferred tax liability, net, non-current, intangible assets and goodwill by $22.7 million, $13.8 million and $9.0 million, respectively. The measurement period adjustment primarily related to the refinement of the estimated state tax rate for Celator.

Identifiable intangible assets acquired comprise IPR&D, which represents incomplete research and development projects at Celator related to Vyxeos. Management estimated the fair value of Vyxeos IPR&D to be approximately $1.8 billion. The fair value of acquired IPR&D was determined using the income approach, including the application of probability factors related to the likelihood of success of Vyxeos reaching final development and commercialization. This approach also took into consideration information and certain program-related documents and forecasts prepared by management. The fair value of acquired IPR&D was capitalized as of the closing date of the Celator Acquisition and is subsequently accounted for as an indefinite-lived intangible asset until completion or abandonment of the associated research and development efforts. Accordingly, during the development period after the closing date of the Celator Acquisition, this asset will not be amortized into earnings; instead, this asset will be subject to periodic impairment testing. Upon successful completion of the development process for an acquired IPR&D project, determination as to the useful life of the asset will be made. The asset would then be considered a finite-lived intangible asset and amortization of the asset into earnings would begin over the remaining estimated useful life of the asset.

The excess of the total acquisition consideration over the fair value amounts assigned to the assets acquired and the liabilities assumed represents the goodwill amount resulting from the Celator Acquisition. We believe that the factors that contributed to goodwill included the Celator workforce, which will complement our clinical experience in hematology/oncology and our expertise in reaching targeted physicians who treat serious medical conditions, and the deferred tax consequences of intangible assets recorded for financial statement purposes. We do not expect any portion of this goodwill to be deductible for tax purposes.

Pro Forma Financial Information (Unaudited)

The following unaudited supplemental pro forma information presents our combined historical results of operations with pro forma adjustments as if the Celator Acquisition had been completed on January 1, 2015. The primary pro forma adjustments include:

- The exclusion of acquisition-related and integration expenses of $13.6 million in 2016 and the inclusion of these expenses in 2015.
- An increase in interest expense of $13.7 million in 2016 and $25.9 million in 2015 incurred on additional borrowings made to partially fund the Celator Acquisition as if the borrowings had occurred on January 1, 2015.

The unaudited pro forma results do not assume any operating efficiencies as a result of the consolidation of operations and are as follows (in thousands, except per share data):

	Year Ended December 31,	
	2016	2015
Revenues	$ 1,488,118	$ 1,326,246
Net income attributable to Jazz Pharmaceuticals plc	$ 386,342	$ 283,113
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - basic	$ 6.39	$ 4.62
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - diluted	$ 6.24	$ 4.49

License and Option Agreement

In July 2016, we entered into an agreement with Pfenex Inc., or Pfenex, under which Pfenex granted us worldwide rights to develop and commercialize multiple early-stage hematology product candidates. The agreement also includes an option for us to negotiate a license for a recombinant pegaspargase product candidate with Pfenex. Under the agreement, Pfenex received upfront, option and development milestone payments totaling $15.8 million and may be eligible to receive additional payments of up to $165 million based on the achievement of certain development, regulatory and sales milestones.

Equity Method Investment

In May 2016, we committed to invest $25.0 million in Arrivo Bioventures LLC, or Arrivo, over a five-year period. The first installment of $5.0 million was invested in the year ended December 31, 2016. We account for our investment in Arrivo under the equity method of accounting. Our equity method investment is included within other non-current assets on the consolidated balance sheet as of December 31, 2016. We record our share of losses in our equity method investment in the consolidated statements of income.

Acquisition of Alizé Pharma II S.A.S.

In March 2016, we acquired all of the outstanding shares of Alizé Pharma II S.A.S., a privately held biotechnology company, for an upfront payment of $8.8 million. In connection with the acquisition, we obtained intellectual property and know-how related to recombinant crisantaspase. The transaction includes contingent regulatory milestone payments of up to €10 million. The transaction was accounted for as an asset acquisition and the upfront payment was charged to acquired IPR&D expense upon closing of the transaction.

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. In 2015, 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 and investments consisted of the following (in thousands):

	December 31, 2016					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 215,963	$ —	$ —	$ 215,963	$ 215,963	$ —
Time deposits	210,000	—	—	210,000	150,000	60,000
Totals	$ 425,963	$ —	$ —	$ 425,963	$ 365,963	$ 60,000

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

Cash equivalents and investments 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. Our investments balance represents time deposits with original maturities of greater than three months.

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, 2016		December 31, 2015	
	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value
Time deposits	$ 210,000	$ 210,000	$ 713,840	$ 713,840

As of December 31, 2016, 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 2016 or in 2015.

As of December 31, 2016, the estimated fair value of our 2021 Notes, which had a carrying value of $473.9 million, was approximately $553 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 revolving credit facilities 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,	
	2016	2015
Raw materials	$ 1,547	$ 2,608
Work in process	18,689	11,836
Finished goods	13,815	5,007
Total inventories	$ 34,051	$ 19,451

6. Property and Equipment

Property and equipment consisted of the following (in thousands):

	December 31,	
	2016	2015
Land and buildings	$ 46,033	$ 1,775
Construction-in-progress	33,427	63,008
Manufacturing equipment and machinery	19,596	5,828
Computer software	17,832	15,797
Computer equipment	10,980	10,963
Leasehold improvements	9,328	9,301
Furniture and fixtures	2,436	2,580
Subtotal	139,632	109,252
Less accumulated depreciation and amortization	(32,142)	(23,680)
Property and equipment, net	$ 107,490	$ 85,572

The decrease in construction-in-progress, or CIP, from December 31, 2015 to December 31, 2016 is primarily due to the reclassification of building and equipment costs related to our Ireland manufacturing and development facility from CIP to the appropriate property and equipment category on the balance sheet following FDA approval of the facility in June 2016.

