Jazz Pharmaceuticals plc
Form 10-K
February 26, 2019
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018
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.)

Fifth Floor, Waterloo Exchange
Waterloo 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 ý 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 ý
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 ý No ¨
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes ý 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. ý

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

Large accelerated filer x	Accelerated filer ¨	Non-accelerated filer ¨	Smaller reporting company ¨	Emerging growth company ¨

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ¨

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, as of June 30, 2018, the last business day of the registrant’s most recently completed second fiscal quarter, was approximately $7,515,311,963 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 16,768,983 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 19, 2019, a total of 57,055,731 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 2019 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.

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2018 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), CombiPlex®, Vyxeos® (daunorubicin and cytarabine) liposome for injection, Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion and FazaClo® (clozapine, USP). 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.

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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," "believ "estimate," "project," "predict," "propose," "intend," "continue," "potential," "possible," "foreseeable," "likely," "unforeseen" 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.

PART I

Item 1. Business

Overview

Jazz Pharmaceuticals plc is a global biopharmaceutical company dedicated to developing life-changing medicines for people with limited or no options. As a leader in sleep medicine and with a growing hematology/oncology portfolio, we have a diverse portfolio of products and product candidates in development.

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 adult and pediatric 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;
- 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; and
- Vyxeos® (daunorubicin and cytarabine) liposome for injection, a product approved in the U.S. and in Europe (where it is marketed as Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia, or t-AML, or acute myeloid leukemia, or AML, with myelodysplasia-related changes, or AML-MRC.

We are also seeking approval in the U.S. and Europe for solriamfetol as a treatment to improve wakefulness and reduce EDS in adult patients with narcolepsy or obstructive sleep apnea, or OSA. The FDA accepted our solriamfetol

new drug application, or NDA, for filing with a standard review in early 2018 and the current Prescription Drug User Fee Act, or PDUFA, date is March 20, 2019. We submitted a solriamfetol marketing authorization application, or MAA, to the European Medicines Agency, or EMA, in the fourth quarter of 2018.

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Our strategy to create shareholder value is focused on:

- Strong financial execution through growth in sales of our current lead marketed products;
- Building a diversified product portfolio and development pipeline through a combination of our internal research and development efforts and obtaining rights to clinically meaningful and differentiated on- or near-market products and early- to late-stage product candidates through acquisitions, collaborations, licensing arrangements, partnerships and venture investments; and
- Maximizing the value of our products and product candidates by continuing to implement our comprehensive global development plans, including through generating additional clinical data and seeking regulatory approval for new indications.

In 2018, in support of our strategy, we continued to expand and advance our research and development pipeline in our sleep and hematology/oncology therapeutic areas, both by conducting activities internally and by leveraging partnerships with third parties. For a summary of our ongoing research and development activities, see "Business—Research and Development" in this Part I, Item 1.

Our Commercialized Products

Xyrem

Xyrem is the only treatment approved by the FDA and marketed in the U.S. for both cataplexy and EDS in patients with narcolepsy. Sodium oxybate, the active pharmaceutical ingredient, or API, in Xyrem, is a formulation of the sodium salt of gamma-hydroxybutyrate, an endogenous neurotransmitter and metabolite of gamma-aminobutyric acid. 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 may lead to difficulties at work, school, or in daily life activities like driving, operating machinery or caring for children. 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.

In the fourth quarter of 2018, the average number of active Xyrem patients in the U.S. was approximately 14,300, and we believe that there are significantly more patients with narcolepsy 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.

Xyrem was approved in the U.S. for the treatment of cataplexy in adult patients with narcolepsy in 2002 and was approved for EDS in adult patients with narcolepsy in 2005. In October 2018, Xyrem was also approved in the U.S. for the treatment of cataplexy or EDS in pediatric narcolepsy patients ages seven and older. The American Academy of Sleep Medicine recommends Xyrem as a standard of care for the treatment of both cataplexy and EDS associated with narcolepsy.

We have had exclusive agreements with Express Scripts Specialty Distribution Services, Inc., or Express Scripts, the central pharmacy for Xyrem, to distribute Xyrem in the U.S. and provide patient support services related to Xyrem since 2002. Our current agreement with Express Scripts expires on July 1, 2019, but we expect to exercise our right to extend the agreement for an additional year. The agreement may be terminated by either party at any time without cause on 180 days' prior written notice to the other party. We own all standard operating procedures, business rules

and the related intellectual property for the services Express Scripts provides related to patient support programs. 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 engage.

Our marketing, sales and distribution of Xyrem in the U.S. are subject to a risk evaluation and mitigation strategy, or REMS, which is required by the FDA to mitigate the risks of serious adverse outcomes resulting from inappropriate prescribing, abuse, misuse and diversion of Xyrem. Under the Xyrem REMS, all of the Xyrem sold in the U.S. must be

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dispensed and shipped directly to patients or caregivers 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 must receive materials concerning the serious risks associated with Xyrem before the physician can prescribe, or a patient can receive, the product. The central certified pharmacy must monitor and report instances of patient or prescriber behavior giving rise to a reasonable suspicion of abuse, misuse or diversion of Xyrem, and maintains enrollment and prescription monitoring information in a central database. The central pharmacy ships the product directly to the patient (or caregiver) by a courier service.

For more information regarding research and development activities in our sleep franchise, see "Business—Research and Development" in this Part I, Item 1.

In 2018, net product sales of Xyrem were $1.4 billion, which represented 75% of our total net product sales.

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. Originally developed by Public Health England, a national executive agency of the United Kingdom, or UK, 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. 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.

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 2011. In 2014, the FDA approved a supplemental BLA for administration of Erwinaze via intravenous infusion in conjunction with chemotherapy.

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 UK 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 supply agreement with PBL, which includes our license for Erwinaze, expires on December 31, 2020. We and PBL had been engaged in discussions related to entry into a replacement agreement to extend the term of our commercial relationship with respect to Erwinaze past 2020, but we did not reach agreement. Unless we and PBL enter into a new agreement, we will lose our license to Erwinaze after December 31, 2020, other than our right to sell certain Erwinaze inventory for a post-termination sales period of 12 months. Either party also has the right to terminate the agreement prior to its expiration in the event of the other party's uncured material breach or insolvency.

To expand our asparaginase franchise beyond Erwinaze, we are pursuing activities related to the development of improved asparaginase products for patients with ALL or other hematological malignancies. For more information, see "Business—Research and Development" in this Part I, Item 1.

In 2018, net product sales of Erwinaze were $174.7 million, which represented 9% of our total net product sales.

Defitelio

Defibrotide, the API in Defitelio, has been approved for the treatment of VOD, a potentially life-threatening complication of HSCT, and is in development for other complications following HSCT, including prevention of VOD, prevention of acute Graft versus Host Disease, or aGvHD, and treatment of transplant-associated thrombotic microangiopathy, or TA-TMA, as well as complications following anti-cancer treatment, including prevention of CAR-T-associated neurotoxicity. Defibrotide is the sodium salt of a complex mixture of single-stranded oligodeoxyribonucleotides derived from porcine DNA. Defibrotide mediates its effects via interaction with

endothelial cells. Non-clinical data suggest that defibrotide stabilizes endothelial cells by reducing endothelial cell activation and by protecting them from further damage.

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.

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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%.

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 in 2013. We commenced a rolling launch of Defitelio in European countries in 2014. In countries where we currently commercialize Defitelio, we are working to maintain current levels of market access.

In 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. We acquired the rights to defibrotide for the treatment and prevention of VOD in North America, Central America and South America from Sigma-Tau Pharmaceuticals, Inc., or Sigma-Tau, in 2014. In exchange for these rights, 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 final payment of $150.0 million upon FDA approval of defibrotide for VOD, paid in the second quarter of 2016.

We launched defibrotide in Canada in 2017. In October 2018, Nippon Shinyaku Co., Ltd., the partner to whom we have granted exclusive rights to develop and commercialize defibrotide in Japan, announced that it had filed an NDA for defibrotide with Japan’s Ministry of Health, Labour and Welfare.

We are also developing defibrotide for other potential indications. For more information regarding defibrotide development activities, see “Business—Research and Development” in this Part I, Item 1.

In 2018, Defitelio/defibrotide product sales were $149.4 million, which represented 8% of our total net product sales.

Vyxeos

Vyxeos is a liposome formulation of a fixed ratio combination of daunorubicin and cytarabine for intravenous infusion that is indicated for the treatment of adults with newly-diagnosed t-AML or AML-MRC and has been shown to have synergistic effects at killing leukemia cells in vitro and in animal models. Vyxeos is the first drug delivery combination product based on our CombiPlex technology platform to be approved by the FDA and the EC.

AML is a rapidly progressing and life-threatening blood cancer that begins in the bone marrow, which produces most of the body's new blood cells. AML cells crowd out healthy cells and move aggressively into the bloodstream to spread cancer to other parts of the body. AML is a relatively rare disease representing about 1% of all new cancer cases and has the lowest survival rate of any form of leukemia. Patients with newly diagnosed t-AML or AML-MRC may have a particularly poor prognosis.

In 2017, we launched Vyxeos in the U.S. after the FDA approved our NDA for the treatment of adults with newly-diagnosed t-AML or AML-MRC. In August 2018, the EC granted marketing authorization for Vyxeos, and, shortly thereafter, we commenced a rolling launch of Vyxeos in the European Union, or EU.

For more information regarding our CombiPlex technology platform and Vyxeos development activities, see “Business—Research and Development” in this Part I, Item 1.

In 2018, Vyxeos product sales were $100.8 million, which represented 5% of our total net product sales.

Other Products

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

In September 2018, we sold substantially all of the assets held by us related to Prialt® (ziconotide) intrathecal infusion to TerSera Therapeutics LLC.

Research and Development

A key aspect of our growth strategy is continued investment in our evolving and expanding research and development pipeline. We actively explore innovative product candidates ranging from small molecules to biologics. While we are primarily focused on opportunities within our sleep and hematology/oncology therapeutic areas, we are also interested in and exploring adjacent therapeutic areas, including central nervous system disorders and solid tumors.

Our development activities encompass all stages of development and currently include clinical testing of new product candidates and activities related to clinical improvements of, or additional indications or new clinical data for, our

commercialized products. We have also recently expanded into preclinical exploration of novel therapies, including precision medicines in hematology and oncology. We conduct most of these activities by leveraging our growing internal research and development function, but we have also entered into collaborations with third parties for the research and development of early-

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stage product candidates and have supported third parties seeking to perform clinical studies that will generate additional data related to our marketed products. We also seek out investment opportunities in support of development of early-stage technologies in our therapeutic areas and adjacencies.

Our current and planned development activities in our sleep therapeutic area are primarily focused on two product candidates, solriamfetol and JZP-258.

Solriamfetol. Solriamfetol is a small molecule new chemical entity being developed for potential treatment of EDS in several disorders and conditions, including OSA and narcolepsy. The FDA accepted our solriamfetol NDA for filing with a standard review in early 2018, and the current PDUFA goal date is March 20, 2019. We submitted a solriamfetol MAA to the EMA in the fourth quarter of 2018. We also recently conducted a Phase 2 clinical trial of solriamfetol in patients with EDS associated with Parkinson's disease and are evaluating future pipeline expansion opportunities in other disorders and conditions, as well as opportunities for geographic expansion. We acquired worldwide development, manufacturing and commercial rights to solriamfetol from Aerial BioPharma LLC, or Aerial, in 2014, other than in certain jurisdictions in Asia where SK Biopharmaceuticals Co., Ltd, or SK, retains rights.

JZP-258. JZP-258 is an oxybate product candidate that contains 90% less sodium than Xyrem and is being developed for the potential treatment of both cataplexy and EDS in patients with narcolepsy and potential treatment of idiopathic hypersomnia, or IH, a chronic neurological disorder that is primarily characterized by EDS. Given the well-accepted relationship between dietary sodium and blood pressure as well as published hypertension guidelines underscoring that excessive consumption of sodium is independently associated with an increased risk of stroke, cardiovascular disease and other adverse outcomes, we believe that lower sodium intake would be beneficial for patients and therefore JZP-258 would offer a clinically meaningful benefit to patients compared to Xyrem. We have conducted a Phase 3 clinical trial of JZP-258 in patients for the treatment of both cataplexy and EDS in narcolepsy and, subject to the results of our Phase 3 clinical trial, we expect to submit an NDA by as early as the end of 2019. We are conducting a Phase 3 clinical trial for the treatment of IH, which currently has no approved therapies in the U.S. We are also pursuing early-stage activities related to the potential development of an extended release oxybate formulation that we believe could provide a clinically meaningful option for some narcolepsy patients.

Our current and planned development activities in our hematology/oncology therapeutic area are focused on exploring additional indications for Defitelio and Vyxeos, generating additional clinical data for Vyxeos, including in combination with other therapeutic agents, and the research and development of new product candidates.

Defitelio. Our Defitelio clinical development strategy generally focuses on the prevention and treatment of serious diseases associated with endothelial cell damage. In addition to clinical trials we are sponsoring, there are more than 20 investigator-sponsored trials ongoing in the U.S. and EU to evaluate defibrotide in multiple conditions.

Vyxeos. Our Vyxeos clinical development strategy is designed to target potential new patient segments across the AML landscape, to pursue indications related to myelodysplastic syndrome, or MDS, and to generate clinical data on Vyxeos when used in combination with other therapeutic agents. As reflected in the table below, we are pursuing this strategy by sponsoring clinical trials, working with cooperative groups who are conducting clinical trials, and partnering with The University of Texas MD Anderson Cancer Center, or MD Anderson. In August 2018, we announced a five-year collaboration with MD Anderson to evaluate potential treatment options for hematologic malignancies, with a near-term focus on Vyxeos, and shortly thereafter, commenced development activities under this collaboration. In addition, there are multiple ongoing investigator-sponsored trials studying Vyxeos.

CombiPlex Platform. We are also evaluating the use of our CombiPlex delivery technology platform in a number of therapeutic combinations in oncology as part of our internal oncology research and development activities. CombiPlex enables the design and rapid evaluation of various combinations of therapies to deliver enhanced anti-cancer activity by identifying an optimal synergistic ratio of drugs in vitro and fixing this ratio in a nanoscale delivery complex that maintains and then coordinates the release of the synergistic combination after administration. CombiPlex utilizes two proprietary nanoscale delivery platforms: liposomes to control the release and distribution of water-soluble drugs and drugs that are both water- and fat-soluble (amphipathic), and nanoparticles to control the release and distribution of non-water-soluble (hydrophobic) drugs. We are conducting preclinical activities using our CombiPlex platform to develop a novel combination of therapeutic agents that are designed to target an undisclosed solid tumor candidate, as

well as other hematology/oncology exploratory activities.

Through third parties, we are also pursuing preclinical and clinical research and development activities in hematology and in precision oncology under a number of licensing and collaboration agreements, including with:

- ImmunoGen, Inc., or ImmunoGen, for opt-in rights to license two hematology-related antibody-drug conjugate, or ADC, product candidates granted orphan drug designation by the FDA, as well as an additional ADC product candidate;

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- Codiak BioSciences, Inc., or Codiak, for an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize potential therapeutic candidates directed at five targets to be developed using Codiak's engEx™ precision engineering platform for exosome therapeutics;
- Pfenex, Inc., or Pfenex, for rights to multiple early-stage hematology product candidates and an option to negotiate a license for a recombinant pegaspargase product candidate; and
- XL-protein GmbH, or XLp, for rights to use XLp's PASylation® technology to extend the plasma half-life of selected asparaginase product candidates.

Below is a summary of ongoing and planned development projects related to our products and pipeline and their corresponding current stages of development:

Sleep	
Product Candidates	Description
Submitted for Regulatory Approval	
Solriamfetol U.S.	EDS in OSA and EDS in narcolepsy
Solriamfetol EU	EDS in OSA and EDS in narcolepsy
In Phase 3	
JZP-258 (oxybate; 90% sodium reduction)	Cataplexy and EDS in narcolepsy
JZP-258 (oxybate; 90% sodium reduction)	IH
In Phase 2	
Solriamfetol	EDS in Parkinson's disease
Preclinical	
Oxybate once-nightly formulation	Narcolepsy

Hematology/Oncology	
Product Candidates	Description
In Phase 3	
Defitelio	Prevention of VOD in high-risk patients following HSCT
Vyxeos	AML or high-risk MDS (AML19) (cooperative group study)
Vyxeos	AML or high-risk MDS (AML18) (cooperative group study)
In Phase 2	
Defitelio	Prevention of aGvHD following allogeneic HSCT
Defitelio	Treatment of TA-TMA (planned pivotal study)
Defitelio	Prevention of chimeric antigen receptor T-cell therapy-, or CAR-T-, associated neurotoxicity (planned study)
Vyxeos + venetoclax	De novo or relapsed/refractory, or R/R, AML (MD Anderson collaboration study)
Vyxeos	MDS (planned cooperative group study)
Vyxeos	R/R AML (cooperative group study)
In Phase 1	
Vyxeos + gemtuzumab	R/R AML or hypomethylating agent failure MDS (MD Anderson collaboration study)
Vyxeos + venetoclax	Low intensity dosing for unfit AML (planned study)
IMGN779	CD33+ AML (Jazz opt-in opportunity with ImmunoGen)
IMGN632	CD123+ hematological malignancies (Jazz opt-in opportunity with ImmunoGen)
Preclinical	
CombiPlex	Solid tumors candidate I

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Product Candidates	Description
CombiPlex	Hematology/oncology exploratory activities
Asparaginase	ALL and other hematological malignancies
Recombinant Pegaspargase	Hematological malignancies (Jazz opt-in opportunity with Pfenex)
Defitelio	Exploratory activities
Exosome NRAS candidate	Hematological malignancies (collaboration with Codiak)
Exosome STAT3 candidate	Hematological malignancies (collaboration with Codiak)
Exosome-based candidates	Solid tumors/hematological malignancies (collaboration with Codiak)

In 2019 and beyond, we expect that our research and development expenses will continue to increase from historical levels, particularly as we prepare for anticipated regulatory submissions and trial data read-outs, initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates.

Sales and Marketing

We have commercial operations primarily in the U.S., Europe and Canada. In the U.S., our products are marketed through our commercial teams, including experienced sales professionals who promote Xyrem, Erwinaze, Defitelio and Vyxeos directly to physicians in specialties appropriate for each product.

In Canada and in approved markets in Europe where we commercialize Erwinaze, Defitelio and Vyxeos, we have a field force of hematology field specialists comprised of sales personnel and medical affairs personnel. In markets where these products either are not approved or are unable to be promoted under local regulation, we have medical science liaisons and medical directors responsible for responding to medical information requests and for providing information consistent with local treatment protocols with respect to such products. Outside the U.S., we directly market Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. We also utilize distributors in certain markets outside the U.S. where we do not market our products directly.

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 also provide reimbursement support for our U.S. markets.

Although we have a relatively small number of sales representatives compared with most other pharmaceutical companies with marketed products, we believe that the size of our sales force is appropriate to effectively reach our target audience in the specialty markets in which we currently operate. We promote Defitelio, Erwinaze and Vyxeos 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, including potentially solriamfetol, may require further expansion of our sales force and sales support organization in the U.S. and internationally.

Competition

The biopharmaceutical industry is highly competitive. Our products compete, and our product candidates may in the future compete, with currently existing therapies, product candidates currently under development by others and/or future product candidates, including new chemical entities that may turn out to be safer or more effective than our products. Any products that we develop may be commercialized in competitive markets, and our competitors, which include large global pharmaceutical companies and small research-based companies and institutions, may succeed in developing products that render our products obsolete or noncompetitive.

We also face competition, and may in the future face additional competition, from manufacturers of generic drugs. 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 when a generic version is available. Generic competition often results in decreases in the prices at which branded products can be sold.

In particular, our products and most advanced product candidates face or may face competition as described below:

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Xyrem. While Xyrem is currently the only product approved by the FDA and marketed in the U.S. for the treatment of both cataplexy and EDS in patients with narcolepsy, we and others may launch products as treatment options in cataplexy and/or EDS in narcolepsy, including other branded sodium oxybate products and other new and existing branded market entrants. In addition, Xyrem will face competition from generics and authorized generics.

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Nine companies have filed abbreviated NDAs, or ANDAs, with the FDA seeking to market generic versions of Xyrem, and we have settled patent litigation against all of them. To date, the FDA has approved or tentatively approved three of these ANDAs, and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs. Under the settlement agreements with the nine ANDA filers, (i) we granted the first ANDA filer, West-Ward Pharmaceuticals Corp. (a wholly owned subsidiary of Hikma Pharmaceuticals PLC) the right to sell an authorized generic version of Xyrem, or AG Product, in the U.S. beginning on January 1, 2023, or earlier under certain circumstances, and a license to launch its own generic sodium oxybate product as early as six months after it has the right to sell the AG Product, unless it elects to continue to sell the AG Product, which it may do for up to a total of five years; (ii) we granted each of three of the other ANDA filers the right to sell a limited volume of an AG Product in the U.S. beginning on July 1, 2023, or earlier under certain circumstances, and a license to launch its own generic sodium oxybate product on or after December 31, 2025, or earlier under certain circumstances; and (iii) we granted each of the five other ANDA filers a license to launch its own generic sodium oxybate product on or after December 31, 2025, or earlier under certain circumstances. We will receive royalties on sales of the AG products. The actual timing of the launch of an AG Product or generic sodium oxybate product is uncertain because the launch dates of the AG Products and generic sodium oxybate products under our ANDA litigation settlement agreements are subject to acceleration under certain circumstances. For a further description of the settlement agreements, including a more complete description of circumstances that might trigger acceleration of such dates, see the risk factor under the heading “The introduction of a new product in the U.S. market that competes with, or otherwise disrupts the market for, Xyrem would adversely affect sales of Xyrem” in Part I, Item 1A of this Annual Report on Form 10-K.

Avadel Pharmaceuticals plc, or Avadel, is conducting a Phase 3 clinical trial of a once-nightly formula of sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy. Avadel has indicated that it intends to seek approval using an NDA approval pathway under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, by referencing Xyrem and relying, to some degree, on the FDA’s approval of Xyrem and related determinations of safety and efficacy. Other companies may develop a sodium oxybate or similar product using, for example, an alternative formulation or a different delivery technology, and seek approval in the U.S. under Section 505(b)(2) or otherwise. For a further description of the approval process for ANDAs and NDAs under the FDA’s Section 505(b)(2) approval pathway, see “Business—Government Regulation—Marketing Exclusivity—The Hatch-Waxman Act” in this Part I, Item 1.

Although Xyrem is currently the only approved treatment for EDS and cataplexy associated with narcolepsy, we are aware that prescribers often prescribe branded or generic medications for these conditions before prescribing or instead of prescribing Xyrem, and that payors often require patients to try such medications before they will cover Xyrem. For example, prescribers often treat mild cataplexy with drugs that have not been approved by the FDA for that indication, including tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors. In addition, we are aware that Harmony Biosciences LLC, or Harmony, has exclusive U.S. rights to seek approval of and commercialize pitolisant, a wake-promoting drug that has already been approved in Europe to treat adult patients with narcolepsy with or without cataplexy. Published data and prescribing patterns in the EU suggest that pitolisant would likely be appropriately used in patients with less severe cataplexy than those treated with Xyrem. While pitolisant is not currently approved in the U.S., Harmony has established an expanded access program for pitolisant, received Breakthrough Therapy and Fast Track designations from the FDA and, in February 2019, announced that the FDA had accepted for filing with priority review its pitolisant NDA. We are also aware that branded or generic stimulants may be prescribed off label for treatment of EDS in narcolepsy. Wake-promoting agents Provigil® (modafinil) and Nuvigil® (armodafinil), and their generic equivalents, are labeled for treatment of EDS in narcolepsy and other conditions, and may be used in conjunction with or instead of Xyrem. It is possible that additional branded or generic products may be introduced to treat symptoms of narcolepsy that will similarly be prescribed before or instead of Xyrem, or that payors will require patients to try before they will cover Xyrem.

- 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. Some new asparaginase treatments 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, including some for the treatment of relapsed or refractory ALL patients. We have experienced frequent intermittent shortages of the product, as described in “Business—Manufacturing” in this Part I, Item 1, that have impacted prescribing habits for Erwinaze, including prescribers’ use of alternate methods to address hypersensitivity reactions. The development of these new treatments could negatively impact our ability to grow sales of Erwinaze in patient populations where the benefit of an asparaginase-containing regimen is not well established. As a biologic product, Erwinaze also faces potential competition from biosimilar products.

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- 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. There are a number of alternative established and recently introduced therapies in AML. A key consideration in the treatment of AML patients is the patient's suitability for chemotherapy. The AML patient population studied in the Vyxeos Phase 3 clinical trial supporting our NDA included fit patients, or those deemed able to tolerate intensive induction chemotherapy. The existing options for the treatment of newly-diagnosed t-AML and AML-MRC in fit patients include cytarabine in combination with an anthracycline (i.e., daunorubicin), known as 7+3. In addition, we are aware of several other products that have been recently approved by the FDA or are in development as treatment options for newly diagnosed AML patients eligible for intensive chemotherapy, such as targeted agents (e.g. midostaurin, enasidenib and ivosidenib), immunotherapies (e.g., gemtuzumab ozogamicin and CAR-T cell therapy), and agents disrupting leukemia cell survival (e.g., glasdegib). We are also aware of the use of venetoclax, an AML treatment recently approved by the FDA. Some of the patient populations being studied for, or treated by, these products overlap with the patient population studied in the Vyxeos Phase 3 clinical trial supporting our NDA. The existence of established treatment options and the development of competing products for the treatment of newly-diagnosed t-AML or AML-MRC could negatively impact our ability to successfully commercialize Vyxeos and achieve the level of sales we expect.
- Solriamfetol. As discussed above, other branded and generic products used to treat EDS in patients with narcolepsy include stimulants, wake-promoting agents such as Provigil and Nuvigil, and generic versions of stimulants and wake-promoting agents. We are also aware that stimulants and wake-promoting agents are prescribed for patients who have OSA. Solriamfetol, if approved by the FDA, will likely face competition from this genericized market. In addition, we are aware of several other products in development to treat excessive sleepiness in patients with narcolepsy or OSA, including, for example, pitolisant, mazindol, modafinil combinations and Avadel's once-nightly sodium oxybate formulation.

An important part of our corporate strategy is to build a diversified product pipeline, including by acquiring or in-licensing and developing additional products and product candidates that we believe are highly differentiated and have significant commercial potential. Our ability to continue to grow our product portfolio requires that we compete successfully with other pharmaceutical companies to acquire or in-license products and product candidates. These competitors include established companies that may have a competitive advantage over us due to their size and financial resources.

For more information on the competitive risks we face generally, see the risk factors under the headings "We face substantial competition from other companies, including companies with larger sales organizations and more experience working with large and diverse product portfolios" and "We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these acquisitions" in Part I, Item 1A of this Annual Report on Form 10-K.

Customers

In the U.S., our lead marketed product, Xyrem, is sold to one specialty pharmacy, a subsidiary of Express Scripts, which ships Xyrem directly to patients. Erwinaze, Defitelio and Vyxeos are sold to hospital customers through subsidiary specialty distributors of McKesson Corporation, or McKesson. We have distribution services agreements made in the ordinary course of business with McKesson and a pharmacy services agreement with Express Scripts that provides for the distribution of Xyrem to patients. For more information regarding our relationship with Express

Scripts, see “Business—Our Commercialized Products” in this Part I, Item 1. Purchases are made on a purchase order basis.

In certain countries in Europe, Erwinase, Defitelio and Vyxeos are sold pursuant to marketing authorizations. We distribute these products through Durbin PLC, a UK-based wholesaler and distributor, and O&M Movianto Nederland BV, our centralized European logistics services provider, to hospitals and local wholesalers in Europe where we market these products directly and, in other markets in Europe and elsewhere where we do not market these products directly, to local distributors and wholesalers. In countries where there is no marketing authorization, Erwinase, Defitelio and Vyxeos are sold pursuant to named patient programs, temporary use authorizations or similar authorizations.

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We directly market Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. Xyrem is also sold in 21 countries by UCB Pharma Limited, or UCB (which has rights to market Xyrem in 54 countries).
Information on our total revenues by product and revenues attributed to customers who represented at least 10% of our total revenues in each of 2018, 2017 and 2016 is included in Note 17, Revenues of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

Manufacturing
We have a manufacturing and development facility in Athlone, Ireland where we manufacture Xyrem and development-stage oxybate product candidates, including JZP-258. We also have a manufacturing plant in Italy where we produce the defibrotide drug substance. Other than these two facilities, we currently do not have our own commercial manufacturing capability for our products and product candidates or their APIs. As a result, our ability to develop and supply products in a timely and competitive manner depends primarily on our third party suppliers, in most cases single source suppliers, being able to meet our ongoing commercial and clinical trial needs.
Lead Marketed Products
Xyrem. Xyrem is manufactured by us in our Athlone facility and by Patheon Pharmaceuticals Inc., which we refer to together with its affiliates as Patheon, under a Master Manufacturing Services Agreement, or the Patheon Agreement, entered into with Patheon in 2015. The Patheon Agreement establishes the general terms and conditions pursuant to which Patheon provides manufacturing services for multiple drug products, including Xyrem, as specified by us in product agreements we enter into from time to time. Although we manufacture Xyrem in our Athlone facility, we expect to rely on Patheon as our sole U.S.-based supplier of Xyrem for the foreseeable future. However, we are not required to purchase Xyrem exclusively from Patheon. The Patheon 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 Patheon Agreement for any reason upon 12 months' prior written notice, and each party has the right to terminate the agreement in the event of the other party's uncured material breach.
Siegfried USA, LLC, or Siegfried, supplies sodium oxybate, the API of Xyrem, to Patheon and, through a Siegfried affiliate in Europe, to our Athlone 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, entered into in 2010, 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. Each party also 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.
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. As a result, its manufacturing and distribution are highly restricted. Quotas from the DEA are required in order to manufacture and package sodium oxybate and Xyrem in the U.S. For information related to DEA quota requirements, see "Business—Government Regulation—Other Post-Approval Pharmaceutical Product Regulation—Controlled Substance Regulations" in this Part I, Item 1.
Erwinaze. Erwinaze is exclusively licensed to us, and manufactured for us, by PBL, a company that is wholly owned by the UK Secretary of State for Health. PBL is our sole supplier for Erwinaze. Our license and supply agreement with PBL, which includes our license for Erwinaze, expires on December 31, 2020. For information related to our agreement with PBL, see "Business—Our Commercialized Products—Erwinaze" in this Part I, Item 1. 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.
A continuing and significant challenge to maintaining sales of Erwinaze and a barrier to increasing sales is PBL's inability to consistently supply product adequate to meet market demand. All Erwinaze that PBL has been able to

supply is currently completely absorbed by demand for the product. In addition, PBL is subject to a January 2017 warning letter issued by the FDA citing significant violations of the FDA's current Good Manufacturing Practices, or cGMP, as well as an inspection report from the UK Medicines and Healthcare Products Regulatory Agency, or MHRA, listing several major findings, including major deficiencies and failures by PBL to comply with cGMP. PBL's product quality and manufacturing issues have resulted, and continue to result, in disruptions in our ability to supply markets from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions during 2019. These supply disruptions will continue to adversely impact our ability to generate sales of and revenues from Erwinaze and our business, financial condition,

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results of operations and growth prospects could be materially adversely affected. For a more complete description of supply issues related to Erwinaze, see the risk factor under the heading "Delays or problems in the supply of our products for sale or our for use in clinical trials, loss of our single source suppliers or 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 from porcine DNA 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 the Patheon Agreement. Patheon is the sole provider of our commercial and clinical supply of Defitelio; however, we are not required to purchase Defitelio exclusively from Patheon. 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.

