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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

☒ **Quarterly report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

For the quarterly period ended September 30, 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)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically 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 ☒ No ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	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 Exchange Act). Yes ☐ No ☒

As of October 31, 2018, 60,321,590 ordinary shares of the registrant, nominal value $0.0001 per share, were outstanding.

JAZZ PHARMACEUTICALS PLC
QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED SEPTEMBER 30, 2018

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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 and Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion. This report also includes trademarks, service marks and trade names of other companies. Trademarks, service marks and trade names appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

JAZZ PHARMACEUTICALS PLC
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands)
(Unaudited)

	September 30, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 499,018	$ 386,035
Investments	565,000	215,000
Accounts receivable, net of allowances	279,437	224,129
Inventories	43,435	43,245
Prepaid expenses	23,189	23,182
Other current assets	54,310	76,686
Total current assets	1,464,389	968,277
Property, plant and equipment, net	198,053	170,080
Intangible assets, net	2,787,281	2,979,127
Goodwill	932,422	947,537
Deferred tax assets, net	37,582	34,559
Deferred financing costs	10,058	7,673
Other non-current assets	56,003	16,419
Total assets	$ 5,485,788	$ 5,123,672
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 37,373	$ 24,368
Accrued liabilities	257,453	198,779
Current portion of long-term debt	33,387	40,605
Income taxes payable	7,139	21,577
Deferred revenue	5,935	8,618
Total current liabilities	341,287	293,947
Deferred revenue, non-current	10,934	16,115
Long-term debt, less current portion	1,560,582	1,540,433
Deferred tax liabilities, net	337,021	383,472
Other non-current liabilities	208,647	176,608
Commitments and contingencies (Note 10)		
Shareholders' equity:		
Ordinary shares	6	6
Non-voting euro deferred shares	55	55
Capital redemption reserve	472	472
Additional paid-in capital	2,078,032	1,935,486
Accumulated other comprehensive loss	(179,466)	(140,878)
Retained earnings	1,128,218	917,956
Total shareholders' equity	3,027,317	2,713,097
Total liabilities and shareholders' equity	$ 5,485,788	$ 5,123,672

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Revenues:				
Product sales, net	$ 465,197	$ 407,971	$ 1,402,139	$ 1,171,304
Royalties and contract revenues	4,176	3,884	12,326	10,990
Total revenues	469,373	411,855	1,414,465	1,182,294
Operating expenses:				
Cost of product sales (excluding amortization of intangible assets)	26,574	31,203	95,207	84,940
Selling, general and administrative	155,873	124,523	521,665	401,106
Research and development	51,160	47,362	169,959	132,447
Intangible asset amortization	46,989	47,313	154,955	99,164
Impairment charges	—	—	42,896	—
Acquired in-process research and development	—	75,000	—	77,000
Total operating expenses	280,596	325,401	984,682	794,657
Income from operations	188,777	86,454	429,783	387,637
Interest expense, net	(18,920)	(19,192)	(59,171)	(56,330)
Foreign exchange loss	(756)	(2,224)	(5,181)	(9,115)
Loss on extinguishment and modification of debt	—	—	(1,425)	—
Income before income tax provision and equity in loss of investees	169,101	65,038	364,006	322,192
Income tax provision	19,348	1,239	75,018	65,914
Equity in loss of investees	437	273	1,360	637
Net income	$ 149,316	$ 63,526	$ 287,628	$ 255,641
Net income per ordinary share:				
Basic	$ 2.47	$ 1.06	$ 4.78	$ 4.26
Diluted	$ 2.41	$ 1.03	$ 4.68	$ 4.17
Weighted-average ordinary shares used in per share calculations - basic	60,476	60,108	60,196	60,030
Weighted-average ordinary shares used in per share calculations - diluted	61,857	61,436	61,493	61,360

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Net income	$ 149,316	$ 63,526	$ 287,628	$ 255,641
Other comprehensive income (loss):				
Foreign currency translation adjustments	(11,984)	50,870	(43,945)	159,302
Unrealized gain (loss) on hedging activities, net of tax expense (benefit) of $107, $56, $758 and ($137), respectively	746	392	5,304	(956)
Other comprehensive income (loss)	(11,238)	51,262	(38,641)	158,346
Total comprehensive income	$ 138,078	$ 114,788	$ 248,987	$ 413,987