7. Goodwill and Intangible Assets

The gross carrying amount of goodwill was as follows (in thousands):

Balance at December 31, 2015	$ 657,139
Goodwill arising from the Celator Acquisition	252,825
Foreign exchange	(16,154)
Balance at December 31, 2016	$ 893,810

The gross carrying amounts and net book values of our intangible assets were as follows (in thousands):

		December 31, 2016			December 31, 2015		
	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	11.3	$ 1,477,618	$ (410,523)	$ 1,067,095	$ 1,321,324	$ (324,044)	$ 997,280
Manufacturing contracts	1.1	11,278	(8,292)	2,986	11,697	(5,676)	6,021
Trademarks	—	2,872	(2,872)	—	2,882	(2,882)	—
Total finite-lived intangible assets		1,491,768	(421,687)	1,070,081	1,335,903	(332,602)	1,003,301
Acquired IPR&D assets		1,941,920	—	1,941,920	182,305	—	182,305
Total intangible assets		$ 3,433,688	$ (421,687)	$ 3,012,001	$ 1,518,208	$ (332,602)	$ 1,185,606

The increase in the gross carrying amount of intangible assets as of December 31, 2016 compared to December 31, 2015 reflects the acquisition of the Vyxeos IPR&D asset in the Celator Acquisition, as described in Note 3, and the capitalization of a $150.0 million milestone payment to Sigma-Tau Pharmaceuticals Inc. that was triggered by the FDA approval of Defitelio on March 30, 2016, partially offset by the negative impact of foreign currency translation adjustments due to the strengthening of the U.S. dollar against the euro. Additionally, after receiving FDA approval of Defitelio, we reclassified $48.4 million of acquired IPR&D from an indefinite-lived intangible asset to an acquired developed technology finite-lived intangible asset. The Defitelio acquired developed technology asset will be amortized over its estimated useful life of 14 years.

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, 2016, 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
2017	$ 102,084
2018	99,379
2019	99,169
2020	98,041
2021	97,118
Thereafter	574,290
Total	$ 1,070,081

8. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2016	2015
Rebates and other sales deductions	$ 72,344	$ 67,454
Employee compensation and benefits	43,363	35,595
Royalties	11,643	4,211
Accrued contract termination fees	11,612	—
Clinical trial accruals	10,139	1,601
Accrued interest	5,179	4,043
Professional fees	4,596	3,038
Sales returns reserve	4,366	6,110
Inventory-related accruals	3,350	1,017
Accrued construction-in-progress	1,597	1,637
Contract claim settlement	—	18,000
Other	25,079	21,364
Total accrued liabilities	$ 193,268	$ 164,070

9. Debt

The following table summarizes the carrying amount of our indebtedness (in thousands):

	December 31,	
	2016	2015
1.875% exchangeable senior notes due 2021	$ 575,000	$ 575,000
Unamortized discount on 1.875% exchangeable senior notes due 2021	(101,094)	(119,467)
1.875% exchangeable senior notes due 2021, net	473,906	455,533
Borrowings under revolving credit facility	850,000	—
Term loan	705,719	732,398
Other borrowings	—	513
Total debt	2,029,625	1,188,444
Less current portion	36,094	37,587
Total long-term debt	$ 1,993,531	$ 1,150,857

Credit Agreement

On June 18, 2015, Jazz Pharmaceuticals plc, as guarantor, and certain of our wholly owned subsidiaries, as borrowers, entered into a credit agreement, which we refer to in this report as the 2015 credit agreement, that provided 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 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.

On July 12, 2016, Jazz Pharmaceuticals plc, as guarantor, and certain of our wholly owned subsidiaries, as borrowers, entered into the amended credit agreement. The amended credit agreement provides for a revolving credit facility of $1.25 billion, which replaces the revolving credit facility of $750.0 million provided for under the 2015 credit agreement, of which $850.0 million was outstanding as of December 31, 2016, and a $750.0 million term loan facility, of which $712.9 million principal amount was outstanding as of December 31, 2016. We used the proceeds of $1.0 billion of loans under the revolving credit facility, together with cash on hand, to fund the Celator Acquisition and expect to use the proceeds from future loans under the revolving credit facility, if any, for general corporate purposes, including corporate development activities. Please see Note 3 for additional information regarding the Celator Acquisition.

Under the amended credit agreement, the term loan matures on July 12, 2021 and the revolving credit facility terminates, and any loans outstanding thereunder become due and payable, on July 12, 2021.

Borrowings under the amended 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, 2016, the interest rate on the term loan was 2.77% and the effective interest rate was 3.0%. As of December 31, 2016, we had undrawn revolving credit facilities totaling $400.0 million of which $0.5 million was committed for an outstanding letter of credit.

Jazz Pharmaceuticals plc and certain of our wholly owned subsidiaries are borrowers under the amended credit agreement. The borrowers' obligations under the amended 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 our 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 2016 and are equal to 5.0% per annum of the principal amount outstanding on July 12, 2016 of $721.9 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 amended credit agreement contains financial covenants that require Jazz Pharmaceuticals plc and our 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, 2016, and are currently, in compliance with these financial covenants.

In connection with our entry into the amended credit agreement, we recorded a loss on extinguishment and modification of debt of $0.6 million in 2016 primarily related to new third party fees associated with modified debt. In 2015, in connection with our entry into the 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, 2016, 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, 2016, 2015 and 2014, we recognized $27.5 million, $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, 2016, 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
2017	$ 36,094
2018	40,606
2019	58,652
2020	76,699
2021	1,925,801
Total	$ 2,137,852

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 2016, 2015 and 2014 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 executive 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, 2016 and December 31, 2015. 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,		
	2016	2015	2014
Lease expense	$ 11,600	$ 10,479	$ 10,678

Future minimum lease payments under our noncancelable operating and facility leases as of December 31, 2016, were as follows (in thousands):

Year ending December 31,	Lease Payments
2017	$ 15,442
2018	12,255
2019	10,881
2020	9,941
2021	9,439
Thereafter	67,914
Total	$ 125,872

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, 2016, we recorded project construction costs of $27.1 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, 2016, we recorded rent expense associated with the ground lease of $1.9 million in our consolidated statements of income.

In August 2016, we entered into an operating lease agreement for office space in Dublin, Ireland for a term of 20 years, with an option to terminate at the end of eight years with no less than one year’s prior written notice and the payment of a termination fee, and a further option to terminate at the end of 15 years with no less than one year’s prior written notice. We are obligated to make minimum lease payments totaling $19.6 million in connection with this lease.