Vyxeos. Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location, using our CombiPlex technology platform. 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. There have been batch failures at Baxter due to mechanical, component and other issues, and batches have been produced that have otherwise not been in compliance with applicable specifications. We are continuing to work with Baxter to address manufacturing complexities. Our manufacturing agreement with Baxter expires in August 2022, subject to automatic three-year renewal terms, unless terminated by either party 24 months prior to the end of the initial term or any renewal term. Each party has the right to terminate the agreement for breach, subject to customary cure periods, and each party may terminate the agreement immediately in the event of the other party's insolvency. While other contract manufacturers may be able to produce Vyxeos, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. The marketing authorization in the EU for Vyxeos also requires us to comply with certain manufacturing-related post-approval commitments.

Product Candidates

Siegfried has supplied us with both the API and finished product for our development activities involving solriamfetol. We expect that Siegfried will manufacture and supply solriamfetol for commercial sale if solriamfetol receives regulatory approval and that, in the short term, Siegfried will be the sole provider of our commercial supply of solriamfetol. We also expect that solriamfetol, if approved, will be subject to scheduling by the DEA after NDA approval.

JZP-258 is currently manufactured at our Athlone facility, and we expect to manufacture this product commercially at our Athlone facility should this candidate proceed through development and receive regulatory approval.

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 "Delays or problems in the supply of our products for sale or our for use in clinical trials, loss of our single source suppliers or 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 product candidates 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, used 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. In addition to patents, our products and product candidates are in some instances protected by various marketing exclusivities. For a description of those exclusivities and their regulatory background, see “Business—Government Regulation—Marketing Exclusivity—The Hatch-Waxman Act” in this Part I, Item 1 and in the risk factor under the heading “It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection” in Part I, Item 1A of this Annual Report on Form 10-K.

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The patents, patent applications and marketing exclusivities that relate to our marketed products and product candidates include:

- Xyrem. We currently have 16 issued patents in the U.S. relating to Xyrem that expire at various times from December 2019 to September 2033. All but four of these patents are listed in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Our patents relate to Xyrem's stable and microbially resistant formulation, its manufacturing process, its method of use, including its restricted distribution system, its method of administration, and a drug-drug interaction, or DDI, between Xyrem and divalproex sodium. In October 2018, as a result of the FDA's grant of pediatric exclusivity, an additional six months was added to the expiration dates of all of our Orange Book-listed patents that have not been invalidated.

  Our Xyrem patents have been subject to patent litigation with the companies who filed ANDAs seeking to market a generic version of Xyrem, including challenge through the inter partes review procedures of the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO. In July 2018, the United States Court of Appeals for the Federal Circuit upheld on appeal PTAB decisions finding that six patents associated with the Xyrem REMS and three claims of a seventh REMS patent are unpatentable. As a result, we will not be able to enforce patents or claims that the PTAB found unpatentable. Although we have settled all patent litigation against the nine companies that filed ANDAs, it is possible that additional companies may challenge our U.S. patents for Xyrem in the future. For a description of our Xyrem settlements, see the risk factor under the heading "Risks Related to Xyrem and Our Other Marketed Products" in Part I, Item 1A of this Annual Report on Form 10-K.

  A Xyrem formulation patent has issued in multiple non-U.S. countries and will expire in December 2019. The European Patent Office has issued a method of administration patent relating to the DDI between Xyrem and divalproex sodium that will expire in February 2034. Those patents are licensed to UCB as the marketing authorization holder outside of the U.S. and Canada, and UCB has the right to enforce them. In addition to our issued patents, we have patent applications relating to Xyrem pending in the U.S. and other countries.

- Erwinaze. Erwinaze has no patent protection. It had been granted orphan drug exclusivity by the FDA 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. 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 U.S. and non-U.S. patents and patent applications relating to various compositions, methods of use and methods of characterization, expiring at various times between June 2019 and November 2035. None of these patents are listed in the Orange Book. Defibrotide has been granted orphan drug exclusivity by the FDA to treat and prevent VOD until March 2023. Defibrotide has also been granted orphan drug designation by the EC and the Korean Ministry of Food and Drug Safety to treat and prevent VOD, by the Commonwealth of Australia-Department of Health for the treatment of VOD and by the EC for the prevention of aGvHD.

- Vyxeos. We have a portfolio of U.S. and non-U.S. patents and patent applications for Vyxeos and the CombiPlex technology platform relating to various compositions and methods of making and use. These include six U.S. patents covering Vyxeos compositions and methods of use expiring between April 2025 and September 2034 and two U.S. patents covering CombiPlex (which also cover Vyxeos) expiring in January 2027. These patents are listed, or in the process of being listed, in the Orange Book. Vyxeos has been granted orphan drug exclusivity by the FDA until August 2024, seven years from its FDA approval, for the treatment of adults with newly-diagnosed t-AML or AML-MRC. In addition, Vyxeos has been granted orphan drug designation by the EC until August 2028, ten years from its EC approval for the treatment of adults with newly-diagnosed t-AML or AML-MRC.

- Solriamfetol. We acquired rights to solriamfetol from Aerial in 2014, including Aerial's patent rights relating to solriamfetol, other than in certain jurisdictions in Asia where SK retains rights. We have a portfolio of U.S. and non-U.S. patents and patent applications for solriamfetol relating to various compositions, formulations and methods of use. Three of our U.S. patents are method of use patents covering treatment of sleep-related conditions expiring between June 2026 and August 2027. A fourth U.S. patent covers the formulation of solriamfetol and expires in

September 2037. We are entitled to apply for a patent term extension for one of these patents.

- JZP-258. We expect that certain patents and patent applications relating to Xyrem will cover our product candidate JZP-258. There are also five additional U.S. patents that will expire in January 2033 covering the formulation and method of making for JZP-258.

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.

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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. For further discussion of the challenges we face in obtaining or maintaining patent and/or trade secret protection, 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.

Government Regulation

As a global pharmaceutical company, our activities are subject to extensive regulation in the U.S., the EU and other countries where we do business. Regulatory requirements encompass the entire life cycle of pharmaceutical products, from research and development activities to marketing approval, manufacturing, labeling, packaging, adverse event and safety reporting, storage, advertising, promotion, sale, pricing and reimbursement, recordkeeping, distribution, importing and exporting. Regulations differ from country to country and are constantly evolving.

Testing and Approval of Pharmaceutical Products

We are not permitted to market a product in a country until we receive approval from the relevant regulatory authority, such as the FDA in the U.S. and the EC or the competent authorities of the EU member states. An application for marketing approval must contain information generated by the applicant, also called a sponsor, demonstrating the quality, safety and efficacy of the product candidate, including data from preclinical and clinical trials, proposed product packaging and labeling and information pertaining to product formulation and the manufacture and analytical testing of the API and the finished product.

In the U.S., the FDA reviews and, if warranted, approves applications for marketing approval. The process for obtaining marketing approval in the U.S. for a drug or biologic product candidate generally includes:

- conducting preclinical laboratory and animal testing and submitting the results to the FDA in an investigational new drug, or IND, application requesting approval to test the product candidate in human clinical trials;
- conducting adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate in the desired indication;
- submitting an NDA, supplemental NDA, or sNDA, or BLA, as appropriate, to the FDA seeking approval for a specific indication; and
- completing inspections by the FDA of the facilities where the product candidate is manufactured, analyzed and stored to demonstrate compliance with cGMP and any requested FDA audits of the clinical trial sites that generated the data supporting the application.

Human clinical trials conducted before approval of a product generally proceed in three sequential phases, although the phases may overlap. In Phase 1, the initial introduction of the product candidate in humans, the product candidate 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 product candidate for a particular indication or indications, dosage tolerance and optimum dosage and to identify common adverse effects and safety risks. If a product candidate 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. Clinical trials must be conducted in accordance with specific protocols, as well as FDA requirements related to conducting the trials and recording and reporting the results, commonly referred to as good clinical practices, to ensure that the resulting data are credible and accurate and that the trial participants are adequately protected. The FDA enforces good clinical practices through periodic inspections of trial sponsors, clinical investigators and trial sites.

Once an NDA, sNDA or BLA has been compiled and submitted, the FDA performs an initial review before it accepts the application for filing. The FDA may refuse to file an application and/or request additional information before acceptance. Once 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 PDUFA for a new molecular entity, the FDA has ten months from the filing decision in which to complete its initial review of a standard application and respond to the applicant, and eight months for a priority application. The FDA does not always meet its PDUFA goal dates, and in certain circumstances,

the PDUFA goal date may be extended. For example, in December 2018, the FDA determined that a submission we made during the course of discussions regarding draft labeling in solriamfetol constituted a major amendment to the NDA, resulting in a three-month extension of the PDUFA goal date to March 20, 2019.

The FDA also has 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, products 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. For example, the FDA granted Vyxeos

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Breakthrough Therapy and Fast Track designations and also granted Priority Review with respect to our NDA for Vyxeos for the treatment of t-AML and AML-MRC that was approved in August 2017. In addition, a priority review voucher, or PRV, such as the PRV that we acquired in May 2018, may be used to obtain priority review by the FDA for one of our future regulatory submissions.

During its review of an application, the FDA evaluates whether the product demonstrates the required level of safety and efficacy for the indication for which approval is sought and also conducts the inspections and audits described above. The FDA may also refer an application to an advisory committee, typically a panel of clinicians, for review, evaluation and a non-binding recommendation as to whether the application should be approved. When the FDA completes its evaluation, it issues either an approval letter or a complete response letter. A complete response letter generally outlines what the FDA considers to be the deficiencies in the application and may indicate that substantial additional testing or information is required in order for the FDA to approve the product. If and when identified deficiencies have been addressed to the FDA's satisfaction in a resubmission of the application, or if the decision is reversed through an administrative appeal, the FDA will issue an approval letter.

Even if a product is approved, the approval may be subject to limitations based on the FDA's interpretation of the data submitted in the application. For example, as a condition of approval, the FDA may require the sponsor to agree to certain post-marketing commitments, such as conducting Phase 4, or post-approval, clinical trials to gain additional safety data or to document a clinical benefit in the case of products approved under Accelerated Approval regulations. The FDA's approval of the BLA for Erwinaze includes a number of post-marketing commitments related to the manufacture of Erwinaze. Several post-marketing commitments and requirements were also mandated by the FDA in connection with its approvals of 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, and its approval of Vyxeos, including the requirement that we conduct a safety study to characterize infusion-related reactions in patients treated with Vyxeos and a clinical trial to determine dosing to minimize toxicity in patients with moderate and severe renal impairment.

In addition, if the FDA determines that a REMS is necessary to ensure that the benefits of the product outweigh the risks, a sponsor may be required to include a proposed REMS (either 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; or conditions on the product's prescribing or distribution referred to as elements to assure safe use. Xyrem is required to have a REMS. For more discussion regarding the Xyrem REMS, see the risk factors under the headings "The distribution and sale of Xyrem are subject to significant regulatory restrictions, including the requirements of a REMS, and these regulatory requirements subject us to 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.

The EU and many individual countries have regulatory structures similar to the U.S. for conducting preclinical and clinical testing and applying for marketing approval or authorization, although specifics may vary widely from country to country. Clinical trials in the EU must be conducted in accordance with the requirements of the EU Clinical Trials Directive, which may be replaced with the new EU Clinical Trials Regulation in 2019, and applicable good clinical practice standards. In the EU, there are several procedures for requesting marketing authorization which can be more efficient than applying for authorization on a country-by-country basis. There is a "centralized" procedure allowing submission of a single marketing authorization application to the EMA. If the EMA issues a positive opinion, the EC will grant a centralized marketing authorization that is valid in all EU member states and three of the four European Free Trade Association countries (Iceland, Liechtenstein and Norway). The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products and biotechnology-derived medicinal products, and optional for others. There is also a "decentralized" procedure allowing companies to file identical applications to several EU member states simultaneously for product candidates that have not yet been authorized in any EU member state and a "mutual recognition" procedure allowing companies that have a product already authorized in one EU member state to apply for that authorization to be recognized by the competent authorities in other EU member states. The UK's planned withdrawal from the EU, commonly referred to as Brexit, has created significant

uncertainty concerning the future relationship between the UK and the EU, and the impact on the process for obtaining or maintaining marketing authorization for pharmaceutical products manufactured or sold in the UK is unknown.

The maximum timeframe for the evaluation of an application in the EU under the centralized procedure is 210 days, subject to certain exceptions. An initial marketing authorization granted in the EU is valid for five years, with renewal subject to re-evaluation of the risk-benefit profile of the product. Once renewed, the authorization is usually valid for an unlimited period unless the national competent authority or the EC decides on justified grounds to proceed with one additional five-year renewal.

In the EU, if an applicant 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, products may be granted marketing authorization “under exceptional circumstances”. A marketing authorization granted under exceptional

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circumstances is valid for five years, subject to an annual reassessment of conditions imposed by the EC. The marketing authorization in the EU for Defitelio was granted 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. As a result, the marketing authorization requires us to comply with a number of post-marketing obligations, including obligations relating to the manufacture 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 to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use. We are in the process of conducting the post-authorization study in the EU to provide further data on long-term safety, health outcomes and patterns of utilization of Defitelio in normal use.

Similar to the use of REMS in the U.S. to ensure that the benefits of a product outweigh its risks, in the EU and other countries we may be required to agree to post-marketing obligations in the marketing authorization for our products, to include a patient package insert or a medication guide to provide information to consumers about the product's risks and benefits, to implement a plan for communication to healthcare providers, and to impose restrictions on the product's distribution. For example, the marketing authorization in the EU for Vyxeos requires us to comply with certain manufacturing-related post-approval commitments.

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 to demonstrate that the product is safe and effective for the new intended use. Such regulatory reviews can result in denial or modification of the planned changes, or requirements to conduct additional tests or evaluations that can substantially delay or increase the cost of the planned changes.

Manufacture of Pharmaceutical Products

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 the third party suppliers of our products are subject to cGMP, which are extensive regulations governing manufacturing processes, stability testing, recordkeeping and quality standards as defined by the FDA, the EC, the EMA, competent authorities of EU member states and other regulatory authorities. The FDA also periodically inspects manufacturing facilities and the sponsor's and manufacturer's records related to manufacturing, and assesses compliance with cGMP. Following such inspections, the FDA may issue notices on Form FDA 483 and warning letters. For example, the FDA issued a warning letter to PBL, our Erwinaze manufacturer, in January 2017 indicating that it was not satisfied with PBL's responses to a Form 483 issued to PBL and citing significant violations of cGMP for finished pharmaceuticals and significant deviations from cGMP for APIs. As recently as August 2018, the FDA conducted an inspection of the PBL manufacturing facility and issued an FDA Form 483 to PBL citing observations related to items referenced in the existing warning letter as well as other manufacturing practices, including data and records management. 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 the EU, a manufacturing authorization is required to manufacture medicinal products, and the manufacturing authorization holder must comply with various requirements set out in applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing products and their APIs, including APIs manufactured outside of the EU with the intention of importing them into the EU. In this regard, in the UK, where PBL's manufacturing facilities are located, PBL is subject to inspections conducted by the MHRA. Following a site inspection of PBL by the MHRA in December 2017, MHRA issued an inspection report listing several major findings, including major deficiencies and failures by PBL to comply with cGMP. In addition to inspection reports, manufacturers and marketing authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in cases of non-compliance with the

EU or EU member states' requirements applicable to manufacturing.

Sales and Marketing of Pharmaceutical Products

Advertising and Promotional Activities

The FDA regulates advertising and promotional activities for products in the U.S., requiring advertising, promotional materials and 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 actively investigates allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. The FDA routinely issues informal and more formal communications such as untitled letters or warning letters interpreting its authority over these matters. While such communications may not be considered final agency decisions, many companies may decide not to contest the agency's

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interpretations so as to avoid disputes with the FDA, even if they believe the claims they were making to be truthful, not misleading and otherwise lawful.

In the EU, the advertising and promotion of our products are subject to laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. For example, applicable 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 in connection with a marketing authorization approval. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU. Other applicable laws at the EU level and in the individual EU member states also apply to the advertising and promotion of medicinal products, including laws that prohibit the direct-to-consumer advertising of prescription-only medicinal products and further limit or restrict the advertising and promotion of our products to the general public and to health care professionals. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment.

Anti-Fraud and Abuse

We are also subject to numerous anti-fraud and abuse laws and regulations globally. In the U.S., there are a variety of federal and state laws restricting certain marketing practices in the pharmaceutical industry pertaining to healthcare fraud and abuse, including anti-kickback laws and false claims laws. Our sales, marketing, patient support and medical activities may be subject to scrutiny under these laws. The U.S. federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving anything of value to induce (or in return for) the referral of business, including the purchase or prescription of a particular drug reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and patients, prescribers, purchasers and formulary managers on the other. 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 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 government may assert that a claim resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim. 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 are subject to regulatory revision or changes in interpretation by the U.S Department of Justice, or DOJ, and the Office of Inspector General of the U.S. Department of Health and Human Services, or OIG. Practices or arrangements that involve remuneration may be subject to scrutiny if they do not qualify for an exemption or safe harbor. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of themselves and the federal government alleging violations of the statute and to share in any monetary recovery. Violations of the False Claims Act may result in significant financial penalties (on a per claim or statement basis), treble damages and exclusion from participation in federal health care programs.

Pharmaceutical companies are subject to other federal false claim and statements laws, some of which extend to non-government health benefit programs. For example, the healthcare fraud provisions 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, impose criminal liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program, including private third party payors, or falsifying or covering up a material fact or making any materially false or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. The majority of individual 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.

Other Post-Approval Pharmaceutical Product Regulation

Safety Reporting/Pharmacovigilance

The FDA, the EMA and other governmental authorities track information on side effects and adverse events reported during clinical studies and after marketing approval. We are required to file periodic safety update reports with the authorities concerning adverse events. If, upon review, an authority determines that any events and/or reports indicate a trend or signal, they can require a change in a product label, restrict sales and marketing, require post-approval safety studies, require a labor intensive collection of data regarding the risks and benefits of marketed products and ongoing assessments of those risks and benefits and/or require or conduct other actions, potentially including withdrawal or suspension of the product from the market. For example, if the EMA has concerns that the risk-benefit profile of a product has changed, it can adopt an opinion advising that the existing marketing authorization for the product be varied and requiring the marketing authorization holder to conduct

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post-authorization safety studies. The opinion is then submitted for approval by the EC. Also, from time to time, the FDA issues drug safety communications on its adverse event reporting system based on its review of reported adverse events.

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. An FDA Form 483 notice, if issued, 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 a warning letter or other regulatory enforcement action. Similarly, the EMA's Pharmacovigilance Risk Assessment Committee may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps. Non-compliance in all cases can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Sunshine Act and Transparency Laws

The Physician Payment Sunshine Act requires extensive tracking of payments and transfers of value to physicians and teaching hospitals and ownership interests held by physicians and their families, and provides for reporting to the federal government and public disclosure of these data. Beginning in 2022, reporting will also be required of information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. 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. Government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports. Other states restrict when pharmaceutical companies may provide meals to prescribers or engage in other marketing-related activities.

Outside the U.S., 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. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products, which is prohibited in the EU, is governed by the national anti-bribery laws of the EU member states, as described below in "Business—Government Regulation—Anti-Corruption Legislation" in this Part I, Item 1. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states require that payments made to physicians 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.

Controlled Substance Regulations

A drug product approved by the FDA may 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 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. The active ingredient of Xyrem, sodium oxybate, is regulated by the DEA as a Schedule I controlled substance. Xyrem, as an FDA-approved drug product, is regulated as a Schedule III controlled substance. We expect that solriamfetol will be subject to scheduling under the CSA, which will need to be completed after any NDA approval and before commercial launch. Individual states also impose similar requirements for controlled substances.

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. Xyrem manufactured at our plant in Ireland enters the U.S. as a Schedule III drug and thus does not require a manufacturing quota.
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.

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Other Regulations

There are many other requirements and restrictions in the U.S. and elsewhere imposed on pharmaceutical companies and their activities, including those related to the posting of information relating to clinical studies and their outcomes, the export and importation of products, required authorizations for distributors, the identification or licensing of sales representatives, restrictions on the ability of manufacturers to offer co-pay support to patients for certain prescription drugs, implementation of required compliance programs or marketing codes of conduct, protection of the environment, taxation and work safety. Non-compliance with such requirements may result in civil, criminal or administrative sanctions.

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 UK Bribery Act of 2010, or the UK Bribery Act. The FCPA and similar anti-corruption laws in other 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. 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 UK and non-UK 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 that carry on a business or part of a business in the UK may be held liable for bribes given, offered or promised to any person, including UK and non-UK 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. As described above, our business is heavily regulated and therefore involves significant interaction with government officials in many countries. Additionally, in certain 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, the UK Bribery Act and similar laws. 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, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We engage in ongoing efforts 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.

Data Protection and Privacy

We are also subject to data protection and privacy laws and regulations governing the processing of personal data. The legislative and regulatory landscape for privacy and data security is subject to increasing focus and continues to evolve. For example, the EU General Data Protection Regulation, or GDPR, which became effective in May 2018, introduced new data protection requirements for all individuals within the EU and the European Economic Area, or EEA. It also addresses the export of personal data outside the EU and EEA areas. Substantial fines may be imposed for violations of GDPR. In addition, certain EU member states have adopted more stringent data protection standards, which add to the complexity of processing personal data in the EU. The California Consumer Privacy Act of 2018, effective beginning January 2020, mirrors a number of the key provisions in the GDPR.

There are legal mechanisms to facilitate the transfer of personal data from the EEA and Switzerland to the U.S., including the EU-U.S. and Swiss-U.S. "Privacy Shield." U.S.-based companies may certify compliance with the Privacy

Shield principles or they may rely on other authorized mechanisms to transfer personal data. Certification for our U.S.-based subsidiaries under the Privacy Shield was approved in 2017. The EC, in its second annual review of the Privacy Shield, concluded that the U.S. continues to ensure an adequate level of protection for personal data transferred under the Privacy Shield. The U.S. Department of Commerce has strengthened the certification process and introduced new oversight procedures and will increase pressure on companies to comply with Privacy Shield. In addition, the privacy and data security landscape in the EU continues to remain in flux as the final decision on UK's withdrawal from the EU may require organizations to revisit the way they transfer personal data from and to the UK. In the U.S., healthcare providers who prescribe our products and research institutions that we collaborate with are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA other than with respect to providing certain employee benefits, we could potentially be subject to criminal penalties if we, our affiliates or our agents

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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.

Marketing Exclusivity

The Hatch-Waxman Act

The marketing 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 an alternative, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, provides two abbreviated approval pathways for certain drug products.

The first path, under Section 505(b)(2) of the FDCA, usually is used for the approval of a product that is similar, but not identical, to a previously-approved brand-name product, 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 on safety and effectiveness only to the extent necessary to bridge the differences between the products. The second abbreviated 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 RLD (i) have the same active ingredient, in the same strength and dosage form, to be delivered via the same route of administration, (ii) are intended for the same uses, and (iii) are bioequivalent. This data and information are provided instead of data and information independently demonstrating the proposed generic product's safety and effectiveness.

The Hatch-Waxman Act requires an ANDA or a Section 505(b)(2) NDA applicant to certify that there are no patents listed for that product in the Orange Book, or that for each Orange Book-listed patent either the listed patent has expired, the listed patent 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 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 Certification." If a relevant patent covers an approved method of use, an ANDA or Section 505(b)(2) applicant can also file a statement, called, in the case of an ANDA, a "section viii statement," that the application does not seek approval of the method of use covered by the listed patent. With such a statement, the applicant must "carve out" the protected method of use (typically an indication and related material) from the proposed product's labeling. If the applicant makes a Paragraph III Certification, the ANDA or the Section 505(b)(2) NDA will not be approved until the listed patents claiming the RLD have expired.

If the applicant has provided a Paragraph IV Certification to the FDA, the applicant must also send a notice of that certification to the NDA holder and the relevant patent holders once the FDA accepts the ANDA or the Section 505(b)(2) NDA for filing. The NDA and patent holders then have 45 days to initiate a patent infringement lawsuit. Filing the lawsuit triggers an automatic stay on FDA's approval of 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, certain settlements of the lawsuit, or a decision in the infringement case that is favorable to the applicant. The FDA may issue tentative approval of an application if the application meets all conditions for approval but cannot receive effective approval because the 30-month stay or a period of regulatory exclusivity has not expired. If an ANDA or Section 505(b)(2) NDA is approved before conclusion of any relevant patent litigation, the applicant can choose to launch the product, but does so "at risk" of being liable for damages, and potentially treble damages, if the RLD sponsor or patent holder ultimately prevails in patent litigation.

Under the Hatch-Waxman Act, newly approved drugs and indications may benefit from statutory periods of non-patent marketing exclusivity that can potentially delay review or approval of an ANDA or Section 505(b)(2)

application. For example, 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 a drug containing an active moiety that the FDA has not previously approved. During this period, the FDA cannot accept for review an ANDA or a Section 505(b)(2) NDA for a product containing the same moiety, except that an application containing a Paragraph IV Certification may be submitted after four years, which may trigger the litigation and stay described above. The Hatch-Waxman Act also provides three years of marketing exclusivity with the approval of an NDA, including a Section 505(b)(2) NDA, for a product containing a previously-approved moiety but that incorporates a change (such as a new indication, dosage form or strength) from an approved product with the same moiety, if the change required clinical data from new investigations that were conducted or sponsored by the applicant. This three-year exclusivity does not preclude submission of the ANDA or Section 505(b)(2) NDA for such a product, but prevents the FDA from giving final approval to such product.

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The Hatch-Waxman Act also permits a patent term extension of up to five years (but not beyond 14 years from the date of approval) for an NDA, including a Section 505(b)(2) NDA, that is approved for a product that contains an active ingredient that has not previously been approved. The extension, which compensates for patent term lost during product development and the FDA regulatory review process, is generally equal to the sum of one-half the time between the effective date of an IND application 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. It is available for only one patent for a given product, and it must be a patent that claims the product or a method of using or manufacturing the product. The USPTO, in consultation with the FDA, reviews and approves applications for patent term extension.

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, which is one that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals, but for which there is no reasonable expectation that the cost of developing the product and making it available in the U.S. for the disease or condition will be recovered from U.S. sales of the product. Orphan drug designation does not shorten the duration of the regulatory review process or lower the approval standards, but can provide important benefits, including consultation with the FDA. If a product is approved for its orphan designated use, it may be entitled to orphan drug exclusivity, which blocks the FDA from approving for seven years any other application for a product that is the same drug for the same indication. If there is a previously-approved product that is the same drug for the same indication, orphan drug designation requires the sponsor to provide a plausible hypothesis of clinical superiority over the approved product, whereas orphan drug exclusivity requires the sponsor to actually demonstrate clinical superiority. Clinical superiority can be by way of greater efficacy, greater safety, or making a major contribution to patient care. Additionally, a later product can be approved if the sponsor holding orphan drug exclusivity consents, or cannot adequately supply the market. Orphan drug exclusivity does not prevent approval of another sponsor's application for different indications or uses of the same drug, or for different drugs for the same indication. Defibrotide has been granted orphan drug exclusivity by the FDA to treat and prevent VOD until March 2023. Vyxeos has been granted orphan drug exclusivity by the FDA for the treatment of AML until August 2024.

Biologic products approved under a BLA are subject to the BPCIA, which authorizes an abbreviated approval pathway for a biological product that is "biosimilar" to an already approved biologic, or reference product. The BPCIA provides periods of exclusivity that protect a reference product from competition by biosimilars. 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. We believe that Erwinaze, which was approved under a BLA in November 2011, is subject to an exclusivity period that will prevent approval of a biosimilar in the U.S. into November 2023.

Under certain circumstances, the exclusivity periods applicable to drugs and biologics and the patent-related protections applicable to drugs may be eligible for a six-month extension if the sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. This exclusivity may be granted even if the data does not support a pediatric indication. We will consider seeking pediatric exclusivity for our products whenever appropriate. For example, in response to a written request from the FDA, we conducted 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, and submitted study results in a supplement to the Xyrem NDA, seeking approval for this indication. In October 2018, FDA approved the sNDA and notified us that we had been granted pediatric exclusivity, extending by six months the preclusive effect of our Orange Book-listed patents for Xyrem that have not been invalidated, as well as the three-year regulatory exclusivity period granted to the Xyrem pediatric indication because of the clinical studies that were necessary for approval of the sNDA.

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. Orphan designated medicinal products are entitled to a range of benefits during the development and regulatory review process and ten years of market exclusivity in all EU

member states upon approval. Similar to in the U.S., a similar medicinal product with the same orphan indication may be approved, notwithstanding orphan product exclusivity, if the exclusivity holder gives consent 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 has been granted orphan drug designation by the EC and the Korean Ministry of Food and Drug Safety to treat and prevent VOD, by the Commonwealth of Australia-Department of Health for the treatment of VOD and by the EC for the prevention of aGvHD. Vyxeos has been granted orphan drug designation by the EC until August 2028.

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Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access

Pricing and Reimbursement

Successful commercialization of our products depends in significant part on adequate financial coverage and reimbursement from third party payors, including governmental payors (such as the Medicaid and Medicare programs in the U.S.), managed care organizations and private health insurers. Third party payors decide which drugs will 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 by examining their cost effectiveness, as demonstrated in pharmacoeconomic and/or clinical studies, in addition to their safety and efficacy. In some cases, for example, third party payors try to encourage the use of less expensive products, when available, through their prescription benefits coverage and reimbursement, co-pay and prior authorization policies. 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 require prior approval before covering a specific product, or may require patients and health care providers to try other covered products first. Third party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. In many instances, third party payors now require rebates with some drug manufacturers in exchange for including a specific product on their formularies. In the past, we have not entered into such arrangements with third party payors for any of our products. The increasing pressure of the pharmaceutical coverage environment may lead us to do so in the future.

Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Medicare is a federal program that is administered by the federal government covering individuals age 65 and over as well as those with certain disabilities. Medicare Part B pays physicians who administer our products. Under the Medicaid Drug Rebate program, as a condition of having federal funds being made available to the states for our drugs under Medicare Part B, 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. Medicaid rebates are based on pricing data we report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services, or CMS, the federal agency that administers the Medicaid Drug Rebate program, several state Medicaid supplemental rebate programs and other governmental pricing programs. 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 applicable sales and associated rebates, discounts and other price concessions. For the federal government to determine Medicare Part B payments to physicians, we are required to provide average sales price, or ASP, information for certain of our products to the CMS on a quarterly basis. The average sales price is calculated based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. This information is used to compute Medicare payment rates, with rates for Medicare Part B drugs outside the hospital outpatient setting and in the hospital outpatient setting consisting of ASP plus a specified percentage. 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.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B program, or 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, which is administered by the Health Resources and Services Administration, or HRSA, requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered drugs used in an outpatient setting. 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, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B

ceiling price calculation and discount requirement. A new regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities became effective on January 1, 2019. HRSA also has announced that it will begin to implement a ceiling price reporting requirement related to the 340B program during the first quarter of 2019. 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.

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 also 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 products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price to certain federal agencies that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non-

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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. 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 addition, in the U.S., 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. There are numerous ongoing efforts at the federal and state level seeking to indirectly or directly regulate drug prices to reduce overall healthcare costs using tools such as price ceilings, value-based pricing and increased transparency and disclosure obligations. The House Oversight Committee of the 116th Congress has announced an investigation into the actions of a number of pharmaceutical companies in raising prescription drug prices in the U.S. Several states have passed or are considering legislation that requires companies to report proprietary pricing information. For example, in 2017, California adopted a prescription drug price transparency state bill requiring advance notice and an explanation for price increases of certain drugs that exceed a specified threshold. Similar bills have been previously introduced at the federal level and additional legislation could be introduced this year.

Similar to what is occurring in 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, including countries representing major markets. 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 compares attributes of individual medicinal products, as 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. On January 31, 2018, the EC adopted a proposal for an HTA regulation intended to boost cooperation among EU member states in assessing health technologies, including new medicinal products. The proposal provides that EU member states will be able to use common HTA tools, methodologies, and procedures across the EU. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social and ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

In the EU, our products are marketed through various channels and within different legal frameworks. The making available or placing on the EU market of unauthorized medicinal products is generally prohibited. However, the competent authorities of the EU member states may exceptionally and temporarily allow and reimburse the supply of such unauthorized 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. 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.