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

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

	Nine Months Ended September 30,	
	2018	**2017**
Operating activities		
Net income	$ 287,628	$ 255,641
Adjustments to reconcile net income to net cash provided by operating activities:		
Intangible asset amortization	154,955	99,164
Share-based compensation	75,718	79,579
Impairment charges	42,896	—
Depreciation	11,363	9,288
Acquired in-process research and development	—	77,000
Loss on disposal of assets	652	360
Deferred income taxes	(44,658)	(53,359)
Provision for losses on accounts receivable and inventory	4,734	1,825
Loss on extinguishment and modification of debt	1,425	—
Amortization of debt discount and deferred financing costs	32,669	19,234
Other non-cash transactions	6,970	14,480
Changes in assets and liabilities:		
Accounts receivable	(55,518)	(22,273)
Inventories	(7,583)	(7,132)
Prepaid expenses and other current assets	6,989	(10,590)
Other long-term assets	(6,494)	(1,825)
Accounts payable	10,116	6,130
Accrued liabilities	65,074	(23,583)
Income taxes payable	(13,999)	8,495
Deferred revenue	(5,623)	23,163
Other non-current liabilities	7,244	12,931
Net cash provided by operating activities	574,558	488,528
Investing activities		
Proceeds from maturity of investments	565,000	150,000
Net proceeds from sale of assets	48,092	—
Acquired in-process research and development	—	(77,000)
Purchases of property, plant and equipment	(15,221)	(20,072)
Acquisition of intangible assets	(111,100)	—
Acquisition of investments	(915,000)	(290,000)
Net cash used in investing activities	(428,229)	(237,072)
Financing activities		
Proceeds from employee equity incentive and purchase plans	84,056	22,793
Proceeds from tenant improvement allowance on build-to-suit lease	1,253	—
Net proceeds from issuance of debt	—	559,484
Repayments under revolving credit facility	—	(850,000)
Payment of debt modification costs	(6,406)	—
Payment of employee withholding taxes related to share-based awards	(17,192)	(17,909)
Repayments of long-term debt	(17,370)	(27,070)
Share repurchases	(77,015)	(56,425)
Net cash used in financing activities	(32,674)	(369,127)
Effect of exchange rates on cash and cash equivalents	(672)	4,323
Net increase (decrease) in cash and cash equivalents	112,983	(113,348)
Cash and cash equivalents, at beginning of period	386,035	365,963
Cash and cash equivalents, at end of period	$ 499,018	$ 252,615

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

JAZZ PHARMACEUTICALS PLC
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)

1. The Company and Summary of Significant Accounting Policies

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

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

- **Xyrem® (sodium oxybate) oral solution**, the only product approved by the U.S. Food and Drug Administration, or FDA, and marketed in the U.S. for the treatment of both cataplexy and excessive daytime sleepiness in patients with narcolepsy;
- **Erwinaze® (asparaginase *Erwinia chrysanthemi*)**, a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia 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.

Our strategy is to create shareholder value by:

- Growing sales of the existing products in our portfolio, including by identifying and investing in growth opportunities such as new treatment indications and new geographic markets;
- Acquiring or licensing rights to clinically meaningful and differentiated products on the market or product candidates at various stages of development; and
- Pursuing targeted development of post-discovery differentiated product candidates.

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

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

Basis of Presentation

These unaudited condensed consolidated financial statements have been prepared following the requirements of the U.S. Securities and Exchange Commission, or SEC, for interim reporting. As permitted under those rules, certain footnotes and other financial information that are normally required by U.S. generally accepted accounting principles, or U.S. GAAP, can be condensed or omitted. The information included in this Quarterly Report on Form 10-Q should be read in conjunction with our annual consolidated financial statements and accompanying notes included in our Annual Report on Form 10-K for the year ended December 31, 2017.

In the opinion of management, these condensed consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and include all adjustments, consisting only of normal recurring adjustments, considered necessary for the fair presentation of our financial position and operating results. The results for the three and nine months ended September 30, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018, for any other interim period or for any future period.

Except for the revenue recognition accounting policy that was updated as a result of adopting Accounting Standards Update No. 2014-09, "Revenue from Contracts with Customers", or ASU No. 2014-09, our significant accounting policies have

not changed substantially from those previously described in our Annual Report on Form 10-K for the year ended December 31, 2017.

These condensed consolidated financial statements include the accounts of Jazz Pharmaceuticals plc and our subsidiaries, and intercompany transactions and balances have been eliminated.

Our operating segment is reported in a manner consistent with the internal reporting provided to the chief operating decision maker, or CODM. Our CODM has been identified as our chief executive officer. We have determined that we operate in one business segment, which is the identification, development and commercialization of meaningful pharmaceutical products that address unmet medical needs.

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 condensed consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates.

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. 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 13, 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 2, 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", or ASU No. 2017-12. ASU No. 2017-12 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	3,133	386,605
Shareholders' Equity:			
Accumulated other comprehensive loss	(140,878)	53	(140,825)
Retained earnings	917,956	(351)	917,605

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 condensed 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).

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 potential U.S. introduction of a generic version of Xyrem 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; the potential U.S. introduction of new products that compete with, or otherwise disrupt the market for, Xyrem in the treatment of cataplexy and/or excessive daytime sleepiness in narcolepsy; changes to or uncertainties around regulatory restrictions, including, among other things, changes to our Xyrem risk evaluation and mitigation strategy, or REMS; any increase in pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors; changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing and REMS programs by government entities; operational disruptions at the Xyrem central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA; and continued acceptance of Xyrem by physicians and patients.