As of December 31, 2016, we had $27.1 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 Patent Certification, or Paragraph IV Certification, from West-Ward Pharmaceuticals Corp., formerly known as Roxane Laboratories, Inc., or 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. 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 were consolidated by the District Court into a single case, which we refer to as the first Roxane consolidated case. In the first Roxane consolidated case, we allege that 10 of our patents covering Xyrem are or will be infringed by Roxane's ANDA, which was approved by the FDA in January 2017, and seek 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, we filed three actions against Roxane in the District Court on February 20, 2015, June 1, 2015 and January 27, 2016 that were consolidated by the District Court into a second case, which we refer to as the second Roxane consolidated case. In the second Roxane consolidated case, we allege that five of our patents covering Xyrem are or will be infringed by Roxane's ANDA and seek a permanent injunction to prevent Roxane from introducing a generic version of Xyrem that would infringe those patents.

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, or REMS, patents.

In July 2016, the District Court determined that it would try all of the patents at issue in the first and second Roxane consolidated cases together, including the REMS patents that were previously bifurcated and stayed, and set trial in this combined consolidated case for the second quarter of 2017. In the first quarter of 2017, the District Court bifurcated and stayed the part of the combined consolidated case involving the REMS patents. Also in the first quarter of 2017, the FDA approved Roxane's ANDA with a REMS that is separate from the Xyrem REMS.

On August 12, 2016, we filed a lawsuit against Roxane in the District Court alleging that an additional later-issued REMS patent 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 September 2016, Roxane moved to dismiss the lawsuit. This motion is pending.

The actual timing of events in our litigation with Roxane may be 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 extended Amneal's 30-month stay period to coincide with the date of Par's 30-month stay period. The stay expired on May 20, 2016.

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. In March 2016, Par moved to dismiss claims involving our patents 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), or our method of administration patents relating to DDI patents. In August 2016, we and Par stipulated to dismiss claims relating to our patents covering the formulation of Xyrem on the grounds that Par had notified FDA that it had converted its Paragraph IV Certifications to a Paragraph III Certification.

On June 4, 2014, we received a notice of Paragraph IV Certification from Ohm Laboratories Inc., formerly known as Ranbaxy, Inc., 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. In May 2016, the Ranbaxy litigation was settled as described below. In the first quarter of 2017, the FDA tentatively approved the ANDAs of Amneal and Ranbaxy.

On October 30, 2014, we received a notice of Paragraph IV Certification from Teva Pharmaceutical Industries Ltd., formerly known as 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. In March 2015, Watson moved to dismiss the portion of the case based on our Orange Book-listed REMS patents on the grounds that these patents do not cover patentable subject matter. In November 2015, the District Court administratively terminated this motion to dismiss (without prejudice) pending the outcome of inter partes review, or 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 had 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 were or would 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. On November 26, 2015, we received an additional notice of Paragraph IV Certification from Wockhardt regarding newly issued patents listed in the Orange Book, and we filed an additional lawsuit against Wockhardt in the District Court alleging that our patents covering Xyrem were or would 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. In April 2016, the Wockhardt litigation was settled as set forth below

On July 23, 2015, we received a Paragraph IV Certification from Lupin Inc., or Lupin, that it had 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.

In January, April and June 2016, the District Court issued orders consolidating all of the cases then pending against Amneal, Par, Ranbaxy, Watson, Wockhardt and Lupin into a single case for all purposes. No trial date has been set in that consolidated case.

We entered into settlement agreements with Wockhardt and Ranbaxy on April 18, 2016 and May 9, 2016, respectively, that resolved our patent litigation against Wockhardt and Ranbaxy. Under the settlement agreements, we granted each of Wockhardt and Ranbaxy a license to manufacture, market, and sell its generic version of Xyrem on or after December 31, 2025, or earlier depending on the occurrence of certain events. The specific terms of the settlement agreements are confidential.

The settlements with Wockhardt and Ranbaxy do not resolve the litigation against Amneal, Par, Watson and Lupin, which is ongoing. We cannot predict the specific timing or outcome of events in this matter with respect to the remaining defendants 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 the six REMS patents. In July 2016, the PTAB issued final decisions that the claims of these six patents are unpatentable; as a result, if the United States Court of Appeals for the Federal Circuit upholds those decisions on appeal, these claims will be canceled. We have filed notices of appeal with respect to these IPR decisions to the United States Court of Appeals for the Federal Circuit. In September 2015, certain of the ANDA filers filed a petition for IPR with respect to the validity of an additional REMS patent. In March 2016, the PTAB partially instituted an IPR on a seventh REMS patent, declining to review 25 of 28 claims. A PTAB decision on the three claims that were tried is expected before the end of the first quarter of 2017.

In October 2015, Ranbaxy and Par filed petitions for IPR with respect to the validity of one of our DDI patents, and Amneal filed an IPR petition on the same patent in February 2016. In April 2016, the PTAB denied Par's petition in its entirety and issued a decision on Ranbaxy's petition, instituting an IPR trial with respect to 16 of the claims under the patent subject to this petition and denying the petition with respect to the other 18 claims. In July 2016, the PTAB denied Amneal's petition in its entirety. In March 2016, Ranbaxy filed a petition for IPR with respect to the validity of the second of our DDI patents. In connection with settlement of our litigation with Ranbaxy, both of the IPR petitions filed by Ranbaxy were terminated.

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 connection with settlement of our patent litigation with Wockhardt, this IPR petition was terminated.

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 pending IPR or other proceeding, the outcome of any appeal of the July 2016 IPR decisions with respect to the six REMS patents or the impact any IPR or other proceeding might have on ongoing ANDA litigation proceedings or other aspects of our Xyrem business.