For more information, see the risk factors under the headings “Adequate coverage and reimbursement from third party payors may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably,” “The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition” and “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” in Part I, Item 1A of this Annual Report on Form 10 K.

Patient Assistance Programs

We have various programs to help patients access our products, including patient assistance programs, which include co-pay coupons for certain of our products, services that help patients determine their insurance coverage for our products, and a free product program. We also make grants to independent charitable foundations that help financially needy patients with their premium, co-pay and co-insurance obligations. There has been enhanced scrutiny of company-sponsored patient assistance

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programs, including insurance premium and co-pay assistance programs and donations to third-party charities that provide such assistance, as well as reimbursement support offerings.

The OIG has established guidelines that permit pharmaceutical manufacturers to make donations to charitable organizations providing 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. In 2016 and 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of charitable organizations that provide financial assistance to Medicare patients. In April 2018, we reached an agreement in principle with the DOJ on a proposal for a civil settlement of potential claims by the DOJ in the amount of $57.0 million, subject to accrual of interest on the settlement amount from the date of the agreement in principle, negotiation of a definitive settlement agreement and other contingencies, which we expect will include entry into a corporate integrity agreement with the OIG. For more information, see Note 12, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

U.S. Healthcare Reform

The Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act of 2010, which we refer to together as the Healthcare Reform Act, was intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals, the provision of subsidies to eligible individuals enrolled in plans offered on the health insurance exchanges, and the expansion of the Medicaid program. This law has substantially changed 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 340B program, fraud and abuse and enforcement. These changes have impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.

Since the November 2016 U.S. election, President Trump and the U.S. Congress have made numerous efforts to repeal or amend the Healthcare Reform Act. Such "repeal and replace" efforts have failed to date. However, additional legislative changes to or regulatory changes under the Healthcare Reform Act remain possible. In this regard, the U.S. Tax Cuts and Jobs Act of 2017, signed into law in December 2017, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment, commonly referred to as the "individual mandate," imposed by the Healthcare Reform Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year. The nature and extent of any additional legislative or regulatory changes to the Healthcare Reform Act are uncertain at this time.

Employees

As of February 19, 2019, we had approximately 1,360 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 involve the controlled storage, use and disposal of chemicals and solvents. Environmental and health and safety authorities in Italy and Ireland administer laws 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. 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.

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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.

Our predecessor, Jazz Pharmaceuticals, Inc., was incorporated in California in March 2003 and was reincorporated in Delaware in January 2004.

Available Information

The mailing address of our headquarters is Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland, and our telephone number at that location is 353-1-634-7800. Our website is www.jazzpharmaceuticals.com.

We file or furnish pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, 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. Through a link on our website, we make copies of our periodic and current reports, amendments to those 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 Our Other Marketed Products

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® (sodium oxybate) oral solution is 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 adult and pediatric patients with narcolepsy. Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which accounted for 75% and 74% of our net product sales for the years ended December 31, 2018 and 2017, respectively. Our future plans assume that sales of Xyrem will increase, but there is no guarantee 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 2019, and there is no guarantee that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes and revenues from Xyrem.

Our ability to maintain or increase Xyrem product sales is subject to a number of risks and uncertainties. The most important of these risks and uncertainties, any of which could have a material adverse effect on our sales of and revenue from Xyrem, are discussed in more detail in this Part I, Item 1A and include those related to:

- the introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, Xyrem in the treatment of cataplexy and/or EDS in narcolepsy;
- the introduction of a generic version of Xyrem in the U.S. market before the entry dates specified in our settlements with the abbreviated new drug application, or ANDA, filers or on terms that are different from those contemplated by

the settlement agreements;

- increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including pressure to agree to discounts, rebates or other restrictive pricing terms for Xyrem;
- 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 and risk evaluation and mitigation strategy, or REMS, programs by government entities;
- changes to or uncertainties around our Xyrem REMS, or any failure to comply with our REMS obligations to the satisfaction of the FDA;

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- challenges to our intellectual property around Xyrem, including the possibility of new ANDA or new drug application, or NDA, filers or new post-grant patent review proceedings;
- operational disruptions at the Xyrem central pharmacy;
- any supply or manufacturing problems, including any problems with our sole source Xyrem active pharmaceutical ingredient, or API, provider;
- continued acceptance of Xyrem by physicians and patients, including as a result of negative publicity that surfaces from time to time; and
- changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell 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, including on our ability to acquire, in-license or develop new products in the future to grow our business.

The introduction of a new product in the U.S. market that competes with, or otherwise disrupts the market for, Xyrem would adversely affect sales of Xyrem.

While Xyrem is currently the only product approved by the FDA and marketed in the U.S. for the treatment of both cataplexy and EDS in patients with narcolepsy, we and others may launch products as treatment options in cataplexy and/or EDS in narcolepsy, including other branded sodium oxybate products and other new and existing branded market entrants. In addition, Xyrem will face competition from generics and authorized generics. We expect that the approval and launch of any other sodium oxybate or alternative product that treats narcolepsy, or the launch of an authorized generic product, or AG Product, or other generic version of Xyrem, could have a material adverse effect on our sales of and revenues from Xyrem and on our business, financial condition, results of operations and growth prospects.

With respect to generic and authorized generic competition, nine companies sent us notices that they filed ANDAs with the FDA seeking approval to market a generic version of Xyrem, and we filed patent lawsuits against each of them, asserting that such generic products would violate our patents covering Xyrem. As of October 2018, we have settled patent litigation with all nine companies. In our settlement with the first filer, West-Ward Pharmaceuticals Corp. (a wholly owned subsidiary of Hikma Pharmaceuticals PLC), or West-Ward, we granted West-Ward the right to sell an AG Product in the U.S. beginning on January 1, 2023, or earlier under certain circumstances. These include circumstances related to the licensing or market entry of another generic sodium oxybate product, a final decision that all unexpired claims of the Xyrem patents are invalid and/or unenforceable, or a substantial reduction in Xyrem net sales over specified periods of time. West-Ward has a right to elect to continue to sell the West-Ward AG Product for a total of up to five years. We also granted West-Ward a license to launch its own generic sodium oxybate product as early as six months after it has the right to sell the West-Ward AG Product, but if it elects to begin selling its own generic product, it cannot continue to sell the West-Ward AG Product. In our settlements with Amneal Pharmaceuticals LLC, or Amneal, Lupin Inc., or Lupin, and Par Pharmaceutical, Inc., or Par, we granted each party the right to sell a limited volume of an AG Product in the U.S. beginning on July 1, 2023, or earlier under certain circumstances, including events related to the acceleration of West-Ward's AG Product launch date, the earlier launch of another party's AG Product, the launch of another generic sodium oxybate product or a final decision that all unexpired claims of the Xyrem patents are invalid and/or unenforceable. We also granted each of Amneal, Lupin and Par a license to launch its own generic sodium oxybate product under its ANDA on or after December 31, 2025, or earlier under certain circumstances, including events related to the launch of another generic sodium oxybate product or a final decision that all unexpired claims of the Xyrem patents are not infringed, or are invalid and/or unenforceable. If an acceleration event occurs, then each of Amneal, Par and Lupin will have the option to elect to market its AG Product until December 31, 2025, but will not be entitled to market its AG Product and its own generic sodium oxybate product simultaneously. Under the terms of our settlement agreements, we are entitled to receive royalty and other revenue based on sales of AG Products. In our settlements with each of the other five ANDA filers, we granted each a license to launch its own generic sodium oxybate product under its ANDA on or after December

31, 2025, or earlier under certain circumstances, including the launch of another generic sodium oxybate product. In order to launch a generic sodium oxybate product, an ANDA filer must obtain and maintain FDA approval of its ANDA. In January 2017, the FDA approved West-Ward's ANDA and tentatively approved two additional ANDAs for generic sodium oxybate products, and we believe that it is likely that the FDA will approve or tentatively approve the additional ANDAs that have been filed.

Any ANDA holder launching an AG Product or another generic sodium oxybate product will establish the price of the AG Product and/or its own generic sodium oxybate product. Generic competition often results in decreases in the prices at which branded products can be sold. After any introduction of a generic product, whether or not it is an AG Product, a significant percentage of the prescriptions written for Xyrem may be filled with the generic product. 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 when a generic version is available. This would result in reduction in sales of, and revenue from, Xyrem, although we would continue to receive royalty and other revenue based on sales of an AG Product in

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accordance with the terms of our settlement agreements. For more information on the impact of generic competition, see the risk factors under the heading “Adequate coverage and reimbursement from third party payors may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably” and “The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition” in this Part I, Item 1A.

It is possible that additional companies may file ANDAs seeking to market a generic version of Xyrem which could lead to additional patent litigation or challenges with respect to Xyrem. Such patent litigation or challenges could potentially trigger acceleration of the launch dates in our settlement agreements. For example, the launch dates in our settlement agreements would be accelerated if a new ANDA filer were to obtain a final decision prior to January 1, 2023 that all unexpired claims of the Xyrem patents are invalid and/or unenforceable. Alternatively, the launch dates in our settlement agreements could be accelerated if a new ANDA filer were to obtain FDA approval for its sodium oxybate product, and launch its generic product through a generic sodium oxybate REMS before the entry dates specified in our settlement agreements, if, for example, we are unable to obtain an injunction or because that party launches “at risk” of being held liable for damages for patent infringement. It is also possible that we could enter into a settlement agreement with a future ANDA filer that would permit such filer to enter the market on or prior to the launch date(s) in our settlement agreements. If a company launches a generic or authorized generic sodium oxybate product in any of these scenarios, except in limited circumstances related to an “at risk” launch, the launch date for West-Ward’s AG Product would be accelerated to a date on or prior to the date of such entry, which could lead to acceleration of the other settling ANDA filers’ AG Product and generic sodium oxybate product launch dates as described above. For further discussion of Xyrem-related patent matters, see the risk factors under the heading “Risks Related to Our Intellectual Property” in this Part 1, Item 1A.

Another circumstance that could trigger acceleration of West-Ward’s launch date for an AG Product, which would also accelerate Amneal, Lupin and Par’s launch dates for their AG Products and ultimately could lead to acceleration of the other settling ANDA filers’ launch dates for their generic sodium oxybate products, is a substantial reduction in Xyrem net sales. Such a reduction could occur under various circumstances, including if we introduce, or a third party introduces, a product to treat EDS or cataplexy in narcolepsy that leads to a substantial decline in Xyrem net sales prior to January 1, 2023. For example, we are developing JZP-258, an oxybate product candidate that contains 90% less sodium than Xyrem. Given the well-accepted relationship between dietary sodium and blood pressure as well as published hypertension guidelines underscoring that excessive consumption of sodium is independently associated with an increased risk of stroke, cardiovascular disease and other adverse outcomes, we believe that lower sodium intake would be beneficial for patients. JZP-258 is being developed for the treatment of both cataplexy and EDS in narcolepsy as well as for other conditions, and, subject to the results of our Phase 3 clinical trial in narcolepsy, we expect to file an NDA for approval of this product by as early as the end of 2019. Other companies may similarly develop a sodium oxybate product for treatment of narcolepsy, using an alternative formulation or a different delivery technology, and seek approval in the U.S. using an NDA approval pathway under Section 505(b)(2) and referencing the safety and efficacy data for Xyrem, which could lead to additional patent litigation or challenges. We are aware that a company called Avadel Pharmaceuticals plc, or Avadel, is conducting a Phase 3 clinical trial of a once-nightly formula of sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy, and has indicated that it intends to seek approval using the Section 505(b)(2) approval pathway. Approval and successful commercialization of JZP-258, or Avadel’s sodium oxybate formulation, or any other new non-generic sodium oxybate or other product for treatment of narcolepsy patients could negatively impact our ability to maintain and grow sales of Xyrem.

Although, as noted above, Xyrem is currently the only product approved by the FDA and marketed in the U.S. for the treatment of cataplexy associated with narcolepsy, we are aware that prescribers often prescribe branded or generic medications for cataplexy before prescribing or instead of prescribing Xyrem, and that payors often require patients to try such medications before they will cover Xyrem, even if they are not labeled for this use. For example, prescribers

often treat mild cataplexy with drugs that have not been approved by the FDA for this indication, including tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors. These drugs have known side effects, including for example, somnolence or insomnia, that can be problematic for patients with narcolepsy. We are also aware that branded or generic stimulants may be prescribed off label for treatment of EDS in narcolepsy. Wake-promoting agents Provigil® (modafinil) and Nuvigil® (armodafinil), and their generic equivalents are labeled for treatment of EDS in narcolepsy and other conditions, and may be used in conjunction with or instead of Xyrem. Prescribers often prescribe these medications before prescribing or instead of prescribing Xyrem, and payors often require patients to try such medications before they will cover Xyrem.

It is possible that additional branded or generic products may be introduced to treat symptoms of narcolepsy that will also be prescribed before or instead of Xyrem, or that payors will require patients to try before they will cover Xyrem. For example, Harmony Biosciences LLC, or Harmony, has exclusive U.S. rights to seek approval of and commercialize pitolisant, a drug that has already been approved in Europe to treat adult patients with narcolepsy with or without cataplexy. Published data and prescribing patterns in the EU suggest that pitolisant would likely be appropriately used in patients with less severe cataplexy

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than those treated with Xyrem. While pitolisant is not currently approved in the U.S., Harmony has established an expanded access program for pitolisant, received Breakthrough Therapy and Fast Track designations from the FDA and, in February 2019, announced that the FDA had accepted for filing with priority review its pitolisant NDA. Non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy, even if not directly competitive with Xyrem, could have the effect of changing treatment regimens and payor coverage of Xyrem, which could materially and adversely affect sales of Xyrem.

The distribution and sale of Xyrem are subject to significant regulatory restrictions, including the requirements of a REMS, and these regulatory requirements subject us to risks and uncertainties, any of which could negatively impact sales of Xyrem.

The active ingredient of Xyrem, sodium oxybate, is the sodium salt of gamma-hydroxybutyric acid, or GHB, a central nervous system depressant known to be associated with facilitated sexual assault as well as with respiratory depression and other serious side effects. As a result, the FDA requires that we maintain a REMS with elements to assure safe use, or ETASU, for Xyrem to help ensure that the benefits of the drug in the treatment of cataplexy and EDS in narcolepsy outweigh the serious risks of the drug. The REMS imposes extensive controls and restrictions on the sales and marketing of Xyrem that we are responsible for implementing. For example, under the Xyrem REMS, all of the Xyrem sold in the U.S. must be dispensed and shipped directly to patients or caregivers through a central pharmacy, and 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 must receive materials concerning the serious risks associated with Xyrem before the physician can prescribe, or a patient can receive, the product. The central certified pharmacy must monitor and report instances of patient or prescriber behavior giving rise to a reasonable suspicion of abuse, misuse or diversion of Xyrem, and maintains enrollment and prescription monitoring information in a central database. Any failure to comply with our REMS obligations, or a determination by the FDA that the Xyrem REMS is not meeting its goals, 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 require us to invest a significant amount of resources, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

While we believe that the Xyrem REMS has met its goal of mitigating the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse and diversion of Xyrem, we cannot guarantee that the FDA will agree or that the Xyrem REMS will continue to do so in the future. We are required to prepare and submit regular assessments of the Xyrem REMS, and the FDA has stated that it will evaluate the 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, or impose additional requirements on, the Xyrem REMS, including in connection with the submission of applications for new oxybate products, new oxybate indications, or the introduction of authorized generics, or whether the FDA will approve modifications to the Xyrem REMS that we consider warranted in connection with the submission of applications for new oxybate products. Any modifications approved, required or rejected by the FDA could change the safety profile of Xyrem, and have a significant negative impact in terms of product liability, public acceptance of Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, any of which could have a material adverse effect on our Xyrem business. Modifications approved, required or rejected by the FDA could also make it more difficult or expensive for us to distribute Xyrem, make distribution easier for sodium oxybate competitors, disrupt continuity of care for Xyrem patients and/or negatively affect sales of Xyrem.

In October 2018, the FDA approved a modification to the Xyrem REMS in connection with our submission of our pediatric supplemental NDA to include information for pediatric patients and their caregivers. We are in the process of implementing the October 2018 modification to the Xyrem REMS. We have also submitted and expect to continue to submit ongoing assessments as required by the FDA. However, we cannot guarantee that our implementation and ongoing assessments will be completed on our expected timing or 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.

We depend on outside vendors, including the central certified pharmacy, to implement the requirements of the Xyrem REMS. We have an exclusive agreement with Express Scripts Specialty Distribution Services, Inc., the central pharmacy for Xyrem, which expires on July 1, 2019, but we expect to exercise our right to extend the agreement for an additional year. The agreement may be terminated by either party at any time without cause on 180 days' prior written notice to the other party. If the central pharmacy fails to meet the requirements of the Xyrem REMS applicable to the central pharmacy or otherwise does not fulfill its contractual obligations to us, 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 or challenges in implementing REMS modifications, 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 payors 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 U.S. Drug Enforcement Administration, or DEA, and certified and would also need to implement

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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.

A generic version of a drug subject to a REMS with ETASU is required to have the same REMS as the brand drug, and generics and brands are mandated to use a single shared system REMS. 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 under certain circumstances. In its approval of West-Ward's ANDA, the FDA waived the shared REMS requirement, approving West-Ward's ANDA with a generic sodium oxybate REMS, on the condition that the generic sodium oxybate REMS 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. However, 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 this REMS. A sodium oxybate distribution system that is less restrictive than the Xyrem REMS, such as the generic sodium oxybate REMS, which provides that generic sodium oxybate products and potentially sodium oxybate products approved under a Section 505(b)(2) NDA approval pathway could be distributed through multiple pharmacies, could increase the risks associated with sodium oxybate distribution. Because patients, consumers and others may not differentiate generic sodium oxybate from Xyrem or differentiate between the different REMS programs, any negative outcomes, including risks to the public, caused by or otherwise related to a separate sodium oxybate REMS, could have a significant negative impact in terms of product liability, our reputation and good will, public acceptance of Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, any of which could have a material adverse effect on our Xyrem business.

We may face pressure to further modify the Xyrem REMS or to license or share intellectual property pertinent to the Xyrem REMS, including proprietary data required for the safe distribution of sodium oxybate, in connection with the FDA's approval of the generic sodium oxybate REMS or otherwise. Our settlement agreements with ANDA filers do not directly impact the FDA's waiver of the single shared system REMS requirement, any other ANDA filer's ability to develop and implement the generic sodium oxybate REMS for its generic sodium oxybate product or our ability to take any action with respect to 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 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 or another separate REMS.

REMS programs have increasingly drawn public scrutiny from the U.S. Congress, the Federal Trade Commission, or FTC, and the FDA, with allegations that such programs are used as a means of improperly blocking or delaying competition. The U.S. Congress, for example, has introduced proposed legislation aimed at preventing companies from using REMS and other restricted distribution programs as a means to deny potential competitors access to product samples needed for bioequivalence testing. The FDA has stated that it will seek to coordinate with the FTC in identifying and publicizing practices the FTC finds to be anticompetitive and has further stated that the FDA has concerns related to the role of REMS programs in delaying approval of generic products. For example, in May 2018, FDA published a list of companies that it said had potentially been blocking access to the samples of their branded products, including one of our subsidiaries that sells FazaClo® (clozapine, USP) through a REMS program. It is possible that the FTC, the FDA, other governmental authorities or other third parties could claim that, or launch an

investigation into whether, we are using our REMS programs in an anticompetitive manner or have engaged in other anticompetitive practices. The Federal Food, Drug and Cosmetic Act further states that a REMS ETASU shall not be used by an NDA holder to block or delay generic drugs or drugs covered by an application under Section 505(b)(2) from entering the market. In its 2015 letter approving the Xyrem REMS, the FDA expressed concern that we were aware that the Xyrem REMS could have the effect of blocking or delaying generic competition. We cannot predict whether we would face a government investigation or a complaint by a third party premised on a claim that the Xyrem REMS is blocking competition, or the outcome or impact of any such claim.

Pharmaceutical companies, including their agents and employees, are required to monitor adverse events occurring during the use of their products and report them to the FDA. The patient counseling and monitoring requirements of the Xyrem REMS provide more extensive information about adverse events, including deaths, than is generally available for other products that are not subject to similar REMS requirements. As required by the FDA and other regulatory agencies, the adverse

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event information that we collect for Xyrem is regularly reported to the FDA and could result in the FDA requiring changes to Xyrem labeling, including additional warnings or additional boxed warnings, or requiring us to take other actions that could have an adverse effect on patient and prescriber acceptance of Xyrem. As required by the FDA, Xyrem's current labeling includes a boxed warning regarding the risk of central nervous system depression and misuse and abuse.

Any failure to demonstrate our substantial compliance with the REMS or any other applicable regulatory requirements to the satisfaction of the FDA or another 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 "In addition to those specifically described in other risk factors, 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.

While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products.

In addition to Xyrem, we are commercializing a portfolio of products, including our other lead marketed products, Erwinaze, Defitelio and Vyxeos, and we are making significant investments in maximizing the value and therapeutic reach of Defitelio and Vyxeos by conducting additional research and development activities, which include generating additional supportive clinical data and seeking regulatory approval for new indications, as appropriate. Our inability to effectively commercialize our lead marketed products and to maximize their potential where possible through successful research and development activities could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Erwinaze

Erwinaze® (asparaginase Erwinia chrysanthemi) is 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. Erwinaze is licensed from, and manufactured by, a single source, Porton Biopharma Limited, or PBL, a company that is wholly owned by the UK Department of Health and Social Care. Our license and supply agreement with PBL, which includes our license for Erwinaze, expires on December 31, 2020. We and PBL had been engaged in discussions related to entry into a replacement agreement to extend the term of our commercial relationship with respect to Erwinaze past 2020, but we did not reach agreement. Unless we and PBL enter into a new agreement, we will lose our license to Erwinaze after December 31, 2020, other than our right to sell certain Erwinaze inventory for a post-termination sales period of 12 months. In such event, we may not be able to replace the product sales we would lose from Erwinaze, which in 2018 totaled $174.7 million, and our business, financial condition, results of operations and growth prospects would be materially adversely affected. In addition, we cannot predict whether uncertainty related to rights to, and availability of, Erwinaze after 2020 will impact sales of and revenues from this product.

A continuing and significant challenge to our ability to maintain sales of Erwinaze and a barrier to increasing sales is PBL's inability to consistently supply product adequate to meet market demand. PBL's product quality and manufacturing issues have resulted, and continue to result, in supply disruptions, and our need for PBL to minimize or avoid additional supply disruptions due to capacity constraints, production delays, quality or regulatory challenges and other manufacturing difficulties. In addition, we have incurred and continue to incur significant internal and external costs and expenses as a result of these issues, including due to managing the increased need for regulatory and customer interaction. See the discussion regarding Erwinaze supply issues in the risk factor under the heading "Delays or problems in the supply of our products for sale or our for use in clinical trials, loss of our single source suppliers or 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.

Our ability to maintain sales of Erwinaze is also subject to a number of additional challenges, including the following as well as other risks and uncertainties described elsewhere in this Part I, Item 1A:

- the limited population of patients with ALL, and the incidence of hypersensitivity reactions to E. coli-derived asparaginase within that population;
- the development of new asparaginase treatments or treatment protocols for ALL that may not include asparaginase-containing regimens and prescribers' use of alternate methods to address hypersensitivity reactions;
- the failure to obtain regulatory approval from the FDA or UK Medicines and Healthcare Products Regulatory Agency, or MHRA, to release batches of Erwinaze requiring batch-specific approval due to quality and manufacturing issues;
- difficulties with obtaining and maintaining favorable pricing and reimbursement arrangements;
- potential competition from future biosimilar products;

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- PBL's ability to meet the manufacturing post-marketing commitments imposed by the FDA in connection with its approval of our biologics license application, or BLA;
- our failure to comply with obligations under our agreement with PBL resulting in PBL claiming an uncured material breach; 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 if we decide to launch promotional efforts in those countries.

If we fail to maintain revenue from sales of Erwinaze, our business, financial condition, results of operations and growth prospects could be materially adversely affected.

To expand our asparaginase franchise beyond Erwinaze, we are pursuing activities related to the development of improved asparaginase products for patients with ALL or other hematological malignancies. Several of our external research and development collaborations are focused on these efforts, including our agreement with Pfenex, Inc. which includes worldwide rights to develop and commercialize multiple early-stage hematology product candidates and an option to negotiate a license for a recombinant pegaspargase product candidate, and our agreement with XL-protein GmbH, or XLp, for rights to use XLp's PASylation® technology to extend the plasma half-life of selected asparaginase product candidates. If these activities are unsuccessful, our growth prospects could be materially adversely affected.

Defitelio

Defitelio® (defibrotide sodium) is a product approved in the U.S. in 2016 for the treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT, and in Europe in 2013 (where it is marketed as Defitelio® (defibrotide)) for the treatment of severe VOD in adults and children undergoing HSCT therapy.

Our ability to maintain and successfully and sustainably grow sales of Defitelio is subject to a number of risks and uncertainties, including the following as well as other risks and uncertainties described elsewhere in this Part I, Item 1A:

- the continued acceptance of Defitelio in the U.S., the EU and other countries by hospital pharmacy and therapeutics committees and the continued availability of favorable pricing and adequate coverage and reimbursement by government programs and third party payors;
- the limited experience of, and need to educate, physicians in recognizing, diagnosing and treating VOD, particularly in adults;
- the possibility that physicians recognizing VOD symptoms may not initiate or may delay initiation of treatment while waiting for those symptoms to improve, or may terminate treatment before the end of the recommended dosing schedule;
- our ability to successfully maintain or grow sales of Defitelio in Europe and other non-U.S. countries, including our ability to obtain marketing approval in new countries;
- 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 and by the European Commission, or EC, in connection with its marketing authorization granted "under exceptional circumstances"; and
- our ability to maintain favorable pricing and reimbursement approvals across Europe, particularly in countries that represent significant markets.

To expand the potential of Defitelio, our clinical development strategy generally focuses on the prevention and treatment of serious diseases associated with endothelial cell damage, including an ongoing Phase 3 clinical trial in prevention of VOD in high-risk patients following HSCT, ongoing Phase 2 trials in prevention of acute Graft versus Host Disease following allogeneic HSCT, and planned Phase 2 trials in the treatment of transplant-associated thrombotic microangiopathy and the prevention of chimeric antigen receptor T-cell therapy-, or CAR-T-, associated

neurotoxicity. In addition to clinical trials we are sponsoring, there are more than 20 investigator-sponsored trials ongoing in the U.S. and EU to evaluate defibrotide in multiple conditions. If these development activities are unsuccessful, our growth prospects could be materially adversely affected.

Because VOD is an ultra-rare disease, we have experienced inter-quarter variability in our Defitelio sales, which makes Defitelio sales difficult to predict from period to period. As a result, Defitelio sales results or trends in any period may not necessarily be indicative of future performance. If sales of Defitelio 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.

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Vyxeos

Vyxeos® (daunorubicin and cytarabine) liposome for injection is a product approved in the U.S. in 2017 and in Europe in August 2018 (where it is marketed as Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia, or t-AML, or acute myeloid leukemia, or AML, with myelodysplasia-related changes, or AML-MRC. We made a significant investment in Vyxeos through the acquisition of Celator Pharmaceuticals, Inc. in 2017. Our ability to realize the anticipated benefits from our investment in Vyxeos by successfully and sustainably growing sales is subject to a number of risks and uncertainties, including the following as well as other risks and uncertainties described elsewhere in this Part I, Item 1A:

- our ability to differentiate Vyxeos from other liposomal chemotherapies and generically available chemotherapy combinations with which physicians and treatment centers are more familiar;
- the acceptance of Vyxeos in the U.S., the EU and other countries by hospital pharmacy and therapeutics committees and the availability of favorable pricing and adequate coverage and reimbursement by government programs and third party payors;
- delays or problems in the supply or manufacture of the product, including the ability of the third parties upon which we rely to manufacture Vyxeos and its APIs to manufacture sufficient quantities in accordance with applicable specifications;
- the increasing complexity of the AML landscape requiring changes in patient identification and treatment selection, including diagnostic tests and monitoring that clinicians may find challenging to incorporate;
- the use of new and novel compounds in AML that are either used off-label or are only approved for use in combination with other agents and that have not been tested in combination with Vyxeos;
- 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; and
- our ability to meet the post-marketing commitments and requirements imposed by the FDA in connection with its approval of our NDA and by the EC in connection with its marketing authorization.

Our U.S. launch of Vyxeos is still at an early stage. The lack of prescriber usage data from U.S. commercialization of Vyxeos makes Vyxeos sales difficult to predict from period to period, and sales results or trends in any period may not necessarily be indicative of future performance. Following receipt of marketing authorization from the EC in late 2018, as part of our rolling launch of Vyxeos in the EU, we are in the process of making pricing and reimbursement submissions. If we experience delays or unforeseen difficulties in obtaining favorable pricing and reimbursement, planned launches in the affected EU member states would be delayed, which could negatively impact anticipated revenue.

To expand the potential of Vyxeos, our clinical development strategy is designed to target potential new patient segments across the AML landscape, to pursue indications related to myelodysplastic syndrome and to generate clinical data on Vyxeos when used in combination with other therapeutic agents. We are pursuing this strategy by sponsoring clinical trials, working with cooperative groups who are conducting clinical trials and partnering with The University of Texas MD Anderson Cancer Center to evaluate potential treatment options for hematologic malignancies, with a near-term focus on Vyxeos. In addition, there are multiple investigator-sponsored trials ongoing. If these development activities are unsuccessful, our growth prospects could be materially adversely affected.

If sales of Vyxeos 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.

For a discussion of the risks inherent in implementing our research and clinical development strategy with respect to Defitelio and Vyxeos, see the discussion in the risk factor 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.

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

Our products compete, and our product candidates may in the future compete, with currently existing therapies, product candidates currently under development by others and/or future product candidates, including new chemical entities that may turn out to be safer or more effective than our products. Any products that we develop may be commercialized in competitive markets, and our competitors, which include large global pharmaceutical companies and small research-based companies and institutions, may succeed in developing products that render our products obsolete or noncompetitive.

We also face competition, and may in the future face additional competition, from manufacturers of generic drugs. Certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician

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mandate, the dispensing of generic products rather than branded products when a generic version is available. Generic competition often results in decreases in the prices at which branded products can be sold.

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.

For a discussion of specific risks relating to the launch of new products that treat cataplexy and/or EDS in narcolepsy, including generic versions of Xyrem or other sodium oxybate products, see the risk factor under the heading "The introduction of a new product in the U.S. market that competes with, or otherwise disrupts the market for, Xyrem would adversely affect sales of Xyrem" in this Part I, Item 1A. We expect that the approval and launch of any other sodium oxybate or alternative product that treats narcolepsy, or the launch of an AG Product or other generic version of Xyrem, could have a material adverse effect on our sales of and revenues from Xyrem and on our business, financial condition, results of operations and growth prospects.

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. Some new asparaginase treatments 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, including some for the treatment of relapsed or refractory ALL patients. We have experienced frequent intermittent shortages of the product that have impacted prescribing habits for Erwinaze, including prescribers' use of alternate methods to address hypersensitivity reactions. The development of these new treatments could negatively impact our ability to maintain, and potentially in the future grow, sales of Erwinaze in patient populations where the benefit of an asparaginase-containing regimen is not well established. As a biologic product, Erwinaze also faces potential competition from biosimilar products.

While there is currently no direct competition to Defitelio to treat severe VOD, changes in the types of conditioning regimens used as part of HSCT may affect the incidence rate of VOD and demand for Defitelio.

With respect to Vyxeos, there are a number of alternative established therapies in AML. A key consideration in the treatment of AML patients is the patient's suitability for chemotherapy. The AML patient population studied in the Vyxeos Phase 3 clinical trial supporting our NDA included fit patients, or those deemed able to tolerate intensive induction chemotherapy. The existing options for the treatment of newly-diagnosed t-AML and AML-MRC in fit patients include cytarabine in combination with an anthracycline (i.e., daunorubicin), known as 7+3. In addition, we are aware of several other products that have been recently approved by the FDA or are in development as treatment options for newly diagnosed AML patients eligible for intensive chemotherapy, such as targeted agents (e.g. midostaurin, enasidenib and ivosidenib), immunotherapies (e.g., gemtuzumab ozogamicin and CAR-T cell therapy), and agents disrupting leukemia cell survival (e.g., glasdegib). We are also aware of the use of venetoclax, an AML treatment recently approved by the FDA. Some of the patient populations being studied for, or treated by, these products overlap with the patient population studied in the Vyxeos Phase 3 clinical trial supporting our NDA. The existence of established treatment options and the development of competing products for the treatment of newly-diagnosed t-AML or AML-MRC could negatively impact our ability to successfully commercialize Vyxeos and achieve the level of sales we expect.

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 and marketing activities. As a result, our competitors may obtain FDA or other regulatory approvals for their product candidates more rapidly than we can 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.

We have a relatively small number of sales representatives compared with most other pharmaceutical companies with marketed products. Each of our sales representatives is responsible for a territory of significant size. Many of our competitors deploy more personnel to market and sell their products than we do. In particular, we compete with companies with extensive sales, marketing and promotional experience in hematology/oncology markets, and our

failure to compete effectively in this area could negatively affect sales of our hematology/oncology products. If our sales force and sales support organization are not appropriately resourced and sized to adequately promote our products, the commercial potential of our current and any future products may be diminished.

The 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 such growth. We may not be able to expand in a timely or cost-effective manner, or we may not have the financial resources to achieve the necessary growth. We also compete with other companies to recruit, hire, train and retain pharmaceutical sales and marketing personnel, and excessive turnover in such personnel could negatively affect sales of our products.

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Adequate coverage and reimbursement from third party payors 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 successfully commercialize and achieve market acceptance of our products depends in significant part on adequate financial coverage and reimbursement from third party payors. Third party payors include governmental payors (such as the Medicare and Medicaid programs in the U.S.), managed care organizations and private health insurers. Without third party payor support, patients may not be able to obtain prescribed medications due to barriers to access, including the inability to afford the medication.

Third party payors' reimbursement practices are complex, vary widely from payor to payor and can impose time-consuming burdens for patients and prescribing physicians. As part of the overall trend toward cost containment, third party payors often require prior authorization for, and require reauthorization for continuation of, prescription products or impose step edits, which require prior use of another medication, usually a generic or preferred brand, prior to approving coverage for a new or more expensive product. Such restrictive conditions for reimbursement and an increase in reimbursement-related activities can extend the time required to fill prescriptions and may discourage patients from seeking treatment. For example, we are experiencing increasingly restrictive conditions for reimbursement required by some third party payors for Xyrem, which have extended the time required to fill some prescriptions and could continue to do so in the future and which may have a material effect on the overall level of reimbursement coverage for Xyrem. We cannot predict actions that third party payors may take, or whether they will limit the access and level of reimbursement for our products or refuse to provide any approvals or coverage. From time to time, third party payors have refused to provide reimbursement for our products, and others may do so in the future.

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 hematology/oncology products, all of which are used primarily or exclusively in the inpatient hospital setting, there may not be sufficient reimbursement under the relevant MS-DRG to fully cover the cost of our products. In addition, in 2017 CMS approved, and reauthorized in 2018, a New Technology Add-on Payment, or NTAP, for Defitelio, and in 2018, approved an NTAP for Vyxeos. An NTAP is in addition to the MS-DRG-based reimbursement that hospitals receive. NTAP designations are reviewed by CMS on a yearly basis, and we cannot guarantee that CMS will continue the NTAP designation. If the NTAPs for Vyxeos or Defitelio are not renewed, the relevant MS-DRG may not fully cover the cost of our products.

In addition, a significant portion of our revenue from our hematology/oncology products, particularly Erwinaze and Vyxeos, is obtained through government payors, including Medicare and Medicaid, and any failure to qualify for or receive adequate reimbursement under those programs, including as a result of legislative changes to these programs, would have a material adverse effect on revenues from such products. Significant 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 affected 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.

On February 6, 2019, the U.S. Department of Health and Human Services, or HHS, published a proposed rule in the Federal Register proposing to modify the scope of the discount safe harbor to carve out discounts or rebates provided to pharmacy benefit managers, or other third party organizations known as PBMs, which are tasked with administering prescription drug programs for large employers, health plans and government programs, for patients receiving benefits under Medicare Part D or a managed Medicaid plan. While the potential impact of such a rule is still unclear, the potential disruption to the marketplace could have the practical effect of limiting our ability, in some

instances, to effectively negotiate with PBMs for access to our products for patients. Medicaid and other governmental programs are described under the heading “Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access” in Part I, Item 1 of this Annual Report on Form 10-K. For a discussion of specific risks relating to our reporting and payment obligations to government payors, see 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” in this Part I, Item 1A. Third party payors outside the federal government are also increasingly considering new metrics as the basis for reimbursement rates, including those used by federal government payors such as average net sales price, average manufacturer price and actual acquisition cost. It is not possible to predict the impact of these evolving reimbursement mechanics on the willingness of payors to cover our products.

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Third party payors increasingly examine the cost effectiveness of pharmaceutical products, in addition to their safety and efficacy, when making coverage and reimbursement decisions. 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 coverage and reimbursement for our products. If our competitors offer their products at prices that provide lower treatment costs than our products, or otherwise suggest that their products are safer, more effective or more cost-effective than our products, this may result in a greater level of access for their products relative to our products, which would reduce our sales and harm our results of operations. 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. Because some of our products compete in a market with both branded and generic products, obtaining and maintaining access and reimbursement coverage for our products may be more challenging than for products that are new chemical entities for which no therapeutic alternatives exist.

A small number of third party payors and PBMs have market power and negotiating leverage to limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication, and to exclude drugs from their formularies in favor of competitor drugs or alternative treatments, or place drugs on formulary tiers with higher patient co-pay obligations, and/or to mandate stricter utilization criteria. Formulary exclusion effectively encourages patients and providers to seek alternative treatments or pay 100% of the cost of a drug. In many instances, third party payors and PBMs may also exert negotiating leverage by requiring incremental rebates from manufacturers in order to maintain their formulary position. In the past, we have not entered into such arrangements with third party payors for any of our products. The increasing pressure of the pharmaceutical coverage environment may require us to do so in the future, which could have a negative impact on our revenue from Xyrem.

Specifically, we are experiencing increasing pressure from third party payors to agree to discounts, rebates or other restrictive pricing terms for Xyrem. As our business becomes more complex, we may need to enter into rebate agreements in order to ensure that patients continue to have access to Xyrem, and to support the long-term success of our sleep franchise, which might result in lower net revenues for Xyrem.

If solriamfetol, our product candidate for the treatment in adult patients in EDS associated with obstructive sleep apnea, or OSA, and EDS associated with narcolepsy, is approved by the FDA, the product will enter a competitive retail pharmacy market of branded and generic products. Any delays or unforeseen difficulties in obtaining access or reimbursement approvals could delay or prevent our commercial launch and our ability to receive a return on our investment in solriamfetol. Third party payors could impose steps edits that require patients to try alternative, including generic, treatments before authorizing payment for solriamfetol, exclude solriamfetol from formulary coverage lists, limit the types of diagnoses for which coverage will be provided or demand rebates, discounts, exclusivity or other concessions for solriamfetol and potentially our other products. Additionally, at launch, many payors impose a moratorium on coverage for products while the payor makes a coverage decision. These potential utilization management strategies could limit patient access to solriamfetol and depress therapy adherence rates. We cannot predict market acceptance of, and our ability to obtain adequate formulary positions, access to and reimbursement coverage for solriamfetol. An inability to obtain adequate formulary positions could increase patient cost-sharing for solriamfetol and cause some patients to determine not to use our product. If we are unsuccessful in obtaining broad coverage for solriamfetol, our anticipated revenue from and growth prospects for an approved solriamfetol product could be negatively affected.

In addition, if approved, new products indicated for the treatment of symptoms of narcolepsy, like solriamfetol or pitolisant, could impact access to Xyrem, particularly for newly diagnosed narcolepsy patients, if, for example, payors impose a step edit requiring a narcolepsy patient to try solriamfetol before authorizing payment for Xyrem. For more information on solriamfetol, see the risk factor under the heading “Our future success depends on our ability to successfully develop and obtain and maintain regulatory approval in the U.S. and Europe for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.” in this Part I, Item

1A.

The demand for, and the profitability of, our products could be materially harmed if the Medicaid program, Medicare program or other third party payors in the U.S. or elsewhere deny reimbursement for our products, limit the indications for which our products will be reimbursed, or provide reimbursement only on unfavorable terms. We are unable to predict what additional legislation, regulations or policies, if any, relating to third party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business.

The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition.

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U.S. We expect there will

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continue to be legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably. The Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act of 2010, together, the Healthcare Reform Act, substantially changed the way healthcare is financed by both governmental and private insurers. These changes have impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment-for-performance initiatives. Additional legislative and regulatory changes remain possible and appear likely. Their nature and extent are uncertain and they will be subject to judicial and other challenges. For example, while "repeal and replace" efforts by President Trump and the U.S. Congress have failed, aspects of the Healthcare Reform Act have been changed legislatively, such as the repeal of the requirement that certain individuals who fail to maintain qualifying health coverage for all or part of a year make a tax-based shared responsibility payment commonly referred to as the "individual mandate." In addition, there have been delays in the implementation of key provisions of the Healthcare Reform Act, including the excise tax on generous employer-based health plans. 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 products.

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 our revenues. For details of the changes to the Medicaid Drug Rebate program and the Public Health Service's 340B program, or the 340B program, see "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1 of this Annual Report on Form 10-K and 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" in this Part I, Item 1A. The U.S. 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.

In addition to the Healthcare Reform Act, we anticipate that the U.S. Congress, state legislatures, regulators and the private sector will continue to consider and may adopt healthcare policies and reforms intended to curb 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, additional 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, 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, several states have passed laws or are considering legislation aimed at increasing transparency relating to drug pricing, and other states may do so in the future.

There also continue to be legislative proposals to amend U.S. laws to allow the importation into the U.S. of prescription drugs, which have not been subject to U.S. regulatory oversight. The potential importation of such prescription drugs could pose significant safety concerns for patients, increase the risk of counterfeit products becoming available in the market, and have a negative impact on prescription drug prices in the U.S.

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 affected, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted. We have periodically increased the price of Xyrem, most

recently in January 2019, 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. There is no guarantee that such price adjustments will not negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our products, 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.

If we become the subject of any government investigation or U.S. Congressional hearing with respect to 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 or hearing 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 Note 12, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K and the risk factor under the heading “In addition to those specifically described in other risk

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factors, 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.

In many countries outside the U.S., procedures to obtain price approvals, coverage and reimbursement can take considerable time after the receipt of marketing approval. The process of maintaining pricing and reimbursement approvals is complex and varies from country to country. Many European countries periodically review their reimbursement of medicinal products, which could have an adverse impact on reimbursement status. We cannot predict the outcome of any periodic reviews required to maintain pricing and reimbursement approvals across Europe. In addition, orphan products that have a 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 maintain favorable pricing and reimbursement approvals across Europe. 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 we are unable to maintain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country's reimbursed price influences other countries, our anticipated revenue from and growth prospects for our products in the EU could be negatively affected.

In August 2018, the EC granted marketing authorization for Vyxeos, and, as part of our rolling launch of Vyxeos in the EU, we are in the process of making pricing and reimbursement submissions in EU member states. If we experience delays or unforeseen difficulties in obtaining favorable pricing and reimbursement approvals, planned launches in the affected EU member states would be delayed, which could negatively impact anticipated revenue from Vyxeos. If we are unable to obtain favorable pricing and reimbursement approvals in the EU member states that represent significant potential markets, our anticipated revenue from and growth prospects for Vyxeos in the EU could be negatively affected.

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, including those representing the larger markets. 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. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU member states.

In the EU, our products are marketed through various channels and within different legal frameworks. In certain EU member states, reimbursement for unauthorized products 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.

We expect that legislators, policymakers and healthcare insurance funds in the EU will continue to propose and implement cost-containing measures to keep healthcare costs down. Such measures could include limitations on the prices we will be able to charge for our products or the amounts of reimbursement available for these products from governmental agencies or third party payors, may increase the tax obligations on pharmaceutical companies, 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. 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. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted, could negatively affect our growth prospects in Europe.

In addition to access, coverage and reimbursement, 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 each of our products by physicians, patients, third party payors and the medical community depends on:

- the clinical indications for which a product is approved and any restrictions placed upon the product in connection with its approval, such as a REMS, patient registry requirements or labeling restrictions;
- the prevalence of the disease or condition for which the product is approved and its diagnosis;

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- 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, particularly with respect to Erwinaze;
- perceived advantages over alternative treatments;
- relative convenience and ease of administration;
- with respect to Xyrem, 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; 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 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.

For additional discussion about payor acceptance, see the risk factor under the heading "Adequate coverage and reimbursement from third party payors 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.

Delays or problems in the supply of our products for sale or for use in clinical trials, loss of our single source suppliers or 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 suppliers 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. In addition, we and our suppliers are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and equivalent rules and regulations prescribed by non-U.S. regulatory authorities. We have cGMP responsibilities for the products we manufacture in our facilities and also have oversight responsibilities for the manufacturing conducted by our third party suppliers operating under contract. If we or any of our suppliers encounter manufacturing, quality or compliance difficulties with respect to any of our products, we may be unable to obtain or maintain regulatory approval or meet commercial demand for such products, which could adversely affect our business, financial condition, results of operations and growth prospects. In addition, the failure of any of our suppliers to comply with cGMP or other rules and regulations while manufacturing products on our behalf could result in regulatory action directed at the adequacy of our oversight of our contract suppliers, which could result in enforcement actions against us by the FDA and other regulatory entities.

We have a manufacturing and development facility in Ireland where we manufacture Xyrem and development-stage oxybate products, including JZP-258, and a manufacturing plant in Italy where we produce the defibrotide drug substance. We currently do not have our own commercial manufacturing or packaging capability for our other products, product candidates or their APIs. 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. For details of our arrangements with our suppliers, see “Business—Manufacturing” in Part I, Item 1 of this Annual Report on Form 10-K. 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. We are the sole supplier of the defibrotide compound. We have a single source for sodium oxybate, the API for Xyrem, for Erwinaze, for the finished vial form of Defitelio and for Vyxeos. Single sourcing puts us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties. There is no guarantee that our suppliers can or will continue to supply on a timely basis, or at all, the quantities of API or finished product that we need. 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 implement and execute the necessary technology transfer to, and to qualify, a new supplier. The FDA and similar international regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and

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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 meet FDA's 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, which could negatively impact our anticipated revenues 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.

Erwinaze is licensed from, and manufactured for us by, a single source, PBL. 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 indicating that it was not satisfied with PBL's response to the FDA Form 483 issued to PBL in March 2016 and citing significant violations of cGMP for finished pharmaceuticals and significant deviations from cGMP for APIs. In March 2017, PBL filed a response to the warning letter with the FDA. In August 2018, the FDA conducted an inspection of the PBL manufacturing facility and issued an FDA Form 483 to PBL citing observations related to items referenced in the warning letter as well as other manufacturing practices, including data and records management. PBL continues to address the issues identified by the FDA in the warning letter and has submitted its response to the August 2018 Form 483.

In the United Kingdom, or UK, where PBL's manufacturing facilities are located, PBL is subject to similar inspections conducted by the MHRA. Following a site inspection of PBL by MHRA in December 2017, MHRA issued an inspection report listing several major findings, including major deficiencies and failures by PBL to comply with cGMP. In January 2018, PBL filed a response to the report with the 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, including any failure by PBL to correct the violations and deviations referenced above to the satisfaction of the FDA and MHRA, could adversely affect Erwinaze supply, particularly in light of the ongoing limited supply of Erwinaze, 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 other competent authorities being suspended, varied, or revoked, product release being delayed or suspended, including potentially the FDA refusing admission of Erwinaze in the U.S., 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 further limit our future maintenance and potential growth of the market for this product. We have incurred and continue to incur significant internal and external costs and expenses as a result of these issues, including due to managing the increased need for regulatory and customer interaction. 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 PBL 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.

All Erwinaze that PBL has been able to supply is currently completely absorbed by demand for the product. As a consequence, there is no product inventory that can be used to absorb supply disruptions resulting from quality, manufacturing, regulatory or other issues. PBL has experienced and continues to experience product quality and manufacturing issues that have resulted, and continue to result, in disruptions in our ability to supply markets from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. We cannot predict whether the required remediation activities by PBL in connection with its January 2017 FDA warning letter, the December 2017 MHRA report or the August 2018 FDA Form 483 will further strain PBL's manufacturing capacity or otherwise further adversely affect Erwinaze supply. As capacity constraints and supply disruptions continue, whether as a result of continued quality or manufacturing challenges at PBL, regulatory issues or otherwise, we will be unable to build product inventory, our ability to supply the market will continue to be compromised and physicians' decisions to use Erwinaze will continue to be negatively impacted.

If PBL's quality, manufacturing or regulatory issues persist and supply disruptions continue, our agreement with PBL only gives us the right to engage a backup supplier for Erwinaze in very limited circumstances, such as following termination of the agreement by us due to 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 disruption in manufacturing or exacerbate the supply shortage. If we continue to fail to obtain a sufficient supply of Erwinaze from PBL, our sales of and revenues from Erwinaze, our future maintenance and potential growth of the market for this product, our reputation and our business, financial condition, results of operations and growth prospects would continue to be materially adversely affected.

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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 by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. Given that our Vyxeos launch is at an early stage, there is limited experience with the complex manufacturing process relating to Vyxeos. Baxter manufactured batches that were used in the Phase 3 clinical trial for Vyxeos; there have since been batch failures due to mechanical, component and other issues, and batches have been produced that have otherwise not been in compliance with applicable specifications. We are continuing to work with Baxter to address manufacturing complexities. Moreover, 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 we fail to obtain a sufficient supply of Vyxeos in accordance with applicable specifications on a timely basis for any reason or due to manufacturing or regulatory challenges, our sales of and revenues from Vyxeos, our future maintenance and potential growth of the market for this product, our ability to conduct ongoing and future clinical trials of Vyxeos, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

In addition, while the APIs in Vyxeos, daunorubicin and cytarabine, 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 provided the qualification data to the FDA. If the FDA 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 successfully commercialize Vyxeos and generate sales of this product at the level we expect and to conduct ongoing and future clinical trials of Vyxeos 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. For example, Siegfried USA, LLC, or Siegfried, is currently our sole supplier of both the API and finished product for our development activities involving solriamfetol, and we expect that Siegfried will manufacture and supply solriamfetol drug product for commercial sale if solriamfetol receives regulatory approval. If Siegfried does not or is not able to supply us with solriamfetol for any reason, it may take time and resources to implement and execute the necessary technology transfer to another provider, and such delay could negatively impact our anticipated revenues from solriamfetol.

We or our suppliers may not be able to produce sufficient supplies of our product candidates in a timely manner or in accordance with applicable specifications. If any of our suppliers 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. 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 chemistry, manufacturing and controls, or 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.

Our manufacturing facilities and manufacturing facilities of our suppliers have been and are subject to periodic unannounced inspection by the FDA, the European Medicines Agency, or 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, recordkeeping 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.

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Risks Related to Growth of Our Product Portfolio and Research and Development

Our future success depends on our ability to successfully develop and obtain and maintain regulatory approval in the U.S. and Europe for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.

In furtherance of our growth strategy, we have made and are making significant investments in a number of product candidates, including solriamfetol and JZP-258. Our inability to obtain and maintain regulatory approval for our product candidates in the U.S. and Europe, and, if approved, to successfully commercialize new products would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Solriamfetol

We are seeking approval in the U.S. and Europe for solriamfetol as a treatment to improve wakefulness and reduce EDS in adult patients with narcolepsy or OSA. The FDA accepted our solriamfetol new drug application, or NDA, for filing with a standard review in early 2018 and the current Prescription Drug User Fee Act, or PDUFA, date is March 20, 2019. We submitted a solriamfetol marketing authorization application, or MAA, to the EMA in the fourth quarter of 2018. We cannot predict whether our NDA or MAA will be approved in a timely manner, or at all, or, in the case of our NDA for solriamfetol, the results of labeling discussions with the FDA. If we fail to obtain approval for solriamfetol in the U.S. and EU, or if the FDA or EC requires product labeling that negatively impacts patient, physician or payor acceptance of the product, our growth prospects could be materially adversely affected.

If approved, solriamfetol will face competition from existing and future products that treat EDS in adult patients with narcolepsy or OSA in a competitive retail pharmacy market of branded and generic products. In particular, we will need to successfully differentiate solriamfetol from other branded and generic treatments for EDS in patients with narcolepsy with which physicians are more familiar, including stimulants, wake-promoting agents, such as Provigil and Nuvigil, and generic versions of stimulants and wake-promoting agents. We are also aware that stimulants and wake-promoting agents are prescribed for patients to treat excessive sleepiness in OSA. Solriamfetol, if approved by the FDA, will likely face competition from this genericized market. In addition, we are aware of several other products in development as potential treatments for excessive daytime sleepiness in patients with narcolepsy or OSA, including, for example, pitolisant, mazindol, modafinil combinations and Avadel’s once-nightly sodium oxybate formulation.

In addition to uncertainties related to obtaining regulatory approval of solriamfetol and potential competition, our ability to realize the anticipated benefits from our investment in solriamfetol is subject to a number of risks and uncertainties, including the following as well as other risks and uncertainties described elsewhere in this Part I, Item 1A:

- our ability to successfully launch and grow sales of any approved solriamfetol product in the U.S. and EU;
- potential launch delays after any approval, including due to the need for DEA scheduling review which will need to be completed after NDA approval, if any, but before commercial launch;
- the availability of adequate formulary positions and pricing and adequate coverage and reimbursement by third party payors, including government programs, including the impact of any delays in coverage decisions by payors;
- restrictions on permitted promotional activities based on limitations on the approved labeling for the product required by the FDA or the EC;
- market acceptance for an approved solriamfetol product, particularly by OSA physicians;
- delays or problems in the supply or manufacture of an approved solriamfetol product; and
- our ability to satisfy post-marketing commitments and requirements, if any, imposed by the FDA in connection with its approval of our NDA and by the EC in connection with its marketing authorization.

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

JZP-258

JZP-258 is an oxybate product candidate that contains 90% less sodium than Xyrem. Given the well-accepted relationship between dietary sodium and blood pressure as well as published hypertension guidelines, we believe that lower sodium intake would be beneficial for patients. We have conducted a Phase 3 clinical trial of JZP-258 in patients for the treatment of cataplexy and EDS in narcolepsy and are conducting a Phase 3 clinical trial for the treatment of idiopathic hypersomnia, a chronic neurological disorder that is primarily characterized by EDS. Subject to the results of our Phase 3 clinical trial in narcolepsy, we expect to submit an NDA to the FDA for JZP-258 by as early as the end of 2019. Any failure or delay in successfully completing necessary clinical trials and conducting other activities, including CMC activities, that are required to complete our planned NDA submission and obtain regulatory approval could materially and adversely affect our growth prospects.

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Avadel has announced that it has obtained an orphan drug designation from the FDA for its once-nightly sodium oxybate formulation for the treatment of EDS and cataplexy in patients with narcolepsy. To obtain orphan drug exclusivity upon approval, Avadel will have to show clinical superiority to Xyrem, or, if applicable, clinical superiority to JZP-258. However, if the FDA approves Avadel's product and grants it orphan drug exclusivity before we obtain approval for JZP-258, there is a risk that JZP-258 will not be approvable for seven years unless it can establish clinical superiority to Avadel's product. We cannot predict the timing of the two submissions or how FDA will evaluate any clinical superiority arguments that either company may make, but a delay in our ability to obtain approval for JZP-258, if at all, could be detrimental to our business.

For a discussion of the risks inherent in product development and regulatory approval, see the discussions in the risk factors under the headings "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" and "The regulatory approval process is expensive, time-consuming and uncertain and may prevent us or our partners from obtaining and maintaining approvals for the commercialization of some or all of our product candidates" in this Part I, Item 1A. If we are not successful in the clinical development of these and other future product candidates, if we are unable to obtain regulatory approval for our product candidates 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.

We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these acquisitions.

In addition to continued investment in our research and development pipeline, we intend to grow our business by acquiring or in-licensing, and developing, additional products and product candidates that we believe are highly differentiated and 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, sales and marketing 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 may not be able to successfully manage the risks associated with integrating any products or product candidates into our portfolio 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 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 or for any other reason;
- 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 to identify and manage these risks and uncertainties effectively could have a material adverse effect on our business.

In addition, product and product candidate acquisitions create other uncertainties and risks, particularly when the acquisition takes the form of a merger or other business consolidation. Our business acquisitions have required, and any similar future transactions will also require, significant efforts and expenditures, including with respect to

transition activities and integrating the acquired business with our historical business. We may encounter unexpected difficulties, or incur unexpected costs, in connection with potential acquisitions and similar transactions, which include:

- high acquisition costs;
- the need to incur substantial debt or engage in dilutive issuances of equity securities to pay for acquisitions;
- the potential disruption of our historical core business;
- the strain on, and need to continue to expand, our existing operational, technical, financial and administrative infrastructure;
- the difficulties in assimilating employees and corporate cultures;
- the failure to retain key managers and other personnel;
- the challenges in controlling additional costs and expenses in connection with and as a result of any acquisition;

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- 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 or otherwise manage an 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. 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.

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 in animal models, may not predict the results of human clinical trials. Similarly, results from early clinical trials may not be predictive of results obtained in later and larger clinical trials, and later clinical trials may fail to show the desired safety and efficacy of our product candidates despite successful initial clinical testing. Even if we believe we have successfully completed testing, 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 or the data is otherwise not sufficient for regulatory approval, we will not be able to commercialize it and receive any return on our investment in that product candidate.

If the FDA determines that our safety or efficacy data for solriamfetol or, after NDA submission, JZP-258 do not warrant marketing approval, we may be required to conduct additional clinical trials, which could be costly and time-consuming, or we may not be able to commercialize solriamfetol or JZP-258, in which event we would not receive any return on our investments in these product candidates. The FDA may also require product labeling that negatively impacts patient, physician or payor acceptance of the product. For more information, see the risk factor under the heading "Our future success depends on our ability to successfully develop and obtain and maintain regulatory approval in the U.S. and Europe for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates" in this Part I, Item 1A.

Any adverse events or other data generated during the course of clinical trials of our product candidates and/or clinical trials related to additional indications for our commercialized 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 data could otherwise have a material adverse effect on a related commercial product, including with respect to its safety profile. Any failure or delay in completing such clinical trials 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:

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difficulty identifying or enrolling eligible patients, often based on the number of clinical trials, particularly in hematology and oncology, with enrollment criteria targeting the same patient population;

- 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, known as an ethics committee in Europe, to conduct a clinical trial at a prospective study site;
- delays or failures in recruiting patients to participate in a clinical trial;

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- failure of our clinical trials and clinical investigators to be in compliance with the FDA and other regulatory agencies' requirements, commonly referred to as good clinical practices;
- unforeseen safety issues;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites;
- failure of our third party clinical trial managers to satisfactorily perform their contractual duties, comply with regulations or meet expected deadlines; or
- insufficient funds to complete the trials.

We rely on contract research organizations and other third parties, such as cooperative groups, to assist us in designing, coordinating, managing, monitoring and otherwise conducting clinical trials with our product candidates. If we, contract research organizations assisting us with clinical trials, other third parties conducting clinical trials with our product candidates, or our trial sites fail to comply with applicable good clinical practices, the clinical data generated in these clinical trials may be deemed unreliable, and the FDA and/or other global regulatory agencies may require us to perform additional clinical trials before approving our marketing applications. In addition, clinical trials must be conducted with product candidates 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 completion of clinical trials and the regulatory approval process.

If third parties do not successfully carry out their contractual 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 generate additional clinical data in support of these products.

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

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. 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.

Although PDUFA provides a ten-month deadline for the FDA to review a new drug application, or a six-month deadline for priority review, there is no guarantee that the FDA will meet that deadline, and the FDA can extend a PDUFA action date under certain circumstances. If the FDA fails to meet PDUFA targeted action dates established for any of our product candidates, the commercialization of the affected product candidate could be delayed or impaired. In the first quarter of 2018, the FDA accepted our NDA for solriamfetol for filing with a standard review. In December 2018, the FDA determined that a submission we made during the course of discussions regarding draft labeling for solriamfetol constituted a major amendment to the NDA, resulting in a three-month extension of the PDUFA goal date to March 20, 2019, to provide time for a full review of the submission. However, if the FDA fails to meet the PDUFA target action date for our solriamfetol NDA submission, requires significant labeling restrictions as described below or requires product labeling that negatively impacts patient, physician or payor acceptance of the product, our ability to commercialize solriamfetol in the U.S. could be delayed or impaired. We also submitted an MAA to the EMA in November 2018 for solriamfetol as a treatment to improve wakefulness and reduce EDS in adult patients with narcolepsy (with or without cataplexy) or OSA. We cannot predict whether we will be able to obtain approval of our NDA for solriamfetol in the U.S. or our marketing authorization in the EU in a timely manner and on what terms, or at all.

Moreover, the redemption of a rare pediatric disease priority review voucher may not result in faster review or approval compared to products considered for approval under conventional FDA procedures and, in any event, does not assure ultimate approval by FDA. Any delay or failure in obtaining approval of a product candidate, or receipt of approval for narrower indications than sought, can have a negative impact on our ability to recoup or research and development costs and to successfully commercialize that product and on our financial performance.

If the FDA, the EC or the competent authorities of the EU member states determine that our quality, safety or efficacy data do not warrant marketing approval, we could be required to conduct additional clinical trials as a condition to receiving approval, which could be costly and time-consuming and could delay the approval of our application.

Even if we receive approval, it may be subject to significant labeling restrictions, including limitations on the dosing of the product, indicated uses for which we may market the product, or other warnings and precautions, such as the requirement for a REMS to ensure that the benefits of the drug outweigh the risks or the imposition of a boxed warning included in the

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labeling for the product. 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. The FDA requires a REMS and a boxed warning for Xyrem, and similar restrictions could be imposed on other products in the future.

Regulatory authorities may also impose post-marketing obligations as part of their approval. Post-marketing obligations may lead to additional costs and burdens associated with commercialization of the drug, and may pose a risk to maintaining approval of the drug. We are subject to certain post-marketing requirements and commitments in connection with the approval of certain of our products, including Erwinaze, Defitelio and Vyxeos. For example, for Defitelio, in the U.S. the FDA imposed several post-marketing commitments and requirements in connection with its approval, 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, and in the EU marketing authorization was granted under exceptional circumstances and requires us to comply with a number of post-marketing obligations, including a study to provide further data on long-term safety, health outcomes and patterns of utilization of Defitelio in normal use. Similarly, the FDA imposed post-marketing requirements in connection with its approval of our NDA for Vyxeos, including the requirement that we conduct a safety study to characterize infusion-related reactions in patients treated with Vyxeos and a clinical trial to determine dosing to minimize toxicity in patients with moderate and severe renal impairment, and the marketing authorization in the EU also requires us to comply with certain manufacturing-related post-approval commitments. In the event that we are unable to comply with our post-marketing obligations imposed as part of the marketing approvals in the U.S. or EU, our approval may be varied, suspended or revoked, product supply may be delayed and our sales of and revenues from our products could be materially adversely affected.

A significant proportion of the regulatory framework in the UK is derived from EU laws. For that reason, the results of the formal procedure of withdrawal from the EU, initiated by the UK in March 2017, could materially change the regulatory regime applicable to our operations, including with respect to the approval of our product candidates, as there is significant uncertainty concerning the future relationship between the UK and the EU. For a further discussion, see the risks under the heading “The UK’s planned withdrawal from the EU, commonly referred to as Brexit, may have a negative effect on global economic conditions, financial markets and our business” in this Part I, Item 1A.