Shareholder Litigation Matters Relating to Celator Acquisition. On June 21, 2016, a putative class-action lawsuit challenging our acquisition of Celator Pharmaceuticals, Inc., or Celator, captioned *Dunbar v. Celator Pharmaceuticals, Inc.*, or the Dunbar action, was filed in the Superior Court of New Jersey. We refer to our acquisition of Celator in this report as the Celator Acquisition. The complaint was filed against Celator, each member of the Celator board of directors, Jazz Pharmaceuticals plc and our wholly owned subsidiary Plex Merger Sub, Inc., or Plex. The complaint generally alleges that the Celator directors breached their fiduciary duties in connection with the Celator Acquisition, and that Jazz Pharmaceuticals plc and Plex aided and abetted these alleged breaches of fiduciary duty. The complaint also generally asserts that the Celator directors breached their fiduciary duties to Celator's public stockholders by, among other things, (i) agreeing to sell Celator to us at an inadequate price, (ii) implementing an unfair process, (iii) agreeing to certain provisions of the merger agreement for the Celator Acquisition that allegedly favored us and deterred alternative bids, and (iv) failing to disclose purportedly material information in Celator's Schedule 14D-9 filing with the U.S. Securities and Exchange Commission, or SEC. The plaintiff sought, among other things, an injunction against the consummation of the Celator Acquisition and an award of costs and expenses, including a reasonable allowance for attorneys' and experts' fees.

Between June 27, 2016 and June 29, 2016, two putative class-action lawsuits challenging the Celator Acquisition, captioned *Palmisciano v. Celator Pharmaceuticals, Inc.*, or the Palmisciano action, and *Barreto v. Celator Pharmaceuticals, Inc.*, or the Barreto action, were filed in the District Court. The complaints were filed against Celator and each member of the Celator board of directors. The complaints assert causes of action under sections 14 and 20 of the Securities Exchange Act of 1934, as amended, predicated on Celator's and the Celator directors' alleged failure to disclose purportedly material information in Celator's Schedule 14D-9 filing with the SEC. The plaintiffs sought, among other things, an injunction against the consummation of the Celator Acquisition and an award of costs and expenses, including a reasonable allowance for attorneys' and experts' fees. Neither Jazz Pharmaceuticals plc nor Plex were named defendants in these actions.

On July 6, 2016, the defendants to the Dunbar action, the Palmisciano action and the Barreto action entered into a memorandum of understanding regarding settlement of these actions with the plaintiffs. The memorandum of understanding outlines the terms of the parties' agreement in principle to settle and release all claims which were or could have been asserted in these actions. In consideration for such settlement and release, the parties to these actions agreed, among other things, that Celator would amend its Schedule 14D-9 to include certain supplemental disclosures. The Schedule 14D-9 was amended by Celator on July 6, 2016, and the Celator Acquisition was completed on July 12, 2016. The settlement remains subject to, among other items, confirmatory discovery, the execution of a stipulation of settlement by the parties, final approval of the settlement by the District Court in the Barreto action and dismissal with prejudice of the Dunbar action and the Palmisciano action.

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

In May 2016, we received a subpoena from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients, and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. In October 2016, we received a second subpoena updating and further specifying document requests regarding support to 501(c)(3) organizations that provide financial assistance to Medicare patients and the provision of financial assistance for Medicare patients taking drugs sold by us. In February 2017, we received a third subpoena requesting documents regarding our support to a specific 501(c)(3) organization that established a fund for narcolepsy patients in January 2017. Other companies have disclosed similar

subpoenas and continuing inquiries. We are cooperating with this investigation. We are unable to predict how long this investigation will continue, whether we will receive additional subpoenas in connection with this investigation, or its outcome, but we expect that we will continue to incur significant costs in connection with the investigation, regardless of the outcome. 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.

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. In November 2015, our board of directors authorized another share repurchase program pursuant to which we were authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300.0 million, exclusive of any brokerage commissions. In September 2016, we completed repurchases under the November 2015 share repurchase program. In November 2016, 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 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 depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the amended credit agreement, corporate and regulatory requirements and market conditions. The new share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2016, under the November 2015 and November 2016 repurchase programs, we spent a total of $278.3 million to repurchase 2.2 million of our ordinary shares at an average total purchase price, including brokerage commissions, of $124.09 per share. All ordinary shares repurchased were canceled. As of December 31, 2016, the remaining amount authorized under the November 2016 share repurchase program was $281.5 million.

Authorized But Unissued Ordinary Shares

We had reserved the following shares of authorized but unissued ordinary shares (in thousands):

	December 31, 2016
2011 Equity Incentive Plan	13,988
2007 Equity Incentive Plan	918
2007 Employee Stock Purchase Plan	443
Amended and Restated 2007 Non-Employee Directors Stock Award Plan	485
Amended and Restated Directors Deferred Compensation Plan	178
Total	16,012

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, 2016 and December 31, 2015 were as follows (in thousands):

	Foreign Currency Translation Adjustments	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2015	$ (267,472)	$ (267,472)
Other comprehensive loss	(49,861)	(49,861)
Balance at December 31, 2016	$ (317,333)	$ (317,333)

In 2016, other comprehensive loss reflects foreign currency translation adjustments, primarily due to the strengthening of the U.S. dollar against the euro.

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 identification, development and commercialization of meaningful pharmaceutical products that address unmet medical needs. The following table presents a summary of total revenues (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Xyrem	$ 1,107,616	$ 955,187	$ 778,584
Erwinaze/Erwinase	200,678	203,261	199,665
Defitelio/defibrotide	108,952	70,731	70,537
Prialt® (ziconotide) intrathecal infusion	29,120	26,440	26,421
Psychiatry	17,653	37,135	40,879
Other	13,242	24,065	46,630
Product sales, net	1,477,261	1,316,819	1,162,716
Royalties and contract revenues	10,712	7,984	10,159
Total revenues	$ 1,487,973	$ 1,324,803	$ 1,172,875

The following table presents a summary of total revenues attributed to geographic sources (in thousands):

	Year Ended December 31,		
	2016	2015	2014
United States	$ 1,354,921	$ 1,192,879	$ 1,007,396
Europe	106,146	103,614	126,715
All other	26,906	28,310	38,764
Total revenues	$ 1,487,973	$ 1,324,803	$ 1,172,875

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,		
	2016	2015	2014
Express Scripts	74%	72%	66%
McKesson Corporation and affiliates	15%	7%	—%
Accredo Health Group, Inc.	—%	6%	14%

At the end of the second quarter of 2015, we transitioned the U.S. distribution of Erwinaze from Accredo Health Group, Inc. to McKesson.