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, maintaining and defending intellectual property protection for our products and product candidates, including protection of their use and methods of manufacturing and distribution. 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 adequately protected trade secrets that cover these activities.

The patent position of pharmaceutical companies can be highly uncertain and involve complex and often changing legal, regulatory and factual questions. The degree of 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:

- our patent applications, or those of our licensors or partners, may not result in issued patents;
- others may independently develop similar or therapeutically equivalent products without infringing our patents, or those of our licensors, 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;
- our issued patents, or those of our licensors or partners, may be held invalid or unenforceable as a result of legal challenges by third parties or may be vulnerable to legal challenges as a result of changes in applicable law;
- 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 those of our licensors or partners;

- competitors may manufacture products in countries where we have not applied for patent protection or that have a different scope of patent protection or that do not respect our patents; or
- others may be issued patents that prevent the sale of our products or require licensing and the payment of significant fees or royalties.

We have patents covering many of our products in Europe and other parts of the world where patent laws operate differently and provide a different scope of protection than in the U.S. For example, in the EU, approval of a generic pharmaceutical product can occur independently of whether the reference brand product is covered by patents, and enforcement of such patents generally must await approval and an indication that the generic product is being offered for sale. Patent enforcement generally must be sought on a country-by-country basis, and issues of patent validity and infringement may be judged differently in different countries.

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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, Vyxeos and solriamfetol. 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, and potentially invalidated or held unenforceable, including through patent litigation or through patent office procedures that permit challenges to patent validity. Patents can also be circumvented, potentially including by FDA approval of an ANDA or Section 505(b)(2) application that avoids infringement of our intellectual property.

Xyrem is covered by patents covering its manufacture, formulation, distribution system and method of use, and we have U.S. patents that extend to 2033. We have settled patent litigation with nine companies seeking to introduce generic versions of Xyrem in the U.S. by granting those companies licenses to launch their generic products in advance of the expiration of the last of our patents. Notwithstanding our patents and settlement agreements, additional third parties may also attempt to introduce generic versions of Xyrem or other sodium oxybate products for treatment of cataplexy and/or EDS in narcolepsy that design around our patents or assert that our patents are invalid or otherwise unenforceable. If these efforts are successful, then that third party could launch a generic or 505(b)(2) product referencing Xyrem before the dates provided in our patents or settlement agreements.

For example, we have several method of use patents listed in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book, that expire in 2033 that cover instructions on the Xyrem package insert and Xyrem REMS related to a drug-drug interaction, or DDI, with divalproex sodium. Although the FDA has stated, in granting a Citizen Petition we submitted in 2016, that it would not approve any sodium oxybate ANDA referencing Xyrem that does not include the portions of the currently approved Xyrem package insert related to the DDI patents, we cannot predict whether a future ANDA filer, or a company that files a Section 505(b)(2) application for a drug referencing Xyrem, may pursue regulatory strategies to avoid infringing our DDI patents notwithstanding the FDA's response to the Citizen Petition, or whether any such strategy would be successful. Likewise, we cannot predict whether we will be able to maintain the validity of these patents or will otherwise obtain a judicial determination that a generic or other sodium oxybate product, its package insert or the generic sodium oxybate REMS or another separate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents a future ANDA filer or other company introducing a different sodium oxybate product from marketing its product, or instead require that party to pay damages in the form of lost profits or a reasonable royalty.

Since Xyrem's regulatory exclusivity has expired in the EU, we are aware that generic or hybrid generic applications have been approved by various EU regulatory authorities, and additional generic or hybrid generic applications may be submitted and approved. We cannot predict whether our licensee in the EU will be able to enforce our existing European patents against generic or hybrid generic filers in the EU.

For a discussion regarding the risks associated with our ANDA litigation settlement agreements, the potential launch of AG Products or other generic versions of Xyrem, or the approval and launch of other sodium oxybate or other products that compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see the risk factors under the headings "Risks Related to Xyrem and the Our Other Marketed Products" and "We have incurred and may in the future 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.

We also rely on trade secrets and other unpatented proprietary information to protect our products and their commercial position, particularly with respect to our products with limited or no patent protection, such as Erwinaze, which has no patent protection. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality and invention 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. Enforcing a claim that a third party illegally obtained or is using any of our inventions or trade secrets would be 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.

In some instances, we also rely on regulatory exclusivity to protect our commercial position. In addition to relying on trade secret protection, Erwinaze was granted orphan drug exclusivity by the FDA for the treatment of ALL in the U.S. for a seven-year period from its FDA approval, which had precluded approval of another product with the same principal molecular structure for the same indication until November 2018. As a biologic product approved under a BLA, Erwinaze 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, interpretation of regulatory exclusivity under the BPCIA may evolve over time based on FDA issuance of guidance documents, proposed regulations or decisions made by the FDA in the course of considering specific applications. In addition, the BPCIA exclusivity period does not prevent another company from independently developing a product that is highly similar to Erwinaze, generating all the

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data necessary for a full BLA and seeking approval. BPCIA exclusivity only assures that another company cannot rely on the FDA's prior approvals of Erwinaze to support the biosimilar product's approval. As a result, it is possible that a potential competing drug product might obtain FDA approval before the expected BPCIA exclusivity period has expired, which would adversely affect sales of Erwinaze. In the EU, the regulatory data protection that provides an exclusivity period for Erwinase has lapsed. 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 employees, consultants, advisors or partners over the ownership of rights to inventions, including 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 may in the future 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. 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 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 inter partes review, or 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, many types of entities, including ANDA filers, have challenged valuable pharmaceutical patents through the IPR process, and six of our Orange Book-listed patents for Xyrem were invalidated through this process.

There is a risk that a court or the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO, could decide that our patents or certain claims in our patents are not valid or infringed, and that we do not have the right to stop a third party from using the inventions covered by those claims, as happened with the decision of the PTAB that certain of our patent claims covering the Xyrem REMS are invalid. In addition, even if we prevail in establishing that another product infringes a valid claim of one of our patents, a court may determine that we can be compensated for the infringement in damages, and refuse to issue an injunction. As a result, we may not be entitled to stop another party from infringing our patents for their full term. For more information, see the risk factors under the headings "Risks Related to Xyrem and Our Other Marketed Products" 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. Lawsuits or proceedings we may file in the future, or our defense against any lawsuits or other proceedings that may be brought against us, may not costly and time-consuming and may not be successful in stopping the infringement of our patents.

Litigation involving patent matters is frequently settled between the parties, rather than continuing to a court ruling, and we have settled patent litigation with all nine Xyrem ANDA filers. The FTC has publicly stated that, in its view,

certain types of agreements between branded 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 have entered into or might enter into in the future constitutes a reasonable and lawful patent settlement. Parties to such settlement agreements in the U.S. are required by law to file the agreements with the FTC and the U.S Department of Justice, or DOJ, for review. Accordingly, we have submitted our ANDA litigation settlement agreements to the FTC and the DOJ for review. We may receive formal or informal requests from the FTC regarding our ANDA litigation settlements, and there is a risk that the FTC may commence a

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formal investigation or action against us, or a third party may initiate civil litigation regarding such settlements, which could divert the attention of management and cause us to incur significant costs, regardless of the outcome. Any claim or finding that we or our business partners have failed to comply with applicable laws and regulations could be costly to us and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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.

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. For further discussion of our Xyrem-related patent matters, see the risk factors under the headings "Risks Related to Xyrem and Our Other Marketed Products" and "Risks Related to Our Intellectual Property" and Note 12, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

Other Risks Related to Our Business and Industry

We have substantially expanded our international footprint and operations, and we may expand further in the future, which subjects us to a variety of risks and complexities which, if not effectively managed, could negatively affect our business.

We are headquartered in Dublin, Ireland and have multiple offices in the U.S., Canada, the UK, Italy and other countries in Europe. Our headcount has grown to approximately 1,360 as of February 2019. This includes employees in 15 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. We may further expand our international operations into other countries in the future, either organically or by acquisition. While we have 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. These risks and complexities include:

- the diverse regulatory, financial and legal requirements in the countries where we are located or do business, including those related to data security and the use of, or access to, commercial and personal information, taxation, trade laws, including tariffs, export quotas, custom duties or other trade restrictions, and any changes to those requirements;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and employment law and other regulations, as well as

- maintaining positive interactions with our unionized employees;
- costs of, and liabilities for, our international operations, products or product candidates; and
- fluctuations in currency rates.

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

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The UK’s planned withdrawal from the EU, commonly referred to as Brexit, may have a negative effect on global economic conditions, financial markets and our business.

Brexit has created significant uncertainty concerning the future relationship between the UK and the EU, particularly if the UK withdraws from the EU without a ratified withdrawal agreement in place. From a regulatory perspective, there is uncertainty about which laws and regulations will apply. A significant portion of the regulatory framework in the UK is derived from EU laws. However, it is unclear which EU laws the UK will decide to replace or replicate in connection with its withdrawal from the EU. In particular, the regulatory regime applicable to our operations, including with respect to the approval of our product candidates, may change, potentially significantly, and the impact on the process for obtaining or maintaining marketing authorization for pharmaceutical products manufactured or sold in the UK is otherwise unknown.

A basic requirement related to the grant of a marketing authorization for a medicinal product in the EU is the requirement that the applicant be established in the EU. Following withdrawal of the UK from the EU, marketing authorizations previously granted to applicants established in the UK through the centralized, mutual recognition or decentralized procedures may no longer be valid. Moreover, depending upon the exact terms of the UK's withdrawal, there is a risk that the scope of a marketing authorization for a medicinal product granted by the EC pursuant to the centralized procedure, or by the competent authorities of other EU member states through the decentralized or mutual recognition procedures, would not encompass the UK. In that circumstance, a separate authorization granted by the UK competent authorities would be required to place medicinal products on the UK market.

In addition, the laws and regulations that will apply after the UK withdraws from the EU may have implications for manufacturing sites that hold certifications issued by the UK competent authorities. Our capability to rely on these manufacturing sites for products intended for the EU market will depend on the terms of the UK's withdrawal and, potentially, on the ability to obtain relevant exemptions under EU law to supply the EU market with products manufactured at UK-certified sites. There is also the risk that if batch release and quality control testing sites for our products are located only in the UK, manufacturers will need to use sites in other EU member states. All of these changes, if they occur, could increase our costs and otherwise adversely affect our business.

Brexit has also given rise to calls for the governments of other EU member states to consider withdrawal from the EU. These developments, or the perception that they could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, including by significantly reducing global market liquidity or restricting the ability of key market participants to operate in certain financial markets. In addition, currency exchange rates for the British Pound and the euro with respect to each other and to the U.S. dollar have already been negatively affected by Brexit. Should this foreign exchange volatility continue or be exacerbated by UK’s withdrawal from the EU, it could cause volatility in our quarterly financial results.

We have an office in Oxford, England which is focused on commercialization of our products outside of the U.S. We do not know to what extent, or when, the UK’s withdrawal from the EU or any other future changes to membership in the EU will impact our business, particularly our ability to conduct international business from a base of operations in the UK. The UK could lose the benefits of global trade agreements negotiated by the EU on behalf of its members, possibly resulting in increased trade barriers, which could make doing business in Europe more difficult and/or costly. Moreover, in the U.S., tariffs on certain U.S. imports have recently been imposed, and the EU and other countries have responded with retaliatory tariffs on certain U.S. exports. We cannot predict what effects these and potential additional tariffs will have on our business, including in the context of escalating global trade and political tensions. However, these tariffs and other trade restrictions, whether resulting from the UK’s withdrawal from the EU or otherwise, could increase our cost of doing business, reduce our gross margins or otherwise negatively impact our financial results.

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. 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 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.

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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 to operate our business. In the ordinary course of our business, we collect, store, process 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, integrity and availability of such information. We have also outsourced some of our operations (including parts of our information technology infrastructure) to a number of third party vendors who may have, or could gain, access to our confidential information. In addition, many of those third parties, in turn, subcontract or outsource some of their responsibilities to third parties.

Our information technology systems are large and complex and store large amounts of confidential information. The size and complexity of these systems make them 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. Attacks of this nature are increasing in frequency, persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, “hacktivists,” nation states and others. In addition to the extraction of important information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of our information. Although the aggregate impact on our operations and financial condition has not been material to date, we have been the target of events of this nature and expect them to continue.

Significant disruptions of our, our third party vendors’ and/or business partners’ 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 further harm us. 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. In addition, failure to maintain effective internal accounting controls related to security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and subject us to regulatory scrutiny.

In addition to those specifically described in other risk factors, 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.

FDA and Equivalent Non-U.S. Regulatory Authorities

Our activities are subject to extensive regulation encompassing the entire life cycle of our products, from research and development activities to marketing approval (including specific post-marketing obligations), manufacturing, labeling, packaging, adverse event and safety reporting, storage, advertising, promotion, sale, pricing and reimbursement, recordkeeping, distribution, importing and exporting. These requirements apply both to us and to third parties we

contract with to perform services and supply us with products. The failure by us or any of our third party partners, including clinical trial sites, 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, restrictions on our products, our suppliers, our other partners or us, the 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 result in a significant drop in our revenues from the affected products and harm to our reputation and could have a significant impact on our sales, business and financial condition.

We monitor adverse events resulting from the use of our 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

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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 may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps or advise that the existing marketing authorization be varied, suspended or revoked. Failure to adequately and promptly correct the observation(s) can result in further regulatory enforcement action, which could include the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures. The failure to adequately address and promptly correct any matters identified by the FDA or other regulatory agencies could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Erwinase, defibrotide and Vyxeos 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 such products 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. Moreover, any failure to maintain revenues from sales of Erwinase, defibrotide and/or Vyxeos 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.

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. Regulatory authorities actively investigate allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. If we are found to have promoted an approved product for off-label uses, we may be subject to significant liability, including civil and administrative financial penalties and other remedies as well as criminal financial penalties, other sanctions and imprisonment. Even if we are not determined to have engaged in off-label promotion, an allegation that we have engaged in such activities could have a significant impact on our 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. 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 also subject to EU member states' laws governing promotion of medicinal products, including limitations on our promotional activities with health care professionals, advertising and promotion of our products to the general public, misleading and comparative advertising and unfair commercial practices. 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 also impose limitations on our promotional activities with health care professionals.

Other Regulatory Authorities

We are also subject to regulation by other regional, national, state and local agencies, including the DEA, the DOJ, the FTC, the United States Department of Commerce, the Office of Inspector General, or OIG, of the HHS and other regulatory bodies, as well as similar governmental authorities in those non-U.S. countries in which we commercialize

our products.

We are subject to numerous anti-fraud and abuse laws and regulations globally and our sales, marketing, patient support and medical activities may be subject to scrutiny under these laws and regulations. For example, the U.S. federal anti-kickback statute is broad and activities that involve providing anything of value to those who prescribe, purchase, or recommend pharmaceutical products may be subject to scrutiny. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common manufacturer business arrangements and activities, the exemptions and safe harbors are drawn narrowly, and practices or arrangements that involve remuneration may be subject to scrutiny if they do not clearly qualify for an exemption or safe harbor. While we maintain a comprehensive compliance program to try to ensure that our practices and the activities of our third-party contractors and employees fall within the scope of such exceptions and safe harbors, regulators and enforcement agencies may disagree with our assessment or find fault with the conduct of our employees or contractors. In addition, existing regulations are subject to regulatory revision or changes in interpretation by the DOJ or OIG. 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.

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The federal civil False Claims Act prohibits, among other things, making a fraudulent claim for payment of federal funds or a false statement to get a false claim paid. The government may assert that a claim resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim under the False Claims Act. Many companies have faced government investigations or lawsuits by whistleblowers who bring a qui tam action under the False Claims Act on behalf of themselves and the government for a variety of alleged improper marketing activities, including providing free product to customers expecting 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, the government and private whistleblowers have pursued False Claims Act cases against 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. If we become the subject of a government False Claims Act or other investigation or whistleblower suit, we could incur substantial legal costs (including settlement costs) and business disruption responding to such investigation or suit, regardless of the outcome. Violations of the False Claims Act may result in significant financial penalties (on a per claim or statement basis), treble damages and exclusion from participation in federal health care programs.

The majority of individual 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.

The Physician Payment Sunshine Act, or Sunshine provisions, currently requires us to track and report to the federal government payments and transfers of value that we make to physicians and teaching hospitals and ownership interests held by physicians and their family, and provides for public disclosures of these data. Public reporting under the Sunshine provisions has resulted in increased scrutiny of the financial relationships between industry, teaching hospitals and physicians. Such scrutiny may negatively impact our ability to engage with physicians on matters of importance to us. In addition, government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports. For example, certain states require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and gifts and payments to individual physicians, and/or restrict when and to what extent pharmaceutical companies may provide meals to prescribers or engage in other marketing related activities. 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 or similar requirements of state or local regulators, we may be subject to significant civil, criminal and administrative penalties, damages or fines.

Outside the U.S., 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. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products, which is prohibited in the EU, is governed by the national anti-bribery laws of the EU member states, as described below. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states require that payments made to physicians 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.

Xyrem is a controlled substance under the Controlled Substances Act, or CSA. Our suppliers, distributors, clinical sites and the central pharmacy for Xyrem are 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 DEA registration and state licenses, when handling Xyrem and its API. 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. DEA quotas are required for any U.S. supplier to manufacture sodium oxybate or Xyrem. New oxybate market entrants, including generic products, may impact the amount of quota available in the U.S., and if, 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.

We expect that solriamfetol will be subject to scheduling review under the CSA before it can be commercially launched. For a further discussion on controlled substance regulations, see the discussion under the heading "Business—Government

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Regulation—Other Post-Approval Pharmaceutical Product Regulation—Controlled Substance Regulations" in Part I, Item 1 of this Annual Report on Form 10-K.

We have various programs to help patients access our products, including patient assistance programs, which include co-pay coupons for certain of our products, services that help patients determine their insurance coverage for our products, and a free product program. Co-pay coupon programs for commercially insured patients, including our program for Xyrem, have received negative publicity related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. In the past, payors brought class action lawsuits challenging the legality of manufacturer co-pay programs under a variety of federal and state laws and insurers have taken actions through their network pharmacies and PBMs to restrict manufacturer co-pay programs. In September 2014, the OIG issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and other 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.

We have established programs to consider grant applications submitted by independent charitable organizations, including organizations that provide co-pay support to patients who suffer from the diseases treated by our drugs. The OIG has established guidelines that suggest that it is lawful for 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, such facts could be used as the basis for an enforcement action against us by the federal government.

In 2016 and 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of charitable organizations that provide financial assistance to Medicare patients. In April 2018, we reached an agreement in principle with the DOJ on a proposal for a civil settlement of potential claims by the DOJ in the amount of $57.0 million, subject to accrual of interest on the settlement amount from the date of the agreement in principle, negotiation of a definitive settlement agreement and other contingencies. We expect any such settlement will involve entry into a corporate integrity agreement, which will impose significant costs and operational burdens on our business. Moreover, a failure to comply with the terms of a corporate integrity agreement could result in monetary penalties or a reduction or elimination of coverage for our products by federal health care programs such as Medicare and Medicaid and state health care programs. If we do not reach a final settlement, or if we are unable to successfully negotiate and enter into a corporate integrity agreement, the outcome of this investigation could include an enforcement action against us. If the federal government were to file an enforcement action against us as a result of the investigation and could establish the elements of a violation of relevant laws, we could be subject to damages, fines and penalties, which could be substantial, along with other criminal, civil or administrative sanctions, including exclusion from participation in federal health care programs. We would expect to incur significant costs in connection with any enforcement action, regardless of the outcome.

We may also become subject to similar investigations by other state or federal governmental agencies or offices. 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. Such investigations may also result in negative publicity or other negative actions that could harm our reputation, impact our business practices, reduce demand for, or patient access to, our products and/or reduce coverage of our products, including by federal health care programs and state health care programs. If any or all of these events occur, our business, financial condition, results of operations and stock price could be materially and adversely affected.

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 UK

Bribery Act of 2010, or the UK Bribery Act. Our heavily regulated business involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in certain 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 and the UK Bribery Act. Recently the U.S. Securities and Exchange Commission, or SEC, and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, private individuals who report original information to the SEC 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

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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 data protection and privacy laws and regulations governing the processing of personal data. 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. Failure to comply with current and future laws and regulations, such as the EU General Data Protection Regulation that became effective in May 2018 and the California Consumer Privacy Act of 2018 that will become effective beginning January 2020, could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors, private litigation and/or adverse publicity that negatively affects 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 for the transfer of personal data are ever deemed inadequate, 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 European Economic Area or Switzerland is restricted, which could adversely impact our operating results. In addition, although we are not directly 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, other than with respect to providing certain employee benefits, we potentially could 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.

Under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, agreements between branded pharmaceutical companies and potential generic competitors settling patent litigation must be submitted to the FTC and the DOJ for review. The FTC has publicly stated that, in its view, certain brand-generic settlement agreements violate the antitrust laws and has 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 have entered into or might enter into in the future constitutes a reasonable and lawful patent settlement. We may receive formal or informal requests from the FTC regarding our Xyrem patent settlements, and there is a risk that the FTC may commence a formal investigation or action against us, or a third party may initiate civil litigation regarding such settlements, which could divert the attention of management and cause us to incur significant costs, regardless of the outcome. We cannot predict the outcome of any potential government investigation of any antitrust claims, including those described above, or the impact of any such claims.

In addition to those described in this and other risk factors, numerous federal, state and non-U.S. statutes and regulations govern 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. Any claim or finding that we or our business partners have failed to comply with applicable laws and regulations could be costly to us and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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.

Our reporting and payment obligations under the Medicaid Drug Rebate program and other governmental programs are described under the heading “Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access” in Part I, Item 1 of this Annual Report on Form 10-K. Our failure to comply with these obligations could negatively impact our financial results.

The Centers for Medicare and Medicaid Services, or CMS, 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.

We also participate in the 340B program, which is described in more detail under the heading “Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access” in Part I, Item 1A of this Annual Report on Form 10-K. The Health Resources and Services Administration, or HRSA, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally

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overcharge covered entities, which became effective on January 1, 2019. Implementation of this regulation could affect our obligations and potential liability under the 340B program in ways we cannot anticipate. HRSA also began to implement a ceiling price reporting requirement related to the 340B program during the first quarter of 2019. There is no guarantee that our submissions will not be found by HRSA to be incomplete or incorrect. 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.

We have obligations to report the average sales price for certain of our drugs to the Medicare program, as described in more detail under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1A of this Annual Report on Form 10-K. Statutory or regulatory changes or CMS 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, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. 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. There is no guarantee that our submissions will not be found by CMS to be incomplete or incorrect.

We participate in the U.S. Department of Veterans Affairs, Federal Supply Schedule, or FSS, pricing program and the Tricare Retail Pharmacy program, as described in more detail under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1A of this Annual Report on Form 10-K. Pursuant to applicable law, knowing provision of false information in connection with price reporting under these programs can subject a manufacturer to civil monetary penalties. These program obligations also contain extensive disclosure and certification requirements.

If we overcharge the government in connection with our arrangements with FSS or Tricare, 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.

Our business and operations could be negatively affected if we become subject to shareholder activism, which could cause us to incur significant expense, hinder execution of our business strategy and impact our stock price.

Shareholder activism, which takes many forms and arises in a variety of situations, has been increasingly prevalent. If we become the subject of certain forms of shareholder activism, such as proxy contests, the attention of our management and our board of directors may be diverted from execution of our strategy. Such shareholder activism could give rise to perceived uncertainties as to our future strategy, adversely affect our relationships with business partners and make it more difficult to attract and retain qualified personnel. Also, we may incur substantial costs, including significant legal fees and other expenses, related to activist shareholder matters. Our stock price could be subject to significant fluctuation or otherwise be adversely affected by the events, risks and uncertainties of any shareholder activism.

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 impairment or even death. This could result in product liability claims against us and/or recalls of one or more of our products. 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 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

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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 therapeutic 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 Italy and Ireland administer laws 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. Our manufacturing facilities are involved in 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 EU laws, 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. In certain cases, laws 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. We may incur significant costs to comply with current or future EU environmental laws.

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, 2018, we had total indebtedness of approximately $1.8 billion, which included $651.0 million in outstanding term loan indebtedness under a secured credit agreement that we entered into in June 2015 and subsequently amended in July 2016 and in June 2018, which we refer to as the amended credit agreement, $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, and $575.0 million of outstanding indebtedness under our 1.50% exchangeable senior notes due 2024, or the 2024 Notes, which were issued in August 2017 and which we refer to, together with the 2021 Notes, as the Exchangeable Senior Notes.

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 the Exchangeable Senior 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.

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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 $667.7 million principal amount term loan due in June 2023 and a $1.6 billion revolving credit facility, with any loans under such revolving credit facility due in June 2023, subject to early mandatory repayments under certain circumstances. The amended credit agreement contains various covenants that, among other things, limit our ability and/or our restricted subsidiaries' ability to:

- 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 indentures governing the Exchangeable Senior Notes.

In addition, the holders of the Exchangeable Senior 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 Exchangeable Senior Notes, unless we elect to deliver only our ordinary shares to settle such exchange, we will be required to make cash payments in respect of the Exchangeable Senior Notes. It is our intent and policy to settle the principal amount of the Exchangeable Senior 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 Exchangeable Senior Notes or to pay cash upon exchanges of the Exchangeable Senior Notes. Our failure to repurchase the Exchangeable Senior Notes at a time when the repurchase is required by the indentures governing the Exchangeable Senior Notes or to pay any cash payable on future exchanges of the Exchangeable Senior Notes as required by the indentures governing the Exchangeable Senior Notes would constitute a default under that indenture. A default under those indentures 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

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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 Public Limited Company, which we refer to as the Azur Merger, and our acquisitions of EUSA Pharma Inc., Gentium S.r.l. and Celator Pharmaceuticals, Inc. To continue to grow our business over the longer term, we will need to commit substantial additional resources to our business and execution of our strategy. Our ongoing capital requirements will depend on many factors, including:

- the revenues from our commercial products, which may be affected by many factors, including the extent of competition for Xyrem or our other products;
- the cost of acquiring and/or in-licensing any new products and product candidates;
- the costs of our commercial operations;
- 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;
- the costs of integration activities related to any future strategic transactions we may engage in; and
- the costs arising from changes in laws and regulations, including, for example, healthcare reform legislation.

Our strategy includes the expansion of our business through acquiring or in-licensing, and developing, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. See the risk factor under the heading “We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these acquisitions” in this Part I, Item 1A. 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. 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 variability in stock prices, which has caused uncertainty with regard to credit availability for many borrowers. 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 UK’s withdrawal from the EU or as a result of tariffs and other trade restrictions potentially contributing to 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 also adversely affect our cost of financing and have an adverse

effect on the market price of our securities.

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, 2018, we had recorded $3.7 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. For example, in connection with entry into an asset purchase agreement in June 2018 to sell substantially all of the assets held by us related to Prialt® (ziconotide) intrathecal infusion, we recognized an impairment charge of $42.9 million in our consolidated statements of income in 2018, primarily related to the carrying balances of intangible assets. Additionally, goodwill and indefinite-lived assets are subject to an impairment test at least annually.

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Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. Our results of operations and financial position in future periods could be negatively impacted should 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. and potential future sales of Vyxeos are or will be 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, as well as our expanding operations, there is no guarantee that we will be able to effectively manage currency transaction and/or translation risks. We use foreign exchange forward contracts to manage currency risk primarily related to certain intercompany balances 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.

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. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various jurisdictions where we operate. Our effective tax rate may fluctuate depending on a number of factors, including, but not limited to, the distribution of our profits or losses between the jurisdictions where we operate and differences in interpretation of tax laws. In addition, the tax laws of any jurisdiction in which we operate may change in the future, which could impact our effective tax rate. We are subject to reviews and audits by the U.S. Internal Revenue Services, or IRS, and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure, transfer pricing arrangements and tax positions through an audit or lawsuit. Responding to or defending against challenges from taxing authorities could be expensive and consume time and other resources. 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.

In December 2015, we received proposed tax assessment notices, and, in October 2018, we received revised tax assessment notices from the French tax authorities for 2012 and 2013 and in December 2018, we received a proposed tax assessment notice for 2015, relating to certain transfer pricing adjustments. The notices propose additional French tax of approximately $43 million for 2012 and 2013 and approximately $4 million for 2015, including interest and penalties through the respective dates of the proposed assessments, translated at the foreign exchange rate at December 31, 2018. We disagree with the proposed assessments and are contesting them vigorously.

On December 22, 2017, the U.S. Tax Cuts and Jobs Act, or U.S. Tax Act, was signed into law. The U.S. Tax Act made broad and complex changes to the U.S. tax code. The U.S. Department of Treasury has issued limited regulations and other interpretive guidance under the U.S. Tax Act, and is expected to issue additional guidance, the impact of which is uncertain but could change the financial impacts that were recorded at December 31, 2018 or are expected to be recorded in future periods. Furthermore, the impact of this tax reform on certain holders of our ordinary shares could be adverse. Among other things, changes to the rules for determining a foreign corporation's status as a controlled foreign corporation could have an adverse effect on U.S. persons who are treated as owning (directly or indirectly) at least 10% of the value or voting power of our ordinary shares. Investors should consult their own advisers regarding the potential application of these rules to their investments.

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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 U.S. Internal Revenue Code, 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. 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. 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 prospective or retroactive application to us, our shareholders, Jazz Pharmaceuticals, Inc. and/or the Azur Merger.

Our U.S. affiliates' ability to use their net operating losses to offset potential taxable income and related income taxes that would otherwise be due is limited under Section 7874 of the Code and 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.

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. Our U.S. affiliates have a significant amount of NOLs. As a result of Section 7874 of the Code, after the Azur Merger, our U.S. affiliates have not been able and will continue to be unable, for a period of time, to utilize their U.S. tax attributes to offset their U.S. taxable income, if any, resulting from certain taxable transactions. While we expect to be able to fully utilize our U.S. affiliates' U.S. NOLs prior to their expiration, as a result of this limitation, it may take our U.S. affiliates longer to use their NOLs.

Our ability to use these NOLs to offset potential future taxable income and related income taxes that would otherwise be due is also dependent upon our generation of future taxable income before the expiration dates of the NOLs, and we cannot predict with certainty when, or whether, our U.S. affiliates will generate sufficient taxable income to use all of the NOLs. In addition, the use 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.

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.

The U.S. Congress, the EU, the Organization for Economic Co-operation and Development, or OECD, and other government agencies in jurisdictions where we and our affiliates do business have had an extended focus on issues related to the taxation of multinational corporations. One example is the OECD's initiative 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. Some countries are beginning to implement legislation and other guidance to align their international tax rules with the OECD's recommendation. As a result of the focus on the taxation of multinational corporations, 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.

A substantial portion of our indebtedness bears interest at variable interest rates based on USD LIBOR and certain of our financial contracts are also indexed to USD LIBOR. Changes in the method of determining LIBOR, or the

replacement of LIBOR with an alternative reference rate, may adversely affect interest rates on our current or future indebtedness and may otherwise adversely affect our financial condition and results of operations.

In July 2017, the Financial Conduct Authority, the authority that regulates LIBOR, announced that it intended to stop compelling banks to submit rates for the calculation of LIBOR after 2021. The Alternative Reference Rates Committee, or ARRC, in the U.S. has proposed that the Secured Overnight Financing Rate, or SOFR, is the rate that represents best practice as the alternative to the U.S. dollar, or USD, LIBOR for use in derivatives and other financial contracts that are currently indexed to USD LIBOR. ARRC has proposed a paced market transition plan to SOFR from USD LIBOR and organizations are currently working on industry-wide and company-specific transition plans as relating to derivatives and cash markets exposed to USD LIBOR. We have certain financial contracts, including the amended credit agreement and our interest rate swaps, that are indexed to USD LIBOR. Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative

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reference rate, may adversely affect interest rates on our current or future indebtedness. Any transition process may involve, among other things, increased volatility or illiquidity in markets for instruments that rely on LIBOR, reductions in the value of certain instruments or the effectiveness of related transactions such as hedges, increased borrowing costs, uncertainty under applicable documentation, or difficult and costly consent processes. We are monitoring this activity and evaluating the related risks, and any such effects of the transition away from LIBOR may result in increased expenses, may impair our ability to refinance our indebtedness or hedge our exposure to floating rate instruments, or may result in difficulties, complications or delays in connection with future financing efforts, any of which could adversely affect our financial condition and results of operations.

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 $184.00 on June 20, 2018 and a low of $113.52 on December 24, 2018 during 2018. 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 trading volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. In particular, 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 our marketed products. The risks and uncertainties associated with our ability to maintain or increase sales of our products 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 Celator Acquisition and/or potential future acquisitions, on our financial or operating results 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 the Exchangeable Senior Notes who may view the Exchangeable Senior 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 the Exchangeable Senior Notes.

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 U.S. jurisdiction.

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Our articles of association, Irish law and the indentures governing the Exchangeable Senior Notes contain provisions that 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 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 to our articles of association, 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 indentures governing the Exchangeable Senior Notes require us to repurchase the Exchangeable Senior Notes for cash if we undergo certain fundamental changes and, in certain circumstances, to increase the exchange rate for a holder of 2021 Notes or 2024 Notes. A takeover of us may trigger the requirement that we purchase the Exchangeable Senior 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, whether alone or together, 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, whether alone or together, could also discourage proxy contests and make it more difficult for our 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, 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. In addition, in the event that we pay a dividend on our ordinary shares, in certain circumstances, as an Irish tax resident company, some shareholders may be subject to withholding tax, which could adversely affect the price of our ordinary shares.

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

In certain circumstances, the transfer of shares in an Irish incorporated company will be subject to Irish stamp duty, which is a legal obligation of the buyer. This duty is currently charged at the rate of 1.0% 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 in respect of transfers by shareholders who hold our

ordinary shares beneficially through brokers which in turn hold those shares through the Depository 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 permits, 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.

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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 2018 fiscal year relating to our periodic or current reports under the Securities Exchange Act of 1934, as amended.

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 lease approximately 45,000 square feet of office space in Dublin, Ireland. This lease expires in December 2036, with an option to terminate in December 2024 with no less than one year's prior written notice and the payment of a termination fee, and a further option to terminate in December 2031 with no less than one year's prior written notice. We own approximately 58,000 square foot manufacturing and development facility in Athlone, Ireland, which is primarily used for the manufacture of Xyrem and development-stage products.

In Palo Alto, California, we occupy a total of approximately 143,000 square feet of office space, 99,000 square feet of which is under a lease that expires in October 2029, or the Palo Alto Lease, and 44,000 square feet of which is under a lease that expires in August 2019. We have an option to extend the term of the Palo Alto Lease twice for a period of five years each and an option to terminate in October 2027 with no less than one year's prior written notice and the payment of a termination fee. In September 2017, we entered into an agreement to lease approximately 99,000 additional square feet of office space in Palo Alto, California. We expect to occupy this office space by the end of 2019. 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 in October 2029 with no less than one year's prior written notice and the payment of a termination fee.

We occupy approximately 46,000 square feet of office space in Philadelphia, Pennsylvania under a lease that expires in April 2029, or the Philadelphia Lease. The Philadelphia Lease also provides for another 14,000 square feet, which we expect to occupy by the end of 2019. In addition, we have offices in Canada, the United Kingdom, Italy, France and elsewhere in Europe. We occupy approximately 26,000 square feet of office space in Oxford, United Kingdom under a lease that expires in December 2027. We own a manufacturing facility in Villa Guardia (Como), Italy, which is primarily used for the manufacture of Defitelio. The manufacturing facility is approximately 37,000 square feet. We also lease approximately 34,000 square feet of office and laboratory space in Villa Guardia (Como), Italy under a lease that expires in December 2023.

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

The information required to be set forth under this Item 3 is incorporated by reference to Note 12, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

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."

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Holders of Ordinary Shares

As of February 19, 2019, 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 2018 and 2017, 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. 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 any current 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, 2018, there were no unregistered sales of equity securities by us during the year ended December 31, 2018.

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, 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.

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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. Regardless of the availability of a DWT exemption, a shareholder who is neither resident nor ordinarily resident in Ireland 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.

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 subject 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 any tax consequences of holding our ordinary shares, including 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, 2013 in (i) our ordinary shares; (ii) the Nasdaq Composite Index; and (iii) the Nasdaq Biotechnology Index through December 31, 2018. 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.

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COMPARISON OF FIVE YEAR CUMULATIVE TOTAL RETURN (2)

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(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.

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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, 2018:

	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, 2018	123,399	$159.86	123,000	$86,074,483
November 1 - November 30, 2018	1,780,091	$147.70	1,780,091	$143,189,015
December 1 - December 31, 2018	1,127,314	$145.54	1,127,314	$379,137,805
Total	3,030,804	$147.39	3,030,405	

(1) This column includes ordinary shares that we reacquired in satisfaction of the exercise price of employee stock options upon exercise, but 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 this column 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. In November and December 2018, our board of directors increased the existing share repurchase program authorization by $320.0 million and $400.0 million, respectively, thereby increasing the total amount authorized for repurchase to $1.02 billion. This authorization has no expiration date.

(4) The dollar amount shown represents, as of the end of each fiscal month, the approximate dollar value of ordinary shares that may yet be purchased under our publicly announced share repurchase program, exclusive of any brokerage commissions. As indicated in footnote (3), our board of directors increased the existing share repurchase program authorization in November and December 2018, and the amounts in this column give effect to those increases in the fiscal month approved. 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, 2018, 2017 and 2016 and the selected consolidated balance sheet data as of December 31, 2018 and 2017 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, 2015 and 2014, and the selected consolidated balance sheet data as of December 31, 2016, 2015 and 2014 are derived from audited consolidated financial statements not included in this

Annual Report on Form 10-K.

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	Year Ended December 31,				
	2018	2017	2016(1)	2015	2014(2)
	(In thousands, except per share amounts)				
Consolidated Statements of Income Data:					
Revenues:					
Product sales, net	$1,869,473	$1,601,399	$1,477,261	$1,316,819	$1,162,716
Royalties and contract revenues	21,449	17,294	10,712	7,984	10,159
Total revenues	1,890,922	1,618,693	1,487,973	1,324,803	1,172,875
Operating expenses:					
Cost of product sales (excluding amortization of intangible assets)	121,544	110,188	105,386	102,526	117,418
Selling, general and administrative	683,530	544,156	502,892	449,119	406,114
Research and development	226,616	198,442	162,297	135,253	85,181
Intangible asset amortization	201,498	152,065	101,994	98,162	126,584
Impairment charges	42,896	—	—	31,523	39,365
Acquired in-process research and development	—	85,000	23,750	—	202,626
Total operating expenses	1,276,084	1,089,851	896,319	816,583	977,288
Income from operations	614,838	528,842	591,654	508,220	195,587
Interest expense, net	(77,075)	(77,756)	(61,942)	(56,917)	(52,713)
Foreign exchange gain (loss)	(6,875)	(9,969)	3,372	1,445	8,683
Loss on extinguishment and modification of debt	(1,425)	—	(638)	(16,815)	—
Income before income tax provision (benefit) and equity in loss of investees	529,463	441,117	532,446	435,933	151,557
Income tax provision (benefit)	80,162	(47,740)	135,236	106,399	94,231
Equity in loss of investees	2,203	1,009	379	—	—
Net income	447,098	487,848	396,831	329,534	57,326
Net loss attributable to noncontrolling interests	—	—	—	(1)	(1,061)
Net income attributable to Jazz Pharmaceuticals plc	$447,098	$487,848	$396,831	$329,535	$58,387
Net income attributable to Jazz Pharmaceuticals plc per ordinary share:					
Basic	$7.45	$8.13	$6.56	$5.38	$0.98
Diluted	$7.30	$7.96	$6.41	$5.23	$0.93
Weighted-average ordinary shares used in per share calculations - basic	59,976	60,018	60,500	61,232	59,746
Weighted-average ordinary shares used in per share calculations - diluted	61,221	61,317	61,870	63,036	62,614

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	As of December 31,				
	2018	2017	2016(1)	2015	2014(2)
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investments	$824,622	$601,035	$425,963	$988,785	$684,042
Working capital	888,518	674,330	490,663	1,031,025	799,044
Total assets	5,203,491	5,123,672	4,800,227	3,332,612	3,308,617
Long-term debt, current and non-current (1)(2)	1,596,412	1,581,038	2,029,625	1,188,444	1,313,161
Retained earnings	841,050	917,956	528,907	302,686	34,704
Total Jazz Pharmaceuticals plc shareholders' equity	2,757,422	2,713,097	1,877,339	1,598,646	1,371,144

(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 that provided 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. In the third quarter of 2017, we completed a private placement of $575.0 million aggregate principal amount of 1.50% exchangeable senior notes due 2024, or the 2024 Notes, resulting in net proceeds to us, after debt issuance costs, of $559.4 million. We used a portion of the net proceeds from the issuance of the 2024 Notes to repay all then outstanding borrowings under the revolving credit facility. In June 2018, we entered into a second amendment of our 2015 credit agreement, which amended agreement we refer to in this report as our amended credit agreement, which increased our revolving credit facility from $1.25 billion to $1.60 billion, extended the maturity dates of our term loan facility and revolving credit facility from July 12, 2021 to June 7, 2023, and reduced the applicable margin for determining the interest rates on outstanding borrowings under the facilities.

(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 $1.0 billion 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.

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

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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 a global biopharmaceutical company dedicated to developing life-changing medicines for people with limited or no options. As a leader in sleep medicine and with a growing hematology/oncology portfolio, we have a diverse portfolio of products and product candidates in development.

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 adult and pediatric 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 who have developed hypersensitivity to E. coli-derived asparaginase;
- 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, 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; and
- Vyxeos® (daunorubicin and cytarabine) liposome for injection, a product approved in the U.S. and in Europe (where it is marketed as Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia, or t-AML, or acute myeloid leukemia, or AML, with myelodysplasia-related changes, or AML-MRC.

We are also seeking approval in the U.S. and Europe for solriamfetol as a treatment to improve wakefulness and reduce EDS in adult patients with narcolepsy or obstructive sleep apnea, or OSA. If we are successful in obtaining FDA approval, we expect to launch the product in the U.S. after scheduling review by the U.S. Drug Enforcement Administration, or DEA, which will need to be completed after approval of our new drug application, or NDA, if any, but before commercial launch.

We are developing JZP-258, an oxybate product candidate that contains 90% less sodium than Xyrem, for the treatment of both cataplexy and EDS in narcolepsy as well as for other conditions. Subject to the results of our Phase 3 clinical trial in narcolepsy, we expect to file an NDA for approval of this product by as early as the end of 2019.

Our strategy to create shareholder value is focused on:

- Strong financial execution through growth in sales of our current lead marketed products;
- Building a diversified product portfolio and development pipeline through a combination of our internal research and development efforts and obtaining rights to clinically meaningful and differentiated on- or near-market products and early- to late-stage product candidates through acquisitions, collaborations, licensing arrangements, partnerships and venture investments; and
- Maximizing the value of our products and product candidates by continuing to implement our comprehensive global development plans, including through generating additional clinical data and seeking regulatory approval for new indications.

Our total net product sales increased by 17% in 2018 compared to 2017, primarily due to an increase in Xyrem net product sales and a full year of net product sales of Vyxeos, which launched in the U.S. in August 2017. We expect total net product sales to increase in 2019 over 2018, primarily due to expected growth in sales of Xyrem and Vyxeos.

In 2018, in support of our strategy, we continued to expand and advance our research and development pipeline in our sleep and hematology/oncology therapeutic areas, both by conducting activities internally and by leveraging partnerships with third parties. A summary of our ongoing development activities is provided under "Business—Research and Development" in Part I, Item 1 of this Annual Report on Form 10-K. In 2019 and beyond, we expect that our

research and development expenses will continue to increase from historical levels, particularly as we prepare for anticipated regulatory submissions and data read-outs from clinical trials, initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates.

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2018 Highlights and Recent Developments

Regulatory Approvals

- In August 2018, the European Commission, or EC, granted marketing authorization for Vyxeos for the treatment of adults with newly-diagnosed t-AML or AML-MRC, and shortly thereafter, we commenced a rolling launch of Vyxeos in the European Union, or EU.
- In October 2018, the FDA approved our supplemental NDA to revise the labeling for Xyrem to include an indication to treat cataplexy or EDS in pediatric narcolepsy patients ages seven and older and granted Xyrem pediatric exclusivity, adding six months to any regulatory or Orange Book patent exclusivity.

Regulatory Submissions

- In March 2018, the FDA accepted for filing our NDA seeking marketing approval for solriamfetol for the treatment of EDS associated with OSA or narcolepsy in adult patients; the target action date for the FDA under the Prescription Drug User Fee Act, or PDUFA, for a new molecular entity, originally December 20, 2018, was extended by the FDA to March 20, 2019.
- In November 2018, we submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for solriamfetol for the treatment of EDS associated with OSA or narcolepsy in adult patients.

Research & Development

- In August 2018, we announced a five-year collaboration with The University of Texas MD Anderson Cancer Center to evaluate potential treatment options for hematologic malignancies, with a near-term focus on Vyxeos, and shortly thereafter, commenced development activities pursuant to this collaboration.
- During 2018, we commenced and/or advanced several development programs in both sleep and hematology/oncology, including (i) completing patient enrollment in our Phase 3 clinical trial evaluating JZP-258 for the treatment of EDS and cataplexy in narcolepsy, (ii) commencing patient enrollment in our Phase 3 clinical trial evaluating JZP-258 for the treatment of idiopathic hypersomnia and (iii) commencing patient enrollment in our Phase 2 clinical trial evaluating defibrotide for the prevention of acute Graft-versus-Host Disease.

Other Significant Developments

- In April 2018, we reached an agreement in principle with the U.S. Department of Justice, or DOJ, on a proposal for a civil settlement of potential claims by the DOJ with respect to an investigation of our support of 501(c)(3) organizations that provide financial assistance to Medicare patients in the amount of $57.0 million, subject to accrual of interest on the settlement amount from the date of the agreement in principle, negotiation of a definitive settlement agreement and other contingencies, which we expect will include entry into a corporate integrity agreement with the Office of Inspector General of the U.S. Department of Health and Human Services.
- In May 2018, we purchased a rare pediatric disease priority review voucher, or PRV, from Spark Therapeutics, Inc. for $110.0 million. We may use the PRV to obtain priority review by the FDA for one of our future regulatory submissions.
- In June 2018, we entered into a second amendment to our 2015 credit agreement, referred to as our amended credit agreement in this report. With the second amendment, we increased the amounts available under our revolving credit facility from $1.25 billion to $1.60 billion, extended the maturity dates of our term loan facility and revolving credit facility from July 12, 2021 to June 7, 2023, and reduced the applicable margin for determining the interest rates on outstanding borrowings under the facilities.
- With entry into a settlement agreement and related agreements resolving our patent infringement litigation against Amneal Pharmaceuticals LLC in October 2018, we settled all outstanding patent infringement litigation against the nine companies that have filed abbreviated new drug applications, or ANDAs, requesting approval to market generic versions of Xyrem.
- We announced increases in our share repurchase authorization of $320 million and $400 million in November and December 2018, respectively. During 2018, we repurchased an aggregate of $523.7 million of our ordinary shares at an average price of $148.33 per share.
- In January 2019, we entered into a strategic collaboration agreement with Codiak BioSciences, Inc., or Codiak, focused on the research, development and commercialization of exosome therapeutics to treat cancer.

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Challenges, Risks and Trends Related to Our Business

Xyrem. Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which accounted for 75% and 74% of our net product sales for the years ended December 31, 2018 and 2017, respectively. Our future plans assume that sales of Xyrem will increase, but there is no guarantee 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 2019, and there is no guarantee that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes and revenues from Xyrem.

As discussed above, we have settled patent litigation with all nine companies that have filed ANDAs with the FDA seeking approval to market a generic version of Xyrem. To date, the FDA has approved or tentatively approved three of these ANDAs, and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs. In connection with the ANDA settlement agreements, we granted four of the filers the right to sell an authorized generic version of Xyrem, or an AG Product, and we granted each of the nine filers a license to launch its own generic sodium oxybate product. The actual timing of the launch of an AG Product or generic sodium oxybate product is uncertain because the launch dates of the AG Products and generic sodium oxybate products under our settlement agreements are subject to acceleration under certain circumstances. In the absence of any circumstances triggering acceleration, the earliest launch of an AG Product would be January 1, 2023. For a further description of the settlement agreements, including a more complete description of potential dates of market entry for an AG Product(s) and generic sodium oxybate product(s) and circumstances that might trigger acceleration of such dates, see the risk factor under the heading “The introduction of a new product in the U.S. market that competes with, or otherwise disrupts the market for, Xyrem would adversely affect sales of Xyrem” in Part I, Item 1A of this Annual Report on Form 10-K.

In addition to generic and authorized generic versions of Xyrem, we and others may launch products as treatment options in cataplexy and/or EDS in patients with narcolepsy, including other branded sodium oxybate products and other new and existing branded market entrants. For example, Avadel Pharmaceuticals plc is conducting a Phase 3 clinical trial of a once-nightly formula of sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy, and has indicated that it intends to seek approval of its product candidate in the U.S. under a Section 505(b)(2) NDA approval pathway. Other companies may also develop a sodium oxybate or similar product using, for example, an alternative formulation or a different delivery technology and pursue a similar regulatory approval strategy in the future.

Non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy, even if not directly competitive with Xyrem, could have the effect of changing treatment regimens and payor coverage of Xyrem, and indirectly materially and adversely affect sales of Xyrem. Prescribers often prescribe stimulants or wake-promoting agents for treatment of EDS, and anti-depressants for cataplexy, before prescribing or instead of prescribing Xyrem, and payors often require patients to try such medications before they will cover Xyrem. It is possible that additional branded or generic products may be introduced to treat symptoms of narcolepsy that will also be prescribed before or instead of Xyrem, or that payors will require patients to try before they will cover Xyrem. Product candidates currently seeking approval for treatment of symptoms of narcolepsy include our product candidate, solriamfetol, which is seeking an indication to treat EDS associated with narcolepsy and with OSA, and pitolisant, a drug that has already been approved in Europe to treat adult patients with narcolepsy with or without cataplexy. Harmony Biosciences LLC, or Harmony, has exclusive U.S. rights to seek approval of and commercialize pitolisant. Harmony has established an expanded access program for pitolisant, received Breakthrough Therapy and Fast Track designations from the FDA, and, in February 2019, announced that the FDA had accepted for filing with priority review its pitolisant NDA.

The receipt of marketing approval and commercialization of an alternative product approved in the U.S. for the treatment of narcolepsy patients could negatively impact our ability to maintain and grow sales of Xyrem, largely due to payor actions taken in response to the disruption of the narcolepsy market. This could have the additional impact of potentially triggering acceleration of market entry of the AG Products or other generic sodium oxybate products under our ANDA litigation settlement agreements. We expect that the approval and launch of any other sodium oxybate or alternative product that treats narcolepsy, or the launch of an AG Product or other generic version of Xyrem, could

have a material adverse effect on our sales of and revenues from Xyrem and on our business, financial condition, results of operations and growth prospects.

Future Xyrem sales may also be impacted by changes to, or uncertainties around, regulatory restrictions, including changes to our current Xyrem risk evaluation and mitigation strategy, or REMS, which requires, among other things, that Xyrem be distributed through a single pharmacy. We cannot predict whether the FDA will request, seek to require or ultimately require modifications to, or impose additional requirements on, the Xyrem REMS, including in connection with the submission of applications for new oxybate products, new oxybate indications or the introduction of authorized generics, or whether the FDA will approve modifications to the Xyrem REMS that we consider warranted in connection with the submission of applications for new oxybate products. We may face pressure to further modify the Xyrem REMS or to license or share intellectual property pertinent to the Xyrem REMS, including proprietary data required for the safe distribution of sodium oxybate, in connection with the FDA's approval of the generic sodium oxybate REMS or otherwise. Any such modifications to the Xyrem REMS approved, required or rejected by the FDA could make it more difficult or expensive for us to distribute

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Xyrem, make distribution easier for sodium oxybate competitors, disrupt continuity of care for Xyrem patients and/or negatively affect sales of Xyrem. We also cannot predict the impact of future implementation of a generic sodium oxybate REMS on the Xyrem REMS.

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 9% and 12% of our net product sales for the years ended December 31, 2018 and 2017, respectively. Erwinaze is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL, a company that is wholly owned by the UK Department of Health and Social Care. Our license and supply agreement with PBL, which includes our license for Erwinaze, expires on December 31, 2020. We and PBL had been engaged in discussions related to entry into a replacement agreement to extend the term of our commercial relationship with respect to Erwinaze past 2020, but we did not reach agreement. Unless we and PBL enter into a new agreement, we will lose our license to Erwinaze after December 31, 2020, other than our right to sell certain Erwinaze inventory for a post-termination sales period of 12 months. In such event, we may not be able to replace the product sales we would lose from Erwinaze, which in 2018 totaled $174.7 million, and our business, financial condition, results of operations and growth prospects would be materially adversely affected. In addition, we cannot predict whether uncertainty related to rights to, and availability of, Erwinaze after 2020 will impact sales of and revenues from this product.

A continuing and significant challenge to maintaining sales of Erwinaze and a barrier to increasing sales is PBL's inability to consistently supply product adequate to meet market demand. All Erwinaze that PBL has been able to supply is currently completely absorbed by demand for the product. In addition, PBL is subject to a January 2017 warning letter issued by the FDA citing significant violations of the FDA's current Good Manufacturing Practices, or cGMP, as well as an inspection report from the UK Medicines and Healthcare Products Regulatory Agency listing several major findings, including major deficiencies and failures by PBL to comply with cGMP. PBL's product quality and manufacturing issues have resulted, and continue to result, in disruptions in our ability to supply markets from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions during 2019. These supply disruptions will continue to adversely impact our ability to generate sales of and revenues from Erwinaze and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Defitelio/defibrotide. Sales of Defitelio/defibrotide accounted for 8% of our net product sales for the years ended December 31, 2018 and 2017. Our ability to maintain and grow sales and to realize the anticipated benefits from our investment in Defitelio is subject to a number of risks and uncertainties, including continued acceptance by hospital pharmacy and therapeutics committees in the U.S., the continued availability of favorable pricing and adequate coverage and reimbursement, the limited experience of, and need to educate, physicians in recognizing, diagnosing and treating VOD, and the limited size of the population of VOD patients who are indicated for treatment with Defitelio. If sales of Defitelio do not reach the levels we expect, our anticipated revenue from the product will be negatively affected and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Vyxeos. Sales of Vyxeos accounted for 5% and 2% of our total net product sales for the years ended December 31, 2018 and 2017, respectively. We began selling Vyxeos in the U.S. in August 2017 following NDA approval, and the launch is still at an early stage. In August 2018, the EC granted marketing authorization for Vyxeos. We have commenced our rolling launch of Vyxeos in the EU, and we are in the process of making pricing and reimbursement submissions in EU member states.

Our ability to realize the anticipated benefits from our investment in Vyxeos is subject to a number of risks and uncertainties, including acceptance by hospital pharmacy and therapeutics committees in the U.S., the EU and other countries, the availability of adequate coverage, pricing and reimbursement approvals, competition from new and existing products and potential competition from products in development, and delays or problems in the supply or manufacture of Vyxeos. If sales of Vyxeos 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.

Solriamfetol. In December 2018, the FDA determined that a submission we made during the course of discussions regarding draft labeling for solriamfetol constituted a major amendment to the NDA we submitted in 2017, resulting in a three-month extension of the PDUFA goal date, from December 20, 2018 to March 20, 2019. In the fourth quarter of 2018, we submitted an MAA to the EMA for solriamfetol. We cannot predict the results of our labeling discussions with the FDA or whether our NDA or MAA will be approved in a timely manner, or at all.

Even if we obtain approval, our ability to realize the anticipated benefits from our investment in solriamfetol is subject to a number of risks and uncertainties, including, among other things, potential launch delays after any approval, including due to the need for DEA scheduling review which will need to be completed after NDA approval, if any, but before commercial launch; the availability of adequate formulary positions and pricing and adequate coverage and reimbursement by government programs and other third party payors, including the impact of any delays in coverage decisions by payors; restrictions on permitted promotional activities based on limitations on the approved labeling for the product required by the FDA or the EC;

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market acceptance for an approved solriamfetol product, particularly by OSA physicians; delays or problems in the supply or manufacture of an approved solriamfetol product; and our ability to satisfy post-marketing commitments and requirements, if any, imposed by the FDA in connection with its approval of our NDA and by the EC in connection with its marketing authorization. If we are unable to obtain approval of our solriamfetol NDA and/or our MAA in a timely manner, or at all, if the FDA or EC requires product labeling that negatively impacts patient, physician or payor acceptance of the product, or if sales of an approved solriamfetol product in the U.S. and EU 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 2019 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 this regard, a key aspect of our growth strategy is our continued and growing investment in research and development activities. Our ability to successfully develop product candidates for one or more indications as well as our ability to identify new indications for existing products are subject to a number of risks and uncertainties, such as 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. In addition, obtaining regulatory approval for product candidates is subject to the inherent uncertainty associated with the regulatory approval process, especially as we continue to increase investment in our product pipeline development projects and undertake planned regulatory submissions for our product candidates.

We also seek to expand our business through corporate development activities. Our ability to identify and acquire, in-license or develop additional products or product candidates to grow our business are subject to a number of risks and uncertainties, including the risks associated with business combination or product or product candidate acquisition transactions, such as the challenges inherent in the integration of acquired businesses with our 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.

We are increasingly experiencing pressure from third party payors to agree to discounts, rebates or other restrictive pricing terms for Xyrem. As our business becomes more complex, we may need to enter into rebate agreements in order to ensure that patients continue to have access to Xyrem, and to support the long-term success of our sleep franchise, which might result in lower net revenues for Xyrem. In addition to increasing pricing pressure from, and restrictions on reimbursement imposed by, governmental and private third party payors, due to the attention being paid globally to healthcare cost containment, drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny by both federal and state governments, including with respect to companies that have increased the price of products after acquiring those products from other companies. In addition, REMS programs have increasingly drawn public scrutiny from the U.S. Congress, the Federal Trade Commission and the FDA, with allegations that such programs are used as a means of improperly blocking or delaying competition. If we become the subject of any government investigation with respect to drug pricing or other business practices, including as they relate to the Xyrem REMS or otherwise, we could incur significant expense and could be distracted from operation of our business and execution of our strategy.

In 2016 and 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of charitable organizations that provide financial assistance to Medicare patients. In April 2018, we reached an agreement in principle with the DOJ on a proposal for a civil settlement of potential claims by the DOJ in the amount of $57.0 million, subject to accrual of interest on the settlement amount from the date of the agreement in principle, negotiation of a definitive settlement agreement and other contingencies. We cannot provide assurances that our efforts to reach a final settlement with the DOJ will be successful or, if they are, the timing or final terms of any such settlement. We expect any such settlement will involve entry into a corporate integrity agreement, which will impose significant costs and operational burdens on our business. Moreover, a failure to comply with the

terms of a corporate integrity agreement could result in monetary penalties or a reduction or elimination of coverage for our products by federal health care programs such as Medicare and Medicaid and state health care programs. 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.

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Results of Operations

The following table presents revenues and expenses for the years ended December 31, 2018, 2017 and 2016 (in thousands except percentages):

	2018	Change	2017	Change	2016 (1)
Product sales, net	$1,869,473	17 %	$1,601,399	8 %	$1,477,261
Royalties and contract revenues	21,449	24 %	17,294	61 %	10,712
Cost of product sales (excluding amortization of intangible assets)	121,544	10 %	110,188	5 %	105,386
Selling, general and administrative	683,530	26 %	544,156	8 %	502,892
Research and development	226,616	14 %	198,442	22 %	162,297
Intangible asset amortization	201,498	33 %	152,065	49 %	101,994
Impairment charges	42,896	N/A(2)	—	N/A(2)	—
Acquired in-process research and development	—	N/A(2)	85,000	N/A(2)	23,750
Interest expense, net	77,075	(1)%	77,756	26 %	61,942
Foreign exchange loss (gain)	6,875	(31)%	9,969	(396)%	(3,372)
Loss on extinguishment and modification of debt	1,425	N/A(2)	—	N/A(2)	638
Income tax provision (benefit)	80,162	(269)%	(47,470)	(135)%	135,236
Equity in loss of investees	2,203	118 %	1,009	166 %	379

(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) 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, 2018, 2017 and 2016 (in thousands except percentages):

	2018	Change	2017	Change	2016
Xyrem	$1,404,866	18 %	$1,186,699	7 %	$1,107,616
Erwinaze/Erwinase	174,739	(11)%	197,340	(2)%	200,678
Defitelio/defibrotide	149,448	12 %	133,650	23 %	108,952
Vyxeos	100,835	198 %	33,790	N/A(1)	—
Prialt	20,839	(24)%	27,361	(6)%	29,120
Other	18,746	(17)%	22,559	(27)%	30,895
Product sales, net	1,869,473	17 %	1,601,399	8 %	1,477,261
Royalties and contract revenues	21,449	24 %	17,294	61 %	10,712
Total revenues	$1,890,922	17 %	$1,618,693	9 %	$1,487,973

(1) Comparison to prior period is not meaningful.

Product Sales, Net

Xyrem product sales increased by 18% in 2018 compared to 2017 primarily due to an increase in sales volume and, to a lesser extent, a higher average net selling price. Xyrem product sales volume increased by 9% in 2018 compared to 2017 primarily driven by an increase in the average number of patients on Xyrem. Price increases were instituted in January 2018 and in January and July 2017. Xyrem product sales increased by 7% in 2017 compared to 2016 primarily due to higher average net selling prices, partially offset by higher gross to net deductions. Sales volumes in 2017 were consistent with 2016; sales growth was impacted by payor mix throughout 2017 and by operational changes that delayed some prescription fulfillment in the second half of 2017. Erwinaze/Erwinase product sales decreased in 2018 and 2017 compared to the immediately preceding years primarily due to lower sales volume as a result of limited supply from the manufacturer. Ongoing supply challenges continue to negatively impact our ability to supply the market. We are experiencing supply disruptions globally and expect further supply disruptions during

2019. Defitelio/defibrotide product sales increased in 2018 compared to 2017, primarily due to higher volumes and, to a lesser extent, the positive impact of foreign exchange rates. Defitelio/defibrotide product sales

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increased in 2017 compared to 2016, primarily due to the impact of a full year of sales in the U.S. in 2017. Vyxeos product sales in 2018 and 2017 were $100.8 million and $33.8 million, respectively, following its launch in the U.S. in August 2017 and rolling launch in the EU beginning in August 2018. Prialt product sales decreased in 2018 and 2017 compared to the immediately preceding years primarily due to a decrease in volume. We completed the sale of our rights to Prialt to TerSera Therapeutics LLC, or TerSera in September 2018. Other product sales decreased in 2018 and in 2017 compared to the immediately preceding years, primarily due to a decrease in sales of our psychiatry products due to generic competition. We expect total product sales will increase in 2019 over 2018, primarily due to expected growth in sales of Xyrem and Vyxeos.

Royalties and Contract Revenues

Royalties and contract revenues increased in 2018 and in 2017 compared to the immediately preceding years, primarily due to higher one-time milestone revenues from out-licensing agreements. We expect royalties and contract revenues to decrease in 2019 compared to 2018 primarily due to lower milestone revenues from out-licensing arrangements.