The following table presents total long-lived assets by location (in thousands):

	December 31,	
	2016	2015
Ireland	$ 62,453	$ 62,795
United States	35,791	12,794
Italy	7,000	7,928
Other	2,246	2,055
Total long-lived assets [1]	$ 107,490	$ 85,572

(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, 2016, a total of 19,036,985 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, 2017, the share reserve under the 2011 Plan automatically increased by 2,692,247 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. The 2007 Plan expires in April 2017.

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, 2016, 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, and (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, 2017.

Amended and Restated 2007 Non-Employee Directors Stock Award Plan

The Amended and Restated 2007 Non-Employee Directors Stock Award Plan, or the 2007 Directors Award 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 Award 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 Award 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 Award Plan will be at the discretion of our board of directors. Since the Azur Merger, all of the new grants under the 2007 Directors Award 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 Award Plan provides the source of shares to fund distributions made prior to August 15, 2010 under the Directors Deferred Compensation Plan described below. In August 2016, our shareholders approved our proposal to expand the types of stock awards that may be granted to our non-employee directors under the 2007 Directors Award Plan and eliminate the final automatic share reserve increase under the 2007 Directors Plan that was scheduled to occur on January 1, 2017. As of December 31, 2016, a total of 869,768 of our ordinary shares had been authorized for issuance under the 2007 Directors Award Plan.

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 2016, 2015 and 2014 related to retainer fees earned and deferred. As of December 31, 2016, 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,		
	2016	2015	2014
Grant date fair value	$ 40.45	$ 57.19	$ 60.29
Volatility	39%	39%	45%
Expected term (years)	4.2	4.2	4.3
Range of risk-free rates	0.8-1.6%	1.1-1.5%	1.1-1.4%
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,		
	2016	2015	2014
Selling, general and administrative	$ 79,037	$ 74,653	$ 55,083
Research and development	15,296	13,356	12,179
Cost of product sales	4,438	3,541	2,376
Total share-based compensation expense, pre-tax	98,771	91,550	69,638
Income tax benefit from share-based compensation expense (1)	(30,022)	(20,071)	(13,550)
Total share-based compensation expense, net of tax	$ 68,749	$ 71,479	$ 56,088

(1) Following adoption of ASU No. 2016-09, the 2016 income tax benefit includes excess tax benefits recognized.

We recognized income tax benefits related to share option exercises of $8.3 million in 2016 and realized $0.4 million and $1.6 million in 2015 and 2014, respectively.

Share Options

The following table summarizes information as of December 31, 2016 and activity during 2016 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, 2016	3,937	$ 102.81		
Options granted	1,308	125.80		
Options exercised	(398)	42.35		
Options forfeited	(269)	142.50		
Options expired	(65)	167.31		
Outstanding at December 31, 2016	4,513	111.52	7.2	$ 104,546
Vested and expected to vest at December 31, 2016	4,288	110.09	7.1	104,417
Exercisable at December 31, 2016	2,541	90.06	6.1	101,401

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 $36.1 million, $93.3 million and $138.2 million during 2016, 2015 and 2014, respectively. We issued new ordinary shares upon exercise of share options.

As of December 31, 2016, total compensation cost not yet recognized related to unvested share options was $81.3 million, which is expected to be recognized over a weighted-average period of 2.5 years.

As of December 31, 2016, total compensation cost not yet recognized related to grants under the ESPP was $5.4 million, which is expected to be recognized over a weighted-average period of less than one year.

Restricted Stock Units

In 2016, we granted RSUs covering an equal number of our ordinary shares to employees with a weighted-average grant date fair value of $125.79. 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 an expense ratably over the vesting period of four years. In 2016, 450,000 RSUs were released with 289,000 ordinary shares issued and 161,000 ordinary shares withheld for tax purposes. The total fair value of shares vested was $59.2 million, $72.2 million and $50.9 million during 2016, 2015 and 2014, respectively.

As of December 31, 2016, total compensation cost not yet recognized related to unvested RSUs was $99.6 million, which is expected to be recognized over a weighted-average period of 2.3 years.

The following table summarizes information as of December 31, 2016 and activity during 2016 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, 2016	1,054	$ 129.40		
RSUs granted	519	125.79		
RSUs released	(450)	105.09		
RSUs forfeited	(126)	137.25		
Outstanding at December 31, 2016	997	137.50	1.3	$ 108,730

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 $3.4 million, $2.2 million and $2.0 million in 2016, 2015 and 2014, 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 $0.8 million, $0.6 million and $0.5 million in 2016, 2015 and 2014, respectively, in connection with the contributions we made under the Irish defined contribution plan. In the U.S., 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. We recorded expense of $1.9 million, $1.1 million and $1.0 million in 2016, 2015 and 2014, 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 $0.6 million, $0.4 million and $0.5 million in 2016, 2015 and 2014, 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 $0.3 million and $0.2 million as of December 31, 2016 and 2015, 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 as of December 31, 2016 and 2015.

17. Restructuring

In 2016 and 2015, we recorded severance costs of $1.5 million and $1.1 million, respectively, for terminated employees in connection with the reorganization of our operations, primarily in France and Italy. 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. As of December 31, 2016, we had incurred total termination benefit costs of $2.6 million in connection with these reorganizations. We do not expect to incur any additional material one-time termination benefit costs relating to these restructuring activities in 2017.

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. We completed these restructuring activities in 2015 and we did not incur any related additional costs in 2016.

The following table summarizes the amounts related to restructuring through December 31, 2016 (in thousands):

	Termination Benefits	Facility Closure Costs	Total
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
Expense	1,516	—	1,516
Payments	(2,590)	—	(2,590)
Balance at December 31, 2016	$ 31	$ —	$ 31

The balances as of December 31, 2016, 2015 and 2014 were included within accrued liabilities in our consolidated balance sheets.