Cost of Product Sales

Cost of product sales increased in 2018 and in 2017 compared to the immediately preceding years, primarily due to changes in product mix and increases in net product sales. Gross margins as a percentage of net product sales were 93.5%, 93.1% and 92.9% in 2018, 2017 and 2016, respectively. The increase in the gross margin percentage in 2018 and in 2017 compared to the immediately preceding years was primarily due to changes in product mix. We expect that our gross margin as a percentage of net product sales will not change materially in 2019 compared to 2018.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased in 2018 compared to 2017 primarily due to an accrued estimated loss contingency, including related interest, of $58.2 million. In April 2018, we reached an agreement in principle with the DOJ on a proposal for a civil settlement of potential claims by the DOJ in the amount of $57.0 million, subject to accrual of interest on the settlement amount from the date of the agreement in principle, negotiation of a definitive settlement agreement and other contingencies. For a further description of this matter, see Note 12, Commitments and Contingencies—Legal Proceedings, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K. Selling, general and administrative expenses in 2018 also included expenses related to the potential commercial launch of solriamfetol in the U.S. and the rolling launch of Vyxeos in the EU, and an increase in compensation-related expenses driven by higher headcount compared to 2017. Selling, general and administrative expenses increased in 2017 compared to 2016, primarily due to an increase in compensation-related expenses, primarily driven by higher headcount, and an increase in other expenses related to the expansion and support of our business, including expenses related to the launch of Vyxeos in the U.S., partially offset by the impact in 2016 of transaction and integration expenses related to the Celator Acquisition of $13.1 million and a one-time contract termination fee of $11.6 million to eliminate a potential future royalty obligation related to Vyxeos. We expect selling, general and administrative expenses in 2019 to increase compared to 2018, primarily due to an increase in compensation-related expenses driven by higher headcount and other expenses related to the expansion and support of our business and an increase in expenses related to the preparation for the potential commercial launch of solriamfetol in the U.S. and the continuation of the commercial launch of Vyxeos in the EU.

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.

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

	Year Ended December 31,		
	2018	2017	2016
Clinical studies and outside services	$117,903	$93,317	$100,165
Personnel expenses	71,158	63,941	47,969
Milestone expense	11,000	19,500	750
Other	26,555	21,684	13,413
Total	$226,616	$198,442	$162,297

Research and development expenses increased by $28.2 million in 2018 compared to 2017. Clinical studies and outside services costs increased in 2018 compared to 2017 primarily due to an increase in expenses related to our ongoing preclinical and clinical development programs and support of partner programs, partially offset by lower clinical trial costs following the completion of three Phase 3 clinical trials for solriamfetol. Personnel expenses increased by $7.2 million in 2018 compared to 2017, primarily due to increased headcount in support of our development programs. Milestone expense of $11.0 million in 2018 related to milestone payments following FDA acceptance of our NDA for solriamfetol in March 2018. Research and development expenses increased by $36.1 million in 2017 compared to 2016. Clinical studies and outside services costs decreased in 2017 compared to 2016 primarily due to lower clinical trial costs following the completion of three Phase 3 clinical trials for solriamfetol, partially offset by an increase in expenses related to other clinical development programs and higher costs in respect of regulatory activities. Personnel expenses increased by $16.0 million in 2017 compared to 2016, primarily driven by increased headcount in support of our development programs. Milestone expense in 2017 related to payments made under the license and option agreement with Pfenex, Inc., or Pfenex, which we entered into in July 2016 and amended in December 2017, for worldwide rights to develop and commercialize multiple early-stage hematology product candidates.

For 2019 and beyond, we expect that our research and development expenses will continue to increase from historical levels, particularly as we prepare for anticipated regulatory submissions and data read-outs from clinical trials, initiate and undertake 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 and regulatory submissions for 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.

Intangible Asset Amortization

Intangible asset amortization increased in 2018 and in 2017 compared to the immediately preceding years, primarily due to the commencement of amortization of the Vyxeos intangible asset upon FDA approval in August 2017. Intangible asset amortization is expected to increase in 2019 compared to 2018 as a result of the reduction in the estimated remaining useful life of the Erwinaze intangible asset due to the receipt of a contract termination notice from PBL in February 2019.

Impairment Charges

In June 2018, we entered into an asset purchase agreement, or APA, with TerSera, pursuant to which TerSera agreed to purchase substantially all of the assets held by us related to Prialt. In connection with the entry into the APA, which was subsequently amended, we reclassified the Prialt assets to be transferred to TerSera as assets held for sale and recorded these assets at fair value, less estimated sales costs, resulting in the recognition of an impairment charge of $42.9 million in 2018. The transaction closed on September 27, 2018.

Acquired In-Process Research and Development

In 2017, acquired in-process research and development, or IPR&D, expense was primarily related to an upfront payment of $75.0 million in connection with a collaboration and option agreement with ImmunoGen, Inc., or ImmunoGen to acquire rights to opt into exclusive, worldwide licenses to develop and commercialize two hematology-related antibody-drug conjugate, or ADC programs, as well as an additional program to be designated

during the term of the agreement.

In 2016, acquired 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 $8.8 million. In July 2016, we made upfront and option payments of $15.0 million to Pfenex.

Interest Expense, Net

Interest expense, net decreased by $0.7 million in 2018 compared to 2017, primarily due to higher interest income, partially offset by the interest expense on our 1.50% exchangeable senior notes due 2024, or the 2024 Notes, which were issued in August 2017. Interest expense, net increased by $15.8 million in 2017 compared to 2016, primarily due to the increase in

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our average debt balance and higher interest rates in 2017. We expect interest expense, net will be lower in 2019 compared to 2018 primarily due to higher interest income.

Foreign Exchange Loss (Gain)

The foreign exchange loss (gain) is primarily related to the translation of euro-denominated net monetary liabilities, primarily intercompany balances, held by subsidiaries with a U.S. dollar functional currency and related foreign exchange forward contracts not designated as hedging instruments.

Loss on Extinguishment and Modification of Debt

In 2018, we recorded a loss of $1.4 million in connection with the second amendment of our 2015 credit agreement in June 2018, related to unamortized debt issuance costs and original issue discount associated with extinguished debt and new third party fees associated with modified debt. In 2016, we recorded a loss of $0.6 million in connection with the first amendment of our 2015 credit agreement in July 2016, which was primarily comprised of new third party fees associated with the modified debt.

Income Tax Provision (Benefit)

Our income tax provision was $80.2 million and $135.2 million in 2018 and 2016, respectively, and our income tax benefit was $47.7 million in 2017. The income tax provision in 2017 included a benefit of $148.8 million relating to the enactment of the U.S. Tax Cuts and Jobs Act, or the U.S. Tax Act. The effective tax rates for 2018, 2017 and 2016 were 15.1%, (10.8)% and 25.4%, respectively. The income tax benefit recognized for 2017 in respect of the enactment of the U.S. Tax Act resulted in a net decrease to our effective tax rate of 33.7%. The effective tax rates for 2018 and 2016 were higher than the Irish statutory rate of 12.5%, primarily due to income taxable at a rate higher than the Irish statutory rate and unrecognized tax benefits, partially offset by the release of reserves related to unrecognized tax benefits upon the expiration of a statute of limitation, originating tax credits and the release of a valuation allowance held primarily against certain foreign net operating losses or NOLs. The effective tax rate for 2017 was lower than the Irish statutory rate of 12.5%, primarily due to the impact of the enactment of the U.S. Tax Act. The increase in the effective tax rate for 2018 compared to 2017 was primarily due to the impact of the enactment of the U.S. Tax Act. Excluding this effect, the effective rate in 2018 would have decreased compared to 2017 primarily due to a decrease in the U.S. corporate income tax rate. The decrease in the effective tax rate in 2017 compared to 2016 was primarily due to the release of a valuation allowance held against certain foreign NOLs and the release of reserves related to unrecognized tax benefits upon the expiration of a statute of limitation, partially offset by a reduction in deductions available in relation to subsidiary equity.

Equity in Loss of Investees

Equity in loss of investees relates to our share in the net loss of companies in which we have made investments accounted for under the equity method of accounting.

Liquidity and Capital Resources

As of December 31, 2018, we had cash, cash equivalents and investments of $824.6 million, borrowing availability under our revolving credit facility of $1.6 billion and a long-term debt principal balance of $1.8 billion. Our long-term debt included $651.0 million aggregate principal amount term loan, $575.0 million principal amount of the 2021 Notes and $575.0 million principal amount of the 2024 Notes. During 2018, 2017 and 2016, we generated cash flows from operations of $798.9 million, $693.1 million and $592.4 million, respectively, and we expect to continue to generate positive cash flow from operations.

We believe that our existing cash, cash equivalents and investments 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 Our Other Marketed Products” 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, development, manufacturing and other operations. In this regard, we have evaluated and expect to continue to evaluate a wide array of

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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 November 2015, 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 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 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 November and December 2018, our board of directors increased the existing share repurchase program authorization by $320.0 million and $400.0 million, respectively, thereby increasing the total amount authorized to $1.02 billion. 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 repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2018, we spent a total of $523.7 million to purchase 3.5 million of our ordinary shares under the share repurchase program at an average total purchase price, including brokerage commissions, of $148.33 per share. In 2017, we spent a total of $98.8 million to repurchase 0.7 million of our ordinary shares at an average total purchase price, including brokerage commissions, of $140.34 per share. All ordinary shares repurchased were canceled. As of December 31, 2018, the remaining amount authorized under the share repurchase program was $379.1 million.

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

	Year Ended December 31,		
	2018	2017	2016
Net cash provided by operating activities	$798,904	$693,087	$592,391
Net cash used in investing activities	(394,487)	(268,950)	(1,751,155)
Net cash provided by (used in) financing activities	(479,130)	(409,111)	540,987
Effect of exchange rates on cash and cash equivalents	(1,700)	5,046	(5,045)
Net increase (decrease) in cash and cash equivalents	$(76,413)	$20,072	$(622,822)

Net cash provided by operating activities of $798.9 million in 2018 related to net income of $447.1 million, adjusted for non-cash items of $328.5 million primarily related to intangible asset amortization, share-based compensation, impairment charges, amortization of debt discount and deferred financing costs and deferred income taxes and a net cash inflow of $23.3 million related to changes in operating assets and liabilities. Net cash provided by operating activities of $693.1 million in 2017 related to net income of $487.8 million, adjusted for acquired IPR&D expense totaling $85.0 million and non-cash items of $93.5 million primarily related to intangible asset amortization, share-based compensation, amortization of debt discount and deferred financing costs and deferred income taxes and a net cash inflow of $26.8 million related to changes in operating assets and liabilities. Net cash provided by operating activities of $592.4 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, amortization of debt discount and deferred financing costs and deferred income taxes. This was partially offset by $20.9 million of net cash outflow related to changes in operating assets and liabilities.

Net cash used in investing activities in 2018 primarily related to the net acquisition of investments of $310.9 million, acquisition of intangible assets of $111.1 million related to the purchase of a PRV and purchases of property, plant and equipment of $20.4 million, partially offset by net proceeds of $47.9 million from the sale of our rights to Prialt to TerSera. Net cash used in investing activities in 2017 primarily related to the net acquisition of investments of $155.0 million, upfront payments for acquired IPR&D of $85.0 million primarily related to a collaboration and option agreement with ImmunoGen and purchases of property, plant and equipment of $29.0 million. 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 Pharmaceuticals, Inc. that was triggered by the FDA approval of Defitelio on March 30, 2016, net acquisition of investments of $65.3 million and upfront and option payments of $23.8 million to acquire IPR&D assets.

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Net cash used in financing activities in 2018 primarily related to repurchase of ordinary shares under our share repurchase program of $523.7 million, repayment of our term loan principal of $25.7 million, payment of employee withholding taxes of $17.9 million related to share-based awards and payment of debt modification costs of $6.4 million, partially offset by proceeds from employee equity incentive and purchase plans of $93.3 million. Net cash used in financing activities in 2017 primarily related to repayment of borrowings under our revolving credit facility of $850.0 million, repurchase of ordinary shares under our share repurchase program of $98.8 million, repayment of our term loan principal of $36.1 million and payment of employee withholding taxes of $18.6 million related to share-based awards, partially offset by net proceeds from issuance of debt of $559.4 million, proceeds from employee equity incentive and purchase plans of $31.8 million and proceeds from a tenant improvement allowance on a build-to-suit lease of $3.2 million. 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 term loan principal, respectively, and payment of employee withholding taxes of $21.2 million related to share-based awards.

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 a 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 to provide for a revolving credit facility of $1.25 billion 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.

On June 7, 2018, we entered into the second amendment to the 2015 credit agreement to provide for a revolving credit facility of $1.60 billion, which replaced the existing revolving credit facility of $1.25 billion, and a new $667.7 million term loan facility, which replaced the $750.0 million term loan facility, of which $651.0 million principal amount was outstanding as of December 31, 2018. We refer to the 2015 credit agreement as amended by the first and second amendments as the amended credit agreement in this report. We expect to use the proceeds from future loans under the revolving credit facility, if any, for permitted capital expenditures and acquisitions, to provide for ongoing working capital requirements and for other general corporate purposes.

Under the amended credit agreement, the term loan matures on June 7, 2023 and the revolving credit facility terminates, and any loans outstanding thereunder become due and payable, on June 7, 2023.

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 1.375% to 1.750% per annum, based upon our secured leverage ratio, or (b) the prime lending rate, plus an applicable margin ranging from 0.375% to 0.750% 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, 2018, the interest rate on the term loan was 3.90% and the effective interest rate was 3.66%. As of December 31, 2018, we had undrawn amounts under our revolving credit facility totaling $1.60 billion.

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 and the 2024 Notes, together referred to as the Exchangeable Senior 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 other exceptions), (2) net cash proceeds from issuances of debt (other than certain permitted debt), and (3) casualty proceeds and condemnation awards (subject to other exceptions). Principal repayments of the term loan, which are due quarterly, are equal to 5.0% per annum of the principal amount outstanding on June 7, 2018 of $667.7 million, with any remaining balance payable on the maturity date.

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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. As of December 31, 2018, we were in compliance with these financial covenants.

Exchangeable Senior Notes

2024 Notes. In the third quarter of 2017, our wholly owned subsidiary Jazz Investments I Limited, completed a private placement of $575.0 million principal amount of 2024 Notes. We used the net proceeds from this offering to repay $500.0 million in outstanding loans under the revolving credit facility under the amended credit agreement and to pay related fees and expenses. We used the remainder of the net proceeds for general corporate purposes. The 2024 Notes are senior unsecured obligations of Jazz Investments I Limited and are fully and unconditionally guaranteed on a senior unsecured basis by Jazz Pharmaceuticals plc and will rank pari passu in right of payment with the existing 2021 Notes. Interest on the 2024 Notes is payable semi-annually in cash in arrears on February 15 and August 15 of each year, beginning on February 15, 2018, at a rate of 1.50% 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 2024 Notes. The 2024 Notes mature on August 15, 2024, unless earlier exchanged, repurchased or redeemed.

The holders of the 2024 Notes have the ability to require us to repurchase all or a portion of their 2024 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, 2024, we may redeem the 2024 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 2024 Notes additional amounts as a result of certain tax-related events. We also may redeem the 2024 Notes on or after August 20, 2021, 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 2024 Notes are exchangeable at an initial exchange rate of 4.5659 ordinary shares per $1,000 principal amount of 2024 Notes, which is equivalent to an initial exchange price of approximately $219.02 per ordinary share. Upon exchange, the 2024 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 2024 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 2024 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2024 Notes who elect to exchange their 2024 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to May 15, 2024, the 2024 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.

2021 Notes. In August 2014, Jazz Investments I Limited completed a private placement of $575.0 million principal amount of the 2021 Notes. The 2021 Notes are 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

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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, 2018 (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	$651,041	$33,387	$66,774	$550,880	$—
Term loan - interest (2)	87,640	21,719	40,089	25,832	—
Exchangeable Senior Notes - principal	1,150,000	—	575,000	—	575,000
Exchangeable Senior Notes - interest (3)	84,094	19,406	38,813	17,250	8,625
Revolving credit facility - commitment fee (4)	17,978	4,056	8,122	5,800	—
Commitment to equity method investees	22,175	7,000	14,000	1,175	—
Purchase and other obligations (5)	146,364	65,075	45,451	29,168	6,670
Operating lease obligations (6)	39,794	8,404	12,040	10,556	8,794
Facility lease obligations (7)	189,843	9,881	29,382	31,171	119,409
Total	$2,388,929	$168,928	$829,671	$671,832	$718,498

(1) This table does not include potential future milestone payments 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. On January 2, 2019, we entered into a strategic collaboration agreement with Codiak for an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize potential therapeutic candidates directed at five targets to be developed using Codiak's engEx™ precision engineering platform for exosome therapeutics. We made an upfront payment of $56.0 million in January 2019. Codiak is eligible to receive up to $20 million in preclinical development milestone payments across all five programs. Codiak is also eligible to receive milestone payments totaling up to $200 million per target based on investigational new drug application acceptance, clinical and regulatory milestones, including approvals in the U.S., the EU and Japan, and certain sales milestones. Codiak is also eligible to receive tiered royalties on net sales of each approved product. In 2014, we signed a definitive agreement with Aerial BioPharma LLC, or Aerial, under which we acquired worldwide development, manufacturing and commercial rights to solriamfetol (other than in certain jurisdictions in Asia where SK Biopharmaceuticals Co., Ltd, or SK, retains rights). Aerial and SK are currently eligible to receive milestone payments up to an aggregate of $259 million based on development, regulatory and sales milestones and tiered royalties from high single digits to mid-teens based on potential future sales of solriamfetol. In July 2016, we entered into an agreement with Pfenex that 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 with Pfenex. This agreement was amended in December 2017. Under the amended agreement, Pfenex received upfront, option and development milestone payments totaling $36 million and may be eligible to receive additional payments of up to $189 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 $85 million. These 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 for variable rate debt was calculated based on the interest rates in effect as of December 31, 2018. The interest rate for our term loan borrowing was 3.90% as of December 31, 2018. Interest that is fixed, associated with our interest rate swaps, is calculated based on the fixed interest swap rate as of December 31, 2018.

(3) We used the fixed interest rates of 1.875% on the 2021 Notes and 1.50% on the 2024 Notes to estimate interest owed as of December 31, 2018 until the respective final maturity dates of these notes.

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(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 0.25% and assumed undrawn amounts of $1.6 billion as of December 31, 2018 to estimate commitment fees owed.

(5) Consists primarily of non-cancelable commitments to our third party manufacturers and to ImmunoGen under our collaboration and option agreement.

(6) Consists primarily of the minimum lease payments for our office buildings and automobile lease payments for our sales force. Operating expenses associated with our leased office buildings are not included in table above.

(7) This includes a lease agreement we entered into in January 2015 to lease office space located in Palo Alto, California in a building subsequently constructed by the landlord, which we occupied beginning in October 2017, and a lease agreement we entered into in September 2017 to lease additional office space located in Palo Alto, California in a second building to be constructed by the same landlord, which we expect to occupy by the end of 2019. Not included in the table above are our estimated costs of approximately $21 million associated with the design, development and construction of tenant improvements under the lease agreement entered into in September 2017, which estimate does not include a tenant improvement allowance to be provided by the landlord.

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, 2018. 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, 2018, 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, 2018, our liability for unrecognized tax benefits amounted to $118.2 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 described in more detail in Note 2, Summary of Significant Accounting Policies, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K, we believe the following accounting estimates and policies to be critical.

Revenue Recognition

Revenues are recognized when control of the promised goods or services is transferred to our customers, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services.

Product Sales, Net

Product sales revenue is recognized when control has transferred to the customer, which occurs at a point in time, 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 is derived from sales of Xyrem. We sell Xyrem in the U.S. to a single central pharmacy, Express Scripts Specialty Distribution Services, Inc., or Express Scripts. In 2018, sales of Xyrem to Express Scripts accounted for 75% of our net product sales. We recognize revenues from sales of Xyrem within the U.S. when control has transferred to the customer, which occurs when Express Scripts removes product from our consigned inventory location at its facility for shipment directly to a patient. We do not accept returns of Xyrem from Express Scripts.

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

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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, 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
Provision, net	144,596	446	41,941	36,642	223,625
Payments/credits	(135,697)	(1,161)	(43,027)	(36,532)	(216,417)
Balance at December 31, 2017	77,162	3,651	3,663	4,309	88,785
Provision, net	160,648	1,203	41,387	42,956	246,194
Payments/credits	(156,696)	(2,344)	(44,642)	(41,808)	(245,490)
Balance at December 31, 2018	$81,114	$2,510	$ 408	$ 5,457	$89,489

Total items deducted from gross product sales were $246.2 million, $223.6 million and $209.6 million, or 11.6%, 12.3% and 12.4% as a percentage of gross product sales, in 2018, 2017 and 2016, 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, 2018, 2017 and 2016.

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 $160.6 million, $144.6 million and $129.6 million, or 7.6%, 7.9% and 7.7% as a percentage of gross product sales, in 2018, 2017 and 2016, respectively. Rebates as a percentage of gross product sales did not change materially in 2018 compared to 2017. We expect that rebates will continue to significantly impact our reported net sales. Rebates as a percentage of gross product sales are expected to decrease in 2019 compared to 2018, primarily due to a decrease in Tricare per unit rebate amounts, partially offset by increased Medicaid utilization for Xyrem.

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 charge of $1.2 million and $0.4 million in 2018 and 2017, respectively, and a credit of $0.5 million in 2016, or 0.1%, 0% and 0% as a percentage of gross product sales in 2018, 2017 and 2016, respectively. Sales returns as a percentage of gross product sales did not change materially in 2018 and 2017 compared to the immediately preceding years. Sales returns as a percentage of gross product sales are not expected to change materially in 2019 compared to 2018.

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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 $41.4 million, $41.9 million and $40.4 million, or 2.0%, 2.3% and 2.4% as a percentage of gross product sales in 2018, 2017 and 2016, respectively. Chargebacks as a percentage of gross product sales did not change materially in 2018 and 2017 compared to the immediately preceding years. We expect that chargebacks will continue to significantly impact our reported net product sales. Chargebacks as a percentage of gross product sales are not expected to change materially in 2019 compared to 2018.

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 $43.0 million, $36.6 million and $40.1 million, or 2.0%, 2.0% and 2.4% as a percentage of gross product sales in 2018, 2017 and 2016, respectively. Discounts and distributor fees as a percentage of gross product sales in 2018 were in line with 2017. Discounts and distributor fees as a percentage of gross product sales decreased in 2017 compared to 2016 primarily due to decreased distributor fees payable to the partner distributors in international markets. 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 2019 compared to 2018.

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 2018 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, 2018, we had $927.6 million of goodwill primarily resulting from the business combination between Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company, which we refer to as the Azur Merger, on January 18, 2012, our acquisition of EUSA Pharma, Inc., or 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:

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- 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.

Finite-lived intangible assets consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives, which range from two to 18 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.

Intangible assets with finite useful lives also includes the PRV we acquired in 2018 which we can use to obtain priority review by the FDA for one of our future regulatory submissions or may sell or transfer to a third party. The PRV is measured at cost and reviewed for impairment when events or circumstances indicate that the carrying value may not be recoverable. At the time we commit to using the PRV to accelerate the review of a drug application, the cost of the PRV will be expensed to the consolidated statement of income. Alternatively, if the PRV is sold, the asset would be derecognized from the consolidated balance sheet.

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, 2018, we had $2.6 billion of finite-lived intangible assets and $0.1 billion of IPR&D assets related to the marketed products and the IPR&D projects that we acquired in the EUSA Acquisition, the Gentium Acquisition and the Celator Acquisition. In relation to the sale of our rights to Prialt to TerSera in 2018, we adjusted the carrying value of the assets held for sale to fair value less costs to sell, which resulted in an impairment charge of $42.9 million in our consolidated statements of income in 2018, primarily related to the carrying balances of intangible assets. We did not recognize an impairment charge related to our intangible assets in 2017 and 2016.

Please refer to Note 9, Goodwill and Intangible assets, of 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, 2018.

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

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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 provision 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,		
	2018	2017	2016
Volatility	35 %	35 %	39 %
Expected term (years)	4.5	4.3	4.2
Range of risk-free rates	2.2-3.0%	1.6-2.1%	0.8-1.6%
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

For a discussion of recent accounting pronouncements, please see Note 2, Summary of Significant Accounting Policies, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

Off-Balance Sheet Arrangements
We do not have any off-balance sheet arrangements.

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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, 2018 consisted of time deposits and money market funds 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 borrowings. On June 7, 2018, we entered into the amended credit agreement to provide for a revolving credit facility of $1.60 billion, which replaced the existing revolving credit facility of $1.25 billion, and a new $667.7 million term loan facility, which replaced the $750.0 million term loan facility, of which $651.0 million principal amount was outstanding as of December 31, 2018. There were no borrowings outstanding under the revolving credit facility as of December 31, 2018. To achieve a desired mix of floating and fixed interest rates on our term loan, we entered into interest rate swap agreements in March 2017 that are designated as cash flow hedges. These derivative instruments are utilized for risk management purposes, and we do not use these derivatives for speculative trading purposes. The interest rate swap agreements have a notional amount of $300.0 million and are effective from March 3, 2017 through July 12, 2021 and convert the floating rate on a portion of our term loan to a fixed rate of 1.895%, plus the borrowing spread. The impact of a hypothetical increase or decrease in interest rates on the fair value of our interest rate swap contracts would be offset by a change in the value of the underlying liability. If interest rates were to increase or decrease by 100 basis points, interest expense for 2019 would increase or decrease by approximately $4 million, based on the unhedged portion of our outstanding variable rate borrowings.

In August 2014, we completed a private placement of $575.0 million aggregate principal amount of the 2021 Notes. In the third quarter of 2017, we completed another private placement of $575.0 million aggregate principal amount of the 2024 Notes. The 2021 Notes and 2024 Notes have fixed annual interest rates of 1.875% and 1.50%, respectively, and we, therefore, do not have economic interest rate exposure on the Exchangeable Senior Notes. However, the fair values of the Exchangeable Senior Notes are exposed to interest rate risk. Generally, the fair values of the Exchangeable Senior Notes will increase as interest rates fall and decrease as interest rates rise. The fair values of the Exchangeable Senior Notes are also affected by volatility in our ordinary share price. As of December 31, 2018, the fair values of the 2021 Notes and the 2024 Notes were estimated to be $558 million and $521 million, respectively.

In July 2017, the Financial Conduct Authority, the authority that regulates LIBOR, announced it intended to stop compelling banks to submit rates for the calculation of LIBOR after 2021. The Alternative Reference Rates Committee, or ARRC, in the U.S. has proposed that the Secured Overnight Financing Rate, or SOFR, is the rate that represents best practice as the alternative to the U.S. dollar, or USD, LIBOR for use in derivatives and other financial contracts that are currently indexed to USD LIBOR. ARRC has proposed a paced market transition plan to SOFR from USD LIBOR and organizations are currently working on industry wide and company specific transition plans as it relates to derivatives and cash markets exposed to USD LIBOR. We have certain financial contracts, including the amended credit agreement and our interest rate swaps, that are indexed to USD LIBOR and are monitoring this activity and evaluating the related risks.

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 or weakening in the rates used to translate the results of our foreign subsidiaries that have functional currencies denominated in the euro would have increased or decreased net income for the year ended December 31, 2018 by approximately $13 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 exchange gain (loss) in the consolidated statements of income. As of December 31, 2018, our primary exposure to transaction risk related to euro net monetary liabilities, including intercompany

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loans, held by subsidiaries with a U.S. dollar functional currency. We have entered into foreign exchange forward contracts to manage this currency risk. 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. As of December 31, 2018, we held foreign exchange forward contracts with notional amounts totaling $271.5 million. The net liability fair value of outstanding foreign exchange forward contracts was $0.3 million as of December 31, 2018. Based on our foreign currency exchange rate exposures as of December 31, 2018, a hypothetical 10% adverse fluctuation in exchange rates would decrease the fair value of our foreign exchange forward contracts by approximately $12 million as of December 31, 2018. The resulting loss on these forward contracts would be offset by a positive impact on the underlying monetary assets and liabilities.

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-45.

	Page
Jazz Pharmaceuticals plc	
Report of Independent Registered Public Accounting Firm	F-1
Consolidated Balance Sheets	F-2
Consolidated Statements of Income	F-3
Consolidated Statements of Comprehensive Income	F-4
Consolidated Statements of Shareholders' Equity	F-5
Consolidated Statements of Cash Flows	F-8
Notes to Consolidated Financial Statements	F-10

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, 2018.

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, 2018, 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

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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, 2018 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, 2018, included herein, and has issued an audit report on our internal control over financial reporting, which is included below.

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Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Jazz Pharmaceuticals plc:

Opinion on Internal Control Over Financial Reporting

We have audited Jazz Pharmaceuticals plc's and subsidiaries' (the "Company") internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, and the related consolidated statements of income, comprehensive income, shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes and financial statements schedule at Item 15(a)2 (collectively, the "consolidated financial statements"), and our report dated February 26, 2019 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

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

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our 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.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ KPMG
Dublin, Ireland
February 26, 2019

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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 2019 annual general meeting of shareholders, or our 2019 Proxy Statement, to be filed pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, or Exchange Act. If our 2019 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 2019 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 2019 Proxy Statement, provided that if the 2019 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 2019 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 2019 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 2019 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 2019 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 2019 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.

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

The information required by this item is to be included in our 2019 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 2019 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 2019 Proxy Statement under the section entitled "Proposal 2—On a Non-Binding Advisory Basis, Ratify Appointment of Independent Registered Accounting Firm 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 2019 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-45 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 herein 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).

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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.
4.3A	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).
4.3B	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).
4.4A	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).
4.4B	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).
4.5A	Indenture, dated as of August 23, 2017, among Jazz Pharmaceuticals Public Limited Company, 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 23, 2017).
4.5B	Form of 1.50% Exchangeable Senior Note due 2024 (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 23, 2017).
10.1	Settlement Agreement, dated as of April 5, 2017, by and between Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited, and Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC (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, 2017, as filed with the SEC on August 8, 2017).
10.2†	

	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).
10.3†	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).

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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	Contract Variation Agreement by and between Porton Biopharma Limited and Jazz Pharmaceuticals France SAS, dated as of December 20, 2018.
10.6†	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).
10.7†	Pharmacy Master Services Agreement, dated as of July 1, 2017, by and between Jazz Pharmaceuticals, Inc. and Express Scripts Specialty Distribution Services, Inc. (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, 2017, as filed with the SEC on August 8, 2017).
10.8A†	Clinical and Commercial Manufacturing and Supply Agreement, dated as of December 22, 2010, between Celator Pharmaceuticals, Inc. and Baxter Oncology GmbH (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the year ended December 31, 2017, as filed with the SEC on February 27, 2018).
10.8B†	Amendment No. 1 Clinical and Commercial Manufacturing and Supply Agreement, dated as of January 18, 2018, by and between Jazz Pharmaceuticals Ireland Limited and Baxter Oncology GmbH (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, 2018, as filed with the SEC on May 8, 2018).
10.9A	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).
10.9B	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).
10.9C	Amendment No. 2, dated as of June 7, 2018, to Credit Agreement, dated as of June 18, 2015 (as previously amended by Amendment No. 1, dated as of July 12, 2016), among Jazz Pharmaceuticals plc, Jazz Securities Designated Activity Company, Jazz Pharmaceuticals, Inc., Jazz Financing I Designated Activity Company, 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 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.10A	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).
10.10B	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).
10.10C	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).
10.11	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).

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10.12A	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).
10.12B	First Amendment, dated as of January 29, 2018, to 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 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.12C	Second Amendment, dated as of July 26, 2018, to 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., as previously amended by the First Amendment to Lease, dated as of January 29, 2018 (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, 2018, as filed with the SEC on November 6, 2018).
10.13A	Commercial Lease, dated as of September 22, 2017, by and between Jazz Pharmaceuticals, Inc. and The Board of Trustees of the Leland Stanford Junior University (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, 2017, as filed with the SEC on November 7, 2017).
10.13B	First Amendment, dated as of January 29, 2018, to Commercial Lease, dated as of September 22, 2017, by and between The Board of Trustees of the Leland Stanford Junior University and Jazz Pharmaceuticals, Inc. (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, 2018, as filed with the SEC on August 7, 2018).
10.14+	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).
10.15+	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).
10.16+	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).
10.17A+	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).
10.17B+	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).
10.17C+	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).
10.17D+	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).
10.18+	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).
10.19A+	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).
10.19B+	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).

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10.19C+	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).
10.19D+	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).
10.21+	Offer Letter from Jazz Pharmaceuticals, Inc. to Daniel N. Swisher, Jr. (incorporated herein by reference to Exhibit 10.21 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the year ended December 31, 2017, as filed with the SEC on February 27, 2018).
10.22A+	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).
10.22B+	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).
10.22C+	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).
10.22D+	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).
10.22E+	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).
10.22F+	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).
10.22G+	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).
10.22H+	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).
10.23A+	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).
10.23B+	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).
10.23C+	Form of Stock Option Grant Notice and Form of 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).
10.23D+	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).

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10.23E+	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).
10.23F+	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).
10.23G+	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).
10.23H+	Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit 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).
10.23I+	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).
10.23J+	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).
10.23K+	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).
10.23L+	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).
10.23M+	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).
10.23N+	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).
10.23O+	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).
10.23P+	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).
10.23Q+	

10.23R+	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).
	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).

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10.23S+	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).
10.23T+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (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, 2018, as filed with the SEC on August 7, 2018).
10.23U+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and 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 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.24+	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).
10.24A+	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).
10.24B+	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).
10.24C+	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).
10.24D+	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).
10.24E+	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).
10.24F+	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 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).
10.24G+	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).
10.24H+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (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, 2018, as filed with the SEC on November 6, 2018).
10.24I+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. 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 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2018, as filed with the SEC on November 6, 2018).
10.25A+	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).

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10.25B+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan Sub-Plan Governing Purchase Rights to Participants in the Republic of Ireland (incorporated herein by reference 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).
10.26A+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved November 3, 2016) (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, 2016, as filed with the SEC on February 28, 2017).
10.26B+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2018) (incorporated herein by reference to Exhibit 10.26C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the year ended December 31, 2017, as filed with the SEC on February 27, 2018).
10.26C+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved October 31, 2018).
10.26D+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2019).
10.27+	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).
10.28+	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).
10.29A+	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).
10.29B+	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).
10.29C+	Amended and Restated Non-Employee Director Compensation Policy (approved May 3, 2018) (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, 2018, as filed with the SEC on August 7, 2018).
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 Principal 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 Principal 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 Principal Executive Officer and Principal 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

+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.

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Item 16. Form 10-K Summary

None.

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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 26, 2019 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)

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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 26, 2019
/s/ MATTHEW P. YOUNG Matthew P. Young	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 26, 2019
/s/ KAREN J. WILSON Karen J. Wilson	Senior Vice President, Finance (Principal Accounting Officer)	February 26, 2019
/s/ PAUL L. BERNS Paul L. Berns	Director	February 26, 2019
/s/ PATRICK G. ENRIGHT Patrick G. Enright	Director	February 26, 2019
/s/ PETER GRAY Peter Gray	Director	February 26, 2019
/s/ HEATHER ANN MCSHARRY Heather Ann McSharry	Director	February 26, 2019
/s/ SEAMUS C. MULLIGAN Seamus C. Mulligan	Director	February 26, 2019
/s/ KENNETH W. O'KEEFE Kenneth W. O'Keefe	Director	February 26, 2019
/s/ ANNE O'RIORDAN Anne O'Riordan	Director	February 26, 2019
/s/ NORBERT G. RIEDEL, PH.D. Norbert G. Riedel, Ph.D.	Director	February 26, 2019
/s/ ELMAR SCHNEE Elmar Schnee	Director	February 26, 2019
/s/ CATHERINE A. SOHN, PHARM.D. Catherine A. Sohn, Pharm.D.	Director	February 26, 2019
/s/ RICK E WINNINGHAM Rick E Winningham	Director	February 26, 2019

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Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Jazz Pharmaceuticals plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Jazz Pharmaceuticals plc and subsidiaries (the "Company") as of December 31, 2018 and 2017, the related consolidated statements of income, comprehensive income, shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2018 and the related notes and financial statement schedule at Item 15(a)2 (collectively, the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated February 26, 2019 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

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

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

/s/ KPMG

We have served as the Company's auditor since 2012.

Dublin, Ireland
February 26, 2019

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

	December 31, 2018	2017
ASSETS		
Current assets:		
Cash and cash equivalents	$309,622	$386,035
Investments	515,000	215,000
Accounts receivable, net of allowances of $534 and $4,162 at December 31, 2018 and 2017, respectively	263,838	224,129
Inventories	52,956	43,245
Prepaid expenses	25,017	23,182
Other current assets	67,572	76,686
Total current assets	1,234,005	968,277
Property, plant and equipment, net	200,358	170,080
Intangible assets, net	2,731,334	2,979,127
Goodwill	927,630	947,537
Deferred tax assets, net	57,879	34,559
Deferred financing costs	9,589	7,673
Other non-current assets	42,696	16,419
Total assets	$5,203,491	$5,123,672
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$40,602	$24,368
Accrued liabilities	264,887	198,779
Current portion of long-term debt	33,387	40,605
Income taxes payable	1,197	21,577
Deferred revenue	5,414	8,618
Total current liabilities	345,487	293,947
Deferred revenue, non-current	9,581	16,115
Long-term debt, less current portion	1,563,025	1,540,433
Deferred tax liabilities, net	309,097	383,472
Other non-current liabilities	218,879	176,608
Commitments and contingencies (Note 12)		
Shareholders' equity:		
Ordinary shares, nominal value $0.0001 per share; 300,000 shares authorized; 57,504 and 59,898 shares issued and outstanding at December 31, 2018 and 2017, 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, 2018 and 2017	55	55
Capital redemption reserve	472	472
Additional paid-in capital	2,113,630	1,935,486
Accumulated other comprehensive loss	(197,791)	(140,878)
Retained earnings	841,050	917,956
Total shareholders' equity	2,757,422	2,713,097
Total liabilities and shareholders' equity	$5,203,491	$5,123,672

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

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JAZZ PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF INCOME
(In thousands, except per share amounts)

	Year Ended December 31,		
	2018	2017	2016
Revenues:			
Product sales, net	$1,869,473	$1,601,399	$1,477,261
Royalties and contract revenues	21,449	17,294	10,712
Total revenues	1,890,922	1,618,693	1,487,973
Operating expenses:			
Cost of product sales (excluding amortization of intangible assets)	121,544	110,188	105,386
Selling, general and administrative	683,530	544,156	502,892
Research and development	226,616	198,442	162,297
Intangible asset amortization	201,498	152,065	101,994
Impairment charges	42,896	—	—
Acquired in-process research and development	—	85,000	23,750
Total operating expenses	1,276,084	1,089,851	896,319
Income from operations	614,838	528,842	591,654
Interest expense, net	(77,075)	(77,756)	(61,942)
Foreign exchange gain (loss)	(6,875)	(9,969)	3,372
Loss on extinguishment and modification of debt	(1,425)	—	(638)
Income before income tax provision (benefit) and equity in loss of investees	529,463	441,117	532,446
Income tax provision (benefit)	80,162	(47,740)	135,236
Equity in loss of investees	2,203	1,009	379
Net income	$447,098	$487,848	$396,831
Net income per ordinary share:			
Basic	$7.45	$8.13	$6.56
Diluted	$7.30	$7.96	$6.41
Weighted-average ordinary shares used in per share calculations - basic	59,976	60,018	60,500
Weighted-average ordinary shares used in per share calculations - diluted	61,221	61,317	61,870

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

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

	Year Ended December 31,		
	2018	2017	2016
Net income	$447,098	$487,848	$396,831
Other comprehensive income (loss):			
Foreign currency translation adjustments	(58,988)	174,973	(49,861)
Unrealized gain on hedging activities, net of income tax provision of $289, $212 and $0, respectively	2,022	1,482	—
Other comprehensive income (loss)	(56,966)	176,455	(49,861)
Total comprehensive income	$390,132	$664,303	$346,970

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

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JAZZ PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(In thousands)

	Ordinary Shares		Non-voting Euro Deferred		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
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	—	—	—	—	—	—	—	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
Issuance of Exchangeable Senior Notes	—	—	—	—	—	149,767	—	—	149,767
Issuance of ordinary shares in conjunction with exercise of share options	428	—	—	—	—	22,683	—	—	22,683
Issuance of ordinary shares under employee stock purchase plan	104	—	—	—	—	9,141	—	—	9,141
Issuance of ordinary shares in conjunction with vesting of restricted stock units	250	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's	—	—	—	—	—	(18,589)	—	—	(18,589)

withholding tax liability									
Share-based compensation	—	—	—	—	—	107,252	—	—	107,252
Shares repurchased	(704)	—	—	—	—	—	—	(98,799)	(98,799)
Other comprehensive income	—	—	—	—	—	—	176,455	—	176,455
Net income	—	—	—	—	—	—	—	487,848	487,848
Balance at December 31, 2017	59,898	$ 6	4,000	$ 55	$ 472	$1,935,486	$ (140,878)	$917,956	$2,713,097

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

	Ordinary Shares		Non-voting Euro Deferred Shares		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2017	59,898	$ 6	4,000	$ 55	$ 472	$1,935,486	$ (140,878)	$917,956	$2,713,097
Cumulative effect adjustment from adoption of new accounting standards	—	—	—	—	—	—	53	(332)	(279)
Issuance of ordinary shares in conjunction with exercise of share options	772	—	—	—	—	82,918	—	—	82,918
Issuance of ordinary shares under employee stock purchase plan	111	—	—	—	—	10,419	—	—	10,419
Issuance of ordinary shares in conjunction with vesting of restricted stock units	253	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(17,925)	—	—	(17,925)
Share-based compensation	—	—	—	—	—	102,732	—	—	102,732
Shares repurchased	(3,530)	—	—	—	—	—	—	(523,672)	(523,672)
Other comprehensive loss	—	—	—	—	—	—	(56,966)	—	(56,966)
Net income	—	—	—	—	—	—	—	447,098	447,098
Balance at December 31, 2018	57,504	$ 6	4,000	$ 55	$ 472	$2,113,630	$ (197,791)	$841,050	$2,757,422

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

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JAZZ PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2018	2017	2016
Operating activities			
Net income	$447,098	$487,848	$396,831
Adjustments to reconcile net income to net cash provided by operating activities:			
Intangible asset amortization	201,498	152,065	101,994
Share-based compensation	102,441	106,900	98,771
Impairment charges	42,896	—	—
Depreciation	15,233	13,089	11,786
Acquired in-process research and development	—	85,000	23,750
Loss on disposal of assets	655	473	47
Deferred tax benefit	(88,815)	(225,591)	(41,163)
Provision for losses on accounts receivable and inventory	4,728	2,190	2,209
Loss on extinguishment and modification of debt	1,425	—	638
Amortization of debt discount and deferred financing costs	43,960	30,026	22,133
Other non-cash transactions	4,499	14,321	(3,741)
Changes in assets and liabilities:			
Accounts receivable	(40,132)	12,278	(25,603)
Inventories	(18,512)	(8,667)	(17,024)
Prepaid expenses and other current assets	6,697	(26,874)	(15,700)
Other non-current assets	(320)	119	267
Accounts payable	17,040	214	361
Accrued liabilities	71,208	(6,578)	11,989
Income taxes payable	(19,735)	16,331	2,962
Deferred revenue	(7,497)	21,009	(1,315)
Other non-current liabilities	14,537	18,934	23,199
Net cash provided by operating activities	798,904	693,087	592,391
Investing activities			
Acquisition of investments	(1,165,915)	(385,000)	(132,181)
Proceeds from maturity of investments	855,000	230,000	66,906
Acquired in-process research and development	—	(85,000)	(23,750)
Purchases of property, plant and equipment	(20,370)	(28,950)	(9,687)
Acquisitions, net of cash acquired	—	—	(1,502,443)
Acquisition of intangible assets	(111,100)	—	(150,000)
Net proceeds from sale of assets	47,898	—	—
Net cash used in investing activities	(394,487)	(268,950)	(1,751,155)
Financing activities			
Net proceeds from issuance of debt	—	559,393	994,647
Proceeds from employee equity incentive and purchase plans	93,337	31,824	24,174
Share repurchases	(523,672)	(98,799)	(278,296)
Payment of employee withholding taxes related to share-based awards	(17,925)	(18,589)	(21,234)
Repayments of long-term debt	(25,717)	(36,094)	(28,304)
Payment of debt modification costs	(6,406)	—	—
Repayments under revolving credit facility	—	(850,000)	(150,000)
Proceeds from tenant improvement allowance on build-to-suit lease	1,253	3,154	—

Net cash provided by (used in) financing activities	(479,130)	(409,111)	540,987
Effect of exchange rates on cash and cash equivalents	(1,700)	5,046	(5,045)
Net increase (decrease) in cash and cash equivalents	(76,413)	20,072	(622,822)
Cash and cash equivalents, at beginning of period	386,035	365,963	988,785
Cash and cash equivalents, at end of period	$309,622	$386,035	$365,963

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JAZZ PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS—(Continued)
(In thousands)

	Year Ended December 31,		
	2018	2017	2016
Supplemental disclosure of cash flow information:			
Cash paid for interest	$42,706	$44,609	$39,898
Cash paid for income taxes	164,217	174,124	160,306
Non-cash investing activities:			
Amounts capitalized in connection with facility lease obligations	27,747	40,970	23,799

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

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JAZZ PHARMACEUTICALS PLC

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

Jazz Pharmaceuticals plc is a global biopharmaceutical company dedicated to developing life-changing medicines for people with limited or no options. As a leader in sleep medicine and with a growing hematology/oncology portfolio, we have a diverse portfolio of products and product candidates in development.

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 adult and pediatric 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 who have developed hypersensitivity to E. coli-derived asparaginase;
- 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, 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; and
- Vyxeos® (daunorubicin and cytarabine) liposome for injection, a product approved in the U.S. and in Europe (where it is marketed as Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia or acute myeloid leukemia with myelodysplasia-related changes.

We are also seeking approval in the U.S. and Europe for solriamfetol as a treatment to improve wakefulness and reduce EDS in adult patients with narcolepsy or obstructive sleep apnea.

We are developing JZP-258, an oxybate product candidate that contains 90% less sodium than Xyrem, for the treatment of both cataplexy and EDS in narcolepsy as well as for other conditions.

Our strategy to create shareholder value is focused on:

- Strong financial execution through growth in sales of our current lead marketed products;
- Building a diversified product portfolio and development pipeline through a combination of our internal research and development efforts and obtaining rights to clinically meaningful and differentiated on- or near-market products and early- to late-stage product candidates through acquisitions, collaborations, licensing arrangements, partnerships and venture investments; and
- Maximizing the value of our products and product candidates by continuing to implement our comprehensive global development plans, including through generating additional clinical data and seeking regulatory approval for new indications.

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.

Use of Estimates

The preparation of financial statements in conformity with U.S. 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.

Adoption of New Accounting Standards

In May 2014, the Financial Accounting Standards Board, or FASB, issued ASU No. 2014-09. 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. We adopted ASU No. 2014-09 on January 1, 2018 on a modified retrospective basis and applied the standard to all contracts as of this date. The adoption of ASU No. 2014-09 did not have a material impact on our results of operations and financial position as the timing of revenue recognition for product sales, net, which is our primary revenue stream, did not change. Refer to Note 17, Revenues, for revenue-related disclosures.

In August 2016, the FASB issued ASU No. 2016-15, “Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments” which addresses how certain cash receipts and cash payments are presented and classified in the statement of cash flows. We adopted this standard on January 1, 2018 and adoption did not have a material impact on our consolidated financial statements.

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. We adopted this standard on January 1, 2018 on a modified retrospective basis and adoption did not have a material impact on our consolidated financial statements.

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. We adopted this standard on January 1, 2018. In the second quarter of 2018, we entered into an asset purchase agreement, or APA, with TerSera Therapeutics LLC, or TerSera, whereby TerSera agreed to purchase substantially all of our assets related to the manufacture, marketing and sale of Prialt® (ziconotide) intrathecal infusion. We entered into an amendment to the APA, and the transaction closed on September 27, 2018. We determined that the disposal group did not constitute a business under the new guidance. Refer to Note 3, Business Combination, Asset Acquisitions and Disposition, for further information on the sale of our rights to Prialt.

In August 2017, the FASB issued ASU No. 2017-12, “Derivatives and Hedging (Topic 815): Targeted Improvements to Accounting for Hedging Activities” which amends and simplifies existing guidance in order to allow companies to more accurately present the economic effects of risk management activities in their financial statements. ASU No. 2017-12 is effective for reporting periods beginning after December 15, 2018, with early adoption permitted. We elected to early adopt this standard on January 1, 2018 on a modified retrospective basis. Adoption of this standard did not have a material impact on our consolidated financial statements.

The cumulative effect of the changes made to our consolidated balance sheet as of January 1, 2018 for the adoption of the above accounting standards was as follows (in thousands):

	Balance at December 31, 2017	Transition Adjustments	Balance at January 1, 2018
Assets:			
Deferred tax assets, net	$ 34,559	$ 595	$35,154

Liabilities:			
Deferred revenue	8,618	(1,120)	7,498
Deferred revenue, non-current	16,115	(1,120)	14,995
Deferred tax liabilities, net	383,472	3,114	386,586
Shareholders' Equity:			
Accumulated other comprehensive loss	(140,878)	53	(140,825)
Retained earnings	917,956	(332)	917,624

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JAZZ PHARMACEUTICALS PLC
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Significant Risks and Uncertainties

Our financial results are significantly influenced by sales of Xyrem. Our ability to maintain or increase Xyrem product sales is subject to a number of risks and uncertainties, including, without limitation, the introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, Xyrem in the treatment of cataplexy and/or EDS in narcolepsy; the introduction of a generic version of Xyrem in the U.S. market before the entry dates specified in our settlements with the abbreviated new drug application, or ANDA, filers or on terms that are different from those contemplated by the settlement agreements; increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including pressure to agree to discounts, rebates or other restrictive pricing terms for Xyrem; 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 and risk evaluation and mitigation strategy, or REMS, programs by government entities; changes to or uncertainties around our Xyrem REMS, or any failure to comply with our REMS obligations to the satisfaction of the FDA; challenges to our intellectual property around Xyrem, including the possibility of new ANDA or new drug application, or NDA, filers or new post-grant patent review proceedings; operational disruptions at the Xyrem central pharmacy; any supply or manufacturing problems, including any problems with our sole source Xyrem active pharmaceutical ingredient, or API, provider; continued acceptance of Xyrem by physicians and patients, including as a result of negative publicity that surfaces from time to time; and changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell Xyrem.

In addition to risks related specifically to Xyrem, 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, including, without limitation, risks and uncertainties associated with: effectively commercializing our other products; competition; obtaining and maintaining adequate coverage and reimbursement for our products; increasing scrutiny of pharmaceutical product pricing and resulting changes in healthcare laws and policy; market acceptance; delays or problems in the supply of our products, loss of single source suppliers or failure to comply with manufacturing regulations; regulatory approval and successful launch of our late-stage product candidates; identifying, acquiring or in-licensing additional products or product candidates; pharmaceutical product development and the inherent uncertainty of clinical success; the regulatory approval process; the challenges of protecting and enhancing our intellectual property rights; complying with applicable regulatory requirements; and possible restrictions on our ability and flexibility to pursue certain future opportunities as a result of our substantial outstanding debt obligations.

Concentrations of Risk

Financial instruments that potentially subject us to concentrations of credit risk consist of cash, cash equivalents, investments and derivative contracts. 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 manage our foreign currency transaction risk and interest rate risk within specified guidelines through the use of derivatives. All of our derivative instruments are utilized for risk management purposes, and we do not use derivatives for speculative trading purposes. As of December 31, 2018 and 2017, we had foreign exchange forward contracts with notional amounts totaling $271.5 million and $511.4 million, respectively. As of December 31, 2018 and 2017, the outstanding foreign exchange forward contracts had a net liability fair value of $0.3 million and a net asset fair value of $10.5 million, respectively. As of December 31, 2018 and 2017, we had interest rate swap contracts with notional amounts totaling $300.0 million. These outstanding interest rate swap contracts had a net asset fair value of $4.1 million and $1.7 million as of December 31, 2018 and 2017, respectively. The counterparties to these contracts are

large multinational commercial banks, and we believe the risk of nonperformance is not significant.

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. As of December 31, 2018, two customers accounted for 89% of gross accounts receivable, Express Scripts Specialty Distribution Services, Inc. and its affiliates, or Express Scripts, which accounted for 74% of gross accounts receivable, and McKesson Corporation and affiliates, or McKesson, which accounted for

15% of gross accounts receivable. As of December 31, 2017, two customers accounted for 86% of gross accounts receivable, Express Scripts, which accounted for 71% of gross accounts receivable, and McKesson, which accounted for 15% of gross accounts receivable.

We depend on single source suppliers for most of our products, product candidates and their active pharmaceutical ingredients, or APIs. With respect to Xyrem, the API is manufactured for us by a single source supplier and the finished product is manufactured both by us in our facility in Athlone, Ireland and by our U.S.-based Xyrem supplier.

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.

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.

Derivative Instruments and Hedging Activities

We record the fair value of derivative instruments as either assets or liabilities on the consolidated balance sheets. Changes in the fair value of derivative instruments are recorded each period in current earnings or other comprehensive income (loss), depending on whether a derivative instrument is designated as part of a hedging transaction and, if it is, the type of hedging transaction. For a derivative to qualify as a hedge at inception and throughout the hedged period, we formally document the nature and relationships between the hedging instruments and hedged item. We assess, both at inception and on an on-going basis, whether the derivative instruments that are used in cash flow hedging transactions are highly effective in offsetting the changes in cash flows of hedged items. Gains or losses on cash flow hedges are reclassified from other comprehensive income (loss) to earnings when the hedged transaction occurs. If we determine that a forecasted transaction is no longer probable of occurring, we discontinue hedge accounting and any related unrealized gain or loss on the derivative instrument is recognized in current earnings. Derivatives that are not designated and do not qualify as hedges are adjusted to fair value through current earnings.

Inventories

Inventories are valued at the lower of cost or net realizable value. 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.

We capitalize inventory costs associated with our products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The determination to capitalize inventory costs is based on various factors, including status and expectations of the regulatory approval process, any known safety or efficacy concerns, potential labeling restrictions, and any other impediments to obtaining regulatory approval. We had no pre-approval inventory on our consolidated balance sheet as of December 31, 2018 or 2017.

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JAZZ PHARMACEUTICALS PLC
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Property, Plant and Equipment

Property, plant 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 and the build-to-suit facility are amortized over the shorter of the noncancelable term of our leases or their economic useful lives. Maintenance and repairs are expensed as incurred.

Operating Leases and Financing Obligations

We recognize rent expense under operating leases on a straight-line basis over the term of the lease with the difference between the expense and cash payments recorded as deferred rent on the consolidated balance sheets.

For certain build-to-suit lease arrangements where we have concluded that we are the “deemed owner” of the building, for accounting purposes only, during the construction period, we are required to record an asset with a corresponding financing obligation for the construction costs incurred by the landlord. The financing obligation is recorded within accrued liabilities and other non-current liabilities in the consolidated balance sheets. We increase the asset and financing obligation as additional building costs are incurred by the landlord during the construction period. Once construction is complete, we evaluate whether the asset qualifies for sale-leaseback accounting treatment. If the lease meets the sale-leaseback criteria, we remove the asset and the related liability from the consolidated balance sheets and treat the lease as either an operating or capital lease based on an assessment of the accounting guidance. If the arrangement does not qualify for sale-leaseback treatment, we reduce the financing obligation over the lease term as payments are made and depreciate the asset over its estimated useful life or lease term, whichever is shorter. Future lease payments associated with build-to-suit leases where we are the deemed owner are allocated between the land and building components. The portion of the lease payments allocated to the land is treated for accounting purposes as operating lease payments, and therefore is recorded as rent expense in the consolidated statements of income. The portion of the lease payments allocated to the building is further bifurcated into a portion allocated to interest expense and a portion allocated to reduce the build-to-suit financing obligation.

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 18 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.

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JAZZ PHARMACEUTICALS PLC
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Intangible assets with finite useful lives also includes a Priority Review Voucher, or PRV, which we can use to obtain priority review by the FDA for one of our future regulatory submissions or may sell or transfer to a third party. The PRV is measured at cost and reviewed for impairment when events or circumstances indicate that the carrying value may not be recoverable. At the time we commit to using the PRV to accelerate the review of a drug application, the cost of the PRV will be expensed to the consolidated statement of income. Alternatively, if the PRV is sold, the asset would be derecognized from the consolidated balance sheet.

Revenue Recognition

Our revenue comprises product sales, net and royalty and contract revenues. Revenues are recognized when control of the promised goods or services is transferred to our customers, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services. Prior to recognizing revenue, we make estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

Product Sales, Net

Product sales revenue is recognized when control has transferred to the customer, which occurs at a point in time, 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.

Reserves for Variable Consideration

Revenues from sales of products are recorded at the net sales price, which includes estimates of variable consideration for which reserves are established and which relate to returns, specialty distributor fees, wholesaler fees, prompt payment discounts, government rebates, government chargebacks, coupon programs and rebates under managed care plans. Calculating certain of these reserves involves estimates and judgments and we determine their expected value 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. These reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. We reassess our reserves for variable consideration at each reporting date. Historically, adjustments to estimates for these reserves have not been material.

Reserves 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. Reserves for government chargebacks and prompt payment discounts are shown as a reduction in accounts receivable.

Royalties and Contract Revenues

We enter into out-licensing agreements under which we license certain rights to our products or product candidates to third parties. If a licensing arrangement includes multiple goods or services, we consider whether the license is distinct. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. If the license to our intellectual property is determined not to be distinct, it is combined with other goods or services into a combined performance obligation. We consider whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. We evaluate the measure of progress each reporting date and, if necessary, adjust the measure of performance and related revenue recognition.

At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price

using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or that of the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price.

For arrangements that include sales-based royalties and milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties and sales-based milestones relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty or sales-based milestone has been allocated has been satisfied (or partially satisfied).

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. Excluded from cost of product sales shown on the consolidated statements of income is amortization of acquired developed technology of $201.3 million, $149.1 million and $99.0 million in 2018, 2017 and 2016, 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 $37.4 million, $36.6 million and $29.5 million in 2018, 2017 and 2016, 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 recognize the benefits of a tax position if it is “more-likely-than-not” of being sustained. 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 exchange 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.

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JAZZ PHARMACEUTICALS PLC
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

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.
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 August 2018, the FASB issued ASU No. 2018-15, “Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer’s Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract”, which aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software. The standard is effective for us beginning January 1, 2020 and early adoption is permitted. 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. 2017-04, “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 February 2016, the FASB issued ASU No. 2016-02, “Leases (Topic 842)”, or ASU No. 2016-02. 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 adoption is permitted. We will adopt ASU No. 2016-02 on a modified retrospective basis at the adoption date of January 1, 2019. The adoption of ASU No. 2016-02 will result in the recognition of right-of-use assets and lease liabilities of approximately $150 million and $170 million, respectively, on the consolidated balance sheet as of January 1, 2019, and the de-recognition of the build-to-suit assets and related financing obligations on the consolidated balance sheet as of December 31, 2018 of $95 million and $110 million, respectively, with the balance impacting retained earnings and deferred rent. The right-of-use assets and lease liabilities primarily relate to real estate leases. We will provide additional lease-related disclosures in the notes to the consolidated financial statements commencing with our consolidated financial statements for the quarter ending March 31, 2019.

3. Business Combination, Asset Acquisitions and Disposition
Celator Acquisition
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. 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 acquisition of Celator, or 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.

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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. Please see Note 11, Debt, 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. In addition, the Celator Acquisition provided us with Celator's proprietary technology platform, CombiPlex, which enables 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 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, plant 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

Identifiable intangible assets acquired comprised IPR&D, which represented 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. After receiving FDA approval of our new drug application, or NDA, for Vyxeos in August 2017, we reclassified the IPR&D balance of $1.8 billion from an indefinite-lived intangible asset to an acquired developed technology finite-lived intangible asset. This acquired developed technology asset is being amortized over its estimated useful life of 18 years.

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.

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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.
- An increase in interest expense of $13.7 million in 2016 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
Revenues	$1,488,118
Net income attributable to Jazz Pharmaceuticals plc	$386,342
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - basic	$6.39
Net income attributable to Jazz Pharmaceuticals plc per ordinary share - diluted	$6.24

Disposition
On June 29, 2018, we entered into an APA with TerSera, pursuant to which TerSera agreed to purchase substantially all of our assets related to the manufacture, marketing and sale of Prialt, but excluding accounts receivable, and to assume certain related liabilities as set forth in the APA. We entered into an amendment to the APA, and the transaction closed, on September 27, 2018. The total sales price was $80.0 million, of which we received $50.0 million at closing, and, subject to certain conditions, we are entitled to receive $15.0 million payable on December 31, 2019 and $15.0 million payable on December 31, 2020, or earlier under certain circumstances.
The related assets met the assets held for sale criteria and were reclassified to assets held for sale as of June 30, 2018. We adjusted the carrying value of the assets held for sale to fair value less costs to sell, which resulted in an impairment charge of $42.9 million in our consolidated statements of income in 2018, primarily related to the carrying balances of intangible assets. Upon closing, we recognized a loss on disposal of $0.5 million within selling, general and administrative expenses in our consolidated statements of income in 2018.
We determined that the disposal of these assets does not qualify for reporting as a discontinued operation since it does not represent a strategic shift that has or will have a major effect on our operations and financial results.
Collaboration and Option Agreement
In August 2017, we entered into a collaboration and option agreement with ImmunoGen, Inc., or ImmunoGen, granting us rights to opt into exclusive, worldwide licenses to develop and commercialize two hematology-related antibody-drug conjugate, or ADC, programs, as well as an additional program to be designated during the term of the agreement. The programs covered under the agreement include IMGN779, a CD33-targeted ADC for the treatment of AML in Phase 1 testing, and IMGN632, a CD123-targeted ADC for hematological malignancies expected to enter clinical testing before the end of 2017.
Under the terms of the agreement, ImmunoGen will be responsible for the development of the three ADC programs prior to any potential opt-in by us. Following any opt-in, we would be responsible for any further development as well as for potential regulatory submissions and commercialization.
As part of the agreement, we paid ImmunoGen a non-refundable upfront payment of $75.0 million, which was charged to acquired IPR&D expense upon closing of the transaction. Additionally, we will pay ImmunoGen up to $100 million in development funding over seven years to support the three ADC programs. For each program, we may exercise our opt-in right at any time prior to a pivotal study or any time prior to a biologics license application upon payment of an option exercise fee. The option exercise fee depends on the timing of exercise and certain other conditions. For each program to which we elect to opt-in, ImmunoGen would be eligible to receive milestone

payments based on receiving regulatory approval of the applicable product, plus tiered royalties as a percentage of commercial sales. After opt-in, we will share with ImmunoGen the costs associated with developing and obtaining regulatory approvals of the applicable product in the U.S. and the European Union, or

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EU. ImmunoGen has the right to co-commercialize one product (or two products, under certain limited circumstances) with us in the U.S. with U.S. profit-sharing in lieu of our payment of applicable U.S. milestone and royalties to ImmunoGen.

License and Option Agreement

In July 2016, we entered into an agreement with Pfenex Inc., or Pfenex, that 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. This agreement was amended in December 2017. Under the amended agreement, Pfenex received upfront, option and development milestone payments totaling $35.3 million and may be eligible to receive additional payments of up to $189 million based on the achievement of certain development, regulatory and sales milestones. In 2017, we recognized expense of $19.5 million within research and development expenses. In 2016, we recognized expenses of $15.8 million, of which $15.0 million was charged to acquired IPR&D expense upon closing of the transaction and $0.8 million was charged to research and development expenses.

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.

4. Cash and Available-for-Sale Securities

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

December 31, 2018	Amortized Cost