18. Income Taxes

The components of income before the income tax provision and equity in loss of investee were as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Ireland	$ 179,570	$ 233,785	$ 238,351
United States	312,904	285,420	222,328
Other	39,972	(83,272)	(309,122)
Total	$ 532,446	$ 435,933	$ 151,557

The following table sets forth the details of the income tax provision (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Current			
Ireland	$ 26,420	$ 29,748	$ 29,337
United States	140,061	116,301	97,679
Other	9,918	28,708	16,469
Total current income tax	176,399	174,757	143,485
Deferred, exclusive of other components below			
Ireland	(7,776)	(6,655)	(3,508)
United States	(9,120)	332	(15,003)
Other	(13,720)	(40,532)	(30,743)
Total deferred, exclusive of other components	(30,616)	(46,855)	(49,254)
Deferred, change in tax rates			
United States	109	294	—
Other	(10,656)	(21,797)	—
Total deferred, change in tax rates	(10,547)	(21,503)	—
Total deferred income tax benefit	(41,163)	(68,358)	(49,254)
Total income tax provision	$ 135,236	$ 106,399	$ 94,231

Our income tax provision was $135.2 million, $106.4 million and $94.2 million in 2016, 2015 and 2014, respectively, related to tax arising on income in Ireland, the U.S. and certain other foreign jurisdictions, certain unrecognized tax benefits and various expenses not deductible for income tax purposes.

The effective tax rates for 2016, 2015 and 2014 were 25.4%, 24.4% and 62.2%, respectively. After adjusting the income before income tax provision and equity in loss of investee 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 rates for 2016 and 2015 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, and various expenses not deductible for income tax purposes, partially offset by originating tax credits, reductions in tax rates in certain jurisdictions and deductions available in relation to subsidiary equity. The effective tax rate for 2014 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, current year losses in some jurisdictions for which no tax benefit is available and various expenses not deductible for income tax purposes, partially offset by changes in U.S. state valuation allowances in 2014 and benefits from certain originating income tax credits. The increase in the effective tax rate in 2016 compared to 2015 was primarily due to a decrease in the impact of the reduction in tax rates in certain jurisdictions and a decrease in originating tax credits, partially offset by changes in income mix among the various jurisdictions in which we operate. 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. We are currently paying taxes in Ireland, the U.S. 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 equity in loss of investee and our effective income tax rate was as follows:

	Year Ended December 31,		
	2016	2015	2014
Statutory income tax rate	12.5 %	12.5 %	12.5 %
Foreign income tax rate differential	16.7 %	19.1 %	50.0 %
Change in unrecognized tax benefits	3.3 %	3.6 %	6.2 %
Financing costs	(2.9)%	(0.4)%	0.7 %
Research and other tax credits	(2.8)%	(3.8)%	(9.4)%
Deduction on subsidiary equity	(2.4)%	(2.7)%	(7.5)%
Acquisition-related costs	2.1 %	— %	3.1 %
Non-deductible compensation	1.8 %	1.9 %	4.6 %
Change in tax rate	(1.8)%	(4.5)%	— %
Excess tax benefits from share-based compensation	(1.5)%	— %	— %
Change in valuation allowance	(0.1)%	(0.6)%	5.7 %
Change in estimates	— %	(1.0)%	(3.0)%
Other	0.5 %	0.3 %	(0.7)%
Effective income tax rate	25.4 %	24.4 %	62.2 %

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,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$ 202,758	$ 57,091
Tax credit carryforwards	114,192	36,797
Intangible assets	15,965	25,384
Share-based compensation	27,522	20,050
Accruals	38,763	32,355
Other	57,893	49,420
Total deferred tax assets	457,093	221,097
Valuation allowance	(53,184)	(33,949)
Net deferred tax assets	403,909	187,148
Deferred tax liabilities:		
Acquired intangible assets	(910,460)	(307,356)
Other	(35,122)	(33,137)
Total deferred tax liabilities	(945,582)	(340,493)
Net deferred tax liabilities	$ (541,673)	$ (153,345)

The net change in valuation allowance was $19.2 million, $4.3 million and $9.0 million in 2016, 2015 and 2014, respectively.

The following table presents the breakdown between non-current deferred tax assets and liabilities (in thousands):

	Year Ended December 31,	
	2016	2015
Non-current deferred tax assets	$ 15,060	$ 130,148
Non-current deferred tax liabilities	(556,733)	(283,493)
Net deferred tax liabilities	$ (541,673)	$ (153,345)

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.

As of December 31, 2016, we had NOL carryforwards and tax credit carryforwards for U.S. federal income tax purposes of approximately $425.7 million and $101.4 million, respectively, available to reduce future income subject to income taxes. The NOL carryforwards are inclusive of $94.6 million from the EUSA Acquisition in 2012 and $229.3 million from the Celator Acquisition in 2016. The federal NOL carryforwards will expire, if not utilized, in the tax years 2017 to 2036, and the federal tax credits will expire, if not utilized, in the tax years 2017 to 2036, with the exception of alternative minimum tax credits, which have no expiration date. In addition, we had approximately $165.0 million of NOL carryforwards and $9.8 million of tax credit carryforwards as of December 31, 2016 available to reduce future taxable income for state income tax purposes. The state NOL carryforwards will expire, if not utilized, in the tax years 2017 to 2036. The state tax credits have no expiration date. The U.S. federal and state NOL carryforwards and tax credit carryforwards are inclusive of $101.9 million of previously unrecognized excess tax benefits which resulted from exercises of employee share options and certain sales by employees of shares issued under other employee equity compensation. These previously unrecognized excess tax benefits were included within a cumulative-effect adjustment to opening retained earnings and deferred tax liabilities, net, non-current on adoption of ASU No. 2016-09. In addition, as of December 31, 2016, there were NOL carryforwards for income tax purposes of approximately $54.2 million and $48.4 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, 2016, 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 U.S. is subject to an 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 $281.2 million, before tax effect, for 2017, $142.0 million, before tax effect, for 2018 and a combined total of $341.9 million, before tax effect, for 2019 to 2032. 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.

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 $53.2 million and $33.9 million as of December 31, 2016 and 2015, respectively, for certain U.S. state and foreign deferred tax assets which we maintain until sufficient positive evidence exists to support reversal. During 2016, as part of the overall change in valuation allowance, we recognized a net income tax expense of $17.9 million relating to the creation of a valuation allowance against certain deferred tax assets primarily associated with NOLs recognized 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 and utilization of certain deferred tax assets primarily associated with NOLs. 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. 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 undistributed earnings of foreign operations that are considered indefinitely reinvested in our foreign subsidiaries totaled approximately $1.2 billion and $983.8 million as of December 31, 2016 and 2015, 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, 2016, it was not practicable to determine the amount of the unrecognized deferred tax liability related to these earnings.

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 recorded an unrecognized tax benefit 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,		
	2016	2015	2014
Balance at the beginning of the year	$ 66,385	$ 40,802	$ 21,637
Increases related to current year tax positions	26,873	23,664	19,837
Increases related to prior year tax positions	1,191	2,833	—
Decreases related to prior year tax positions	(255)	(646)	(672)
Lapse of the applicable statute of limitations	(3,284)	(268)	—
Balance at the end of the year	$ 90,910	$ 66,385	$ 40,802

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 the income tax provision in our consolidated statements of income. As of December 31, 2016 and 2015, 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 $65.3 million and $48.1 million at December 31, 2016 and 2015, respectively, that, if recognized, would affect the effective tax rate on income.

Our most significant tax jurisdictions are Ireland, the U.S. (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 the years ended December 31, 2012 and 2013. 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 $40.3 million, including interest and penalties through the date of the assessment, translated at the foreign exchange rate at December 31, 2016. We disagree with the proposed assessment and intend to contest it vigorously.

19. Quarterly Financial Data (Unaudited)

The following interim financial information presents our 2016 and 2015 results of operations on a quarterly basis (in thousands, except per share amounts):

	2016			
	March 31	June 30	September 30	December 31
Revenues	$ 336,010	$ 381,161	$ 374,181	$ 396,621
Gross margin (1)	310,477	355,130	347,310	358,958
Net income attributable to Jazz Pharmaceuticals plc (2)	75,812	114,502	89,828	116,689
Net income attributable to Jazz Pharmaceuticals plc per ordinary share, basic (2)	1.24	1.89	1.49	1.95
Net income attributable to Jazz Pharmaceuticals plc per ordinary share, diluted (2)	1.21	1.85	1.45	1.91

	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

(1) Gross margin is computed by subtracting cost of product sales (excluding amortization and impairment of intangible assets) from product sales, net.

(2) As described in Note 2, we elected to early adopt ASU No. 2016-09 in the fourth quarter of 2016 retroactive to the beginning of the fiscal year. Previously reported quarterly net income attributable to Jazz Pharmaceuticals plc and the related per-share measures for the first three quarters of 2016 have been recast to reflect the adoption of ASU No. 2016-09. Below is a reconciliation of the net income attributable to Jazz Pharmaceuticals plc and the related per-share measures as previously reported in our quarterly reports on Form 10-Q to the recast amounts reported above.

	2016		
	March 31	June 30	September 30
Net income attributable to Jazz Pharmaceuticals plc, as previously reported	$ 74,121	$ 111,282	$ 87,145
Adoption of ASU No. 2016-09	1,691	3,220	2,683
Net income attributable to Jazz Pharmaceuticals plc, as recast	$ 75,812	$ 114,502	$ 89,828
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - basic, as previously reported	$ 1.21	$ 1.84	$ 1.44
Adoption of ASU No. 2016-09	0.03	0.05	0.05
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - basic, as recast	$ 1.24	$ 1.89	$ 1.49
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - diluted, as previously reported	$ 1.19	$ 1.80	$ 1.41
Adoption of ASU No. 2016-09	0.02	0.05	0.04
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - diluted, as recast	$ 1.21	$ 1.85	$ 1.45

The interim financial information above includes the following items:

- Upfront and milestone payments of $8.8 million and $15.0 million in the first and third quarters of 2016, respectively, and $25.0 million in the third quarter of 2015;
- Transaction costs and integration related costs of $2.2 million, $10.8 million and $0.7 million in the second, third and fourth quarters of 2016, respectively;
- Expenses related to certain legal proceedings and restructuring of $6.1 million in the first quarter of 2016 and $0.5 million and $1.1 million in the first and fourth quarters of 2015, respectively;
- A one-time charge of $11.6 million in respect of a contract termination in the fourth quarter of 2016;
- A loss on extinguishment and modification of debt of $0.6 million in the third quarter of 2016 and $16.8 million in the second quarter of 2015;
- Impairment charges of $31.5 million in the fourth quarter of 2015, which resulted from our decision to terminate a pivotal Phase 2 clinical trial of JZP-416; and
- 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.

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, 2016						
Allowance for doubtful accounts	(1)	$ 489	$ 168	$ —	$ (370)	$ 287
Allowance for sales discounts	(1)	181	1,334	—	(1,397)	118
Allowance for chargebacks	(1)	3,023	41,991	—	(40,265)	4,749
Deferred tax asset valuation allowance	(2)(3)(4)	33,949	19,328	5,544	(5,637)	53,184
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

(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 other comprehensive income and a valuation allowance recognized on purchase accounting.

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).
2.9	Agreement and Plan of Merger, dated as of May 27, 2016, by and among Jazz Pharmaceuticals plc, Plex Merger Sub, Inc., and Celator Pharmaceuticals, 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 May 31, 2016).
3.1	Amended and Restated Memorandum and Articles of Association of Jazz Pharmaceuticals plc, as amended on August 4, 2016 (incorporated herein by reference to Exhibit 3.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
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 Licence 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. (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 2016).
10.6A	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. 001-33500), as filed with the SEC on June 18, 2015).
10.6B	Amendment No. 1, dated as of July 12, 2016, to 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 Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
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).
10.13C+	Amended and Restated Schedule 3 to Employment Agreement by and between Jazz Pharmaceuticals UK Ltd and Iain McGill (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 June 30, 2016, as filed with the SEC on August 9, 2016).
10.13D+	Change in Control Stock Award Acceleration Agreement by and between Jazz Pharmaceuticals plc and Iain McGill (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 June 30, 2016, as filed with the SEC on August 9, 2016).
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 10.17B 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).
10.15C+	Amended and Restated Schedule 3 to Employment Agreement by and between Jazz Pharmaceuticals Ireland Ltd. 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 June 30, 2016, as filed with the SEC on August 9, 2016).
10.15D+	Change in Control Stock Award Acceleration Agreement by and between Jazz Pharmaceuticals plc and Paul Treacy (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 June 30, 2016, as filed with the SEC on August 9, 2016).
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) for the period ended December 31, 2012, 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).
10.18M+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (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 March 31, 2016, as filed with the SEC on May 10, 2016).

10.18N+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (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 March 31, 2016, as filed with the SEC on May 10, 2016).
10.18O+	Amended and Restated 2011 Equity Incentive Plan (approved August 4, 2016) (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, 2016, as filed with the SEC on August 9, 2016).
10.18P+	Amended and Restated 2011 Equity Incentive Plan (approved November 3, 2016) (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, 2016, as filed with the SEC on November 8, 2016).
10.18Q+	Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (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, 2016, as filed with the SEC on November 8, 2016).
10.18R+	Form of U.S. Option Grant Notice and Form of U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 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 September 30, 2016, as filed with the SEC on November 8, 2016).
10.18S+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 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 September 30, 2016, as filed with the SEC on November 8, 2016).
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).
10.20D+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved August 4, 2016) (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, 2016, as filed with the SEC on August 9, 2016).
10.20E+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved November 3, 2016) (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, 2016, as filed with the SEC on November 8, 2016).
10.20F+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (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, 2016, as filed with the SEC on November 8, 2016).
10.20G+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated Non-Employee Directors 2007 Stock Award Plan (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, 2016, as filed with the SEC on November 8, 2016).
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 (approved November 4, 2015) (incorporated herein by reference to Exhibit 10.22B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 2016).
10.22B+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved November 3, 2016).
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) (incorporated herein by reference to Exhibit 10.22D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 2016).
10.22E+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2017).
10.23+	Jazz Pharmaceuticals plc Amended and Restated Executive Change in Control and Severance Benefit Plan (approved February 10, 2016) (incorporated herein by reference to Exhibit 10.23 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2015, as filed with the SEC on February 23, 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 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).
10.25B+	Amended and Restated Non-Employee Director Compensation Policy (approved May 5, 2016) (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, 2016, as filed with the SEC on August 9, 2016).
10.27	Tender and Support Agreement, dated as of May 27, 2016, by and among Jazz Pharmaceuticals plc, Plex Merger Sub, Inc. and each of the persons set forth on Schedule A attached thereto (incorporated herein by reference to Exhibit 99.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on May 31, 2016).
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.

* 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.

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.

A Participant's Target Bonus generally will be based on the Participant's position and/or responsibility level. The Target Bonus 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 Bonuses 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 (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	35%
Executive Director	30%
Senior Director	25%
Director	22%
Associate Director	20%
Senior Manager	18%
Manager	15%
Analyst	12%
Support	8%

If a Participant moves to a position and/or responsibility level with a higher Target Bonus during a Plan Year, the Participant's Target Bonus 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 during a Plan Year, the Participant's Target Bonus 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) such Participant's applicable Target Bonus , provided that in the case of any Participant who is an executive officer of Jazz Pharmaceuticals plc, such Participant's Target Bonus 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 the applicable Target Bonus (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***" means, for a Participant for a Plan Year, the percentage 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, and as amended and restated on 2 November 2016.

Exhibit 10.22E

JAZZ PHARMACEUTICALS

CASH BONUS PLAN
(IRELAND AND OTHER SPECIFIED AFFILIATES)

(Calendar Year 2017)

1. Purpose of the Plan.

The Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2017) (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 2017 and ending 31 December 2017.

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., Jazz Pharmaceuticals Italy S.p.A. and any other Specified Affiliate in Italy (other than Jazz Healthcare Italy S.r.l.), only employees who are classified as "dirigenti" under Italian employment laws and are individually notified in a separate writing of their eligibility 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.

The Target Bonus 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 pursuant to any previous target bonus (whether set forth in a written plan or otherwise). The Board or the Compensation Committee retains the sole discretion to determine the Target Bonuses 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 and the below table does not apply to such Participants. For other Participants, the following table provides

a general guideline as to the Target Bonuses which may typically be assigned to various categories of employees:

Position	Target Bonus (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	35%
Executive Director	30%
Senior Director	25%
Director	22%
Associate Director	20%
Senior Manager	18%
Manager	15%
Analyst	12%
Support	8%

As additional general guidelines, if a Participant moves to a position and/or responsibility level with a higher Target Bonus during a Plan Year, the Participant's Target Bonus 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 during a Plan Year, the Participant's Target Bonus 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) such Participant's applicable Target Bonus , provided that in the case of any Participant who is an executive officer of Jazz Pharmaceuticals plc, such Participant's Target Bonus 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 the applicable Target Bonus (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 2017).

"***Plan Year***" means the calendar year beginning 1 January 2017 and ending 31 December 2017, 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***" means, for a Participant for a Plan Year, the percentage 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.

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As approved by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on 2 November 2016.

AGREEMENT AND ACCEPTANCE

I acknowledge that this Cash Bonus Plan for the Plan Year beginning 1 January 2017 and ending 31 December 2017 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:

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 Designated Activity Company	Ireland
Jazz Capital Limited	Ireland
Jazz Pharmaceuticals, Inc.	Delaware
Celator Pharmaceuticals, Inc.	Delaware
Jazz Pharmaceuticals Europe Holdings Limited	Gibraltar
Jazz Pharmaceuticals France SAS	France
Jazz Pharmaceuticals France Holdings SAS	France
Jazz Pharmaceuticals Lux S.à r.l.	Luxembourg
Gentium S.R.L.	Italy
Jazz Pharmaceuticals Italy 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, No. 333-179075 and No. 333-209767) on Form S-8 of Jazz Pharmaceuticals plc of our reports dated February 28, 2017, with respect to the consolidated balance sheets of Jazz Pharmaceuticals plc as of December 31, 2016 and 2015, 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, 2016, and the related financial statement schedule, and the effectiveness of internal control over financial reporting as of December 31, 2016, which reports appear in the December 31, 2016 annual report on Form 10-K of Jazz Pharmaceuticals plc.

/s/ KPMG

Dublin, Ireland
February 28, 2017

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 28, 2017

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 28, 2017

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, 2016, 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 28, 2017

/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.