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 and 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; our dependence on sole source suppliers for most of our products, including delays or problems in the supply or manufacture of our products and product candidates; competition; complying with applicable regulatory requirements; changes in healthcare laws and policy and related reforms; government investigations and other actions; obtaining and maintaining appropriate pricing and reimbursement for our products; business combination or product or product candidate acquisition transactions; 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 September 30, 2018, we had foreign exchange forward contracts with notional amounts totaling $210.1 million. As of September 30, 2018, the net liability fair value of outstanding foreign exchange forward contracts was $1.0 million. As of September 30, 2018, we had interest rate swap contracts with notional amounts totaling $300.0 million. These outstanding interest rate swap contracts had a fair value of $7.8 million as of September 30, 2018. 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 and as of September 30, 2018 and December 31, 2017, allowances on receivables were not material. As of September 30, 2018, two customers accounted for 91% of gross accounts receivable, including Express Scripts Specialty Distribution Services, Inc. and its affiliates, or Express Scripts, which accounted for 77% of gross accounts receivable, and McKesson Corporation and affiliates, or McKesson, which accounted for 14% of gross accounts receivable. As of December 31, 2017, two customers accounted for 86% of gross accounts receivable including 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.

Recent Accounting Pronouncements

In August 2018, the FASB issued ASU 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. ASU No. 2016-02 must be adopted on a modified retrospective transition basis at the beginning of the earliest comparative period presented in the consolidated financial statements or at the adoption date. The adoption of ASU No. 2016-02 will result in a significant increase in our consolidated balance sheet for right-of-use assets and lease liabilities. While we are continuing to assess all potential impacts of the standard, we currently believe the most significant impact relates to our accounting for the lease agreements we entered into in January 2015 and September 2017 to lease office space located in Palo Alto, California in buildings constructed or to be constructed by the landlord, which are accounted for as build-to-suit arrangements under existing accounting standards, and the lease agreement we entered into in August 2016 for office space in Dublin, Ireland. The future minimum lease payments under these leases at September 30, 2018 were $208.6 million. Based on our initial evaluation of the impact of ASU No. 2016-02 on our build-to-suit facility leases, we expect to de-recognize existing build-to-suit assets and liabilities upon the adoption of ASU No. 2016-02.

2. 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 condensed consolidated statements of income for the nine months ended September 30, 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 for the three and nine months ended September 30, 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.

3. Cash and Available-for-Sale Securities

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

	September 30, 2018					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 281,047	$ —	$ —	$ 281,047	$ 281,047	$ —
Time deposits	590,000	—	—	590,000	25,000	565,000
Money market funds	192,971	—	—	192,971	192,971	—
Totals	$ 1,064,018	$ —	$ —	$ 1,064,018	$ 499,018	$ 565,000

	December 31, 2017					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 225,235	$ —	$ —	$ 225,235	$ 225,235	$ —
Time deposits	235,000	—	—	235,000	20,000	215,000
Money market funds	140,800	—	—	140,800	140,800	—
Totals	$ 601,035	$ —	$ —	$ 601,035	$ 386,035	$ 215,000

Cash equivalents and investments are considered available-for-sale securities. We use the specific-identification method for calculating realized gains and losses on securities sold and include them in interest expense, net in the condensed consolidated statements of income. Our investment balances represent time deposits with original maturities of greater than three months and less than one year.

4. Fair Value Measurement

The following table summarizes, by major security type, our available-for-sale securities and derivative contracts as of September 30, 2018 and December 31, 2017 that were measured at fair value on a recurring basis and were categorized using the fair value hierarchy (in thousands):

	September 30, 2018			December 31, 2017		
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value
Assets:						
Available-for-sale securities:						
Time deposits	$ —	$ 590,000	$ 590,000	$ —	$ 235,000	$ 235,000
Money market funds	192,971	—	192,971	140,800	—	140,800
Interest rate contracts	—	7,824	7,824	—	2,138	2,138
Foreign exchange forward contracts	—	261	261	—	15,495	15,495
Totals	$ 192,971	$ 598,085	$ 791,056	$ 140,800	$ 252,633	$ 393,433
Liabilities:						
Interest rate contracts	$ —	$ —	$ —	$ —	$ 392	$ 392
Foreign exchange forward contracts	—	1,258	1,258	—	5,017	5,017
Totals	$ —	$ 1,258	$ 1,258	$ —	$ 5,409	$ 5,409

As of September 30, 2018, our available-for-sale securities included time deposits and money market funds, and their carrying values were approximately equal to their fair values. Time deposits were measured at fair value using Level 2 inputs and money market funds were measured using quoted prices in active markets, which represent Level 1 inputs. Level 2 inputs, obtained from various third party data providers, represent quoted prices for similar assets in active markets, or these inputs were derived from observable market data, or if not directly observable, were derived from or corroborated by other observable market data.

Our derivative assets and liabilities include interest rate and foreign exchange derivatives that are measured at fair value using observable market inputs such as forward rates, interest rates, our own credit risk as well as an evaluation of our counterparties' credit risks. Based on these inputs, the derivative assets and liabilities are classified within Level 2 of the fair value hierarchy.

There were no transfers between the different levels of the fair value hierarchy in 2018 or in 2017.

As of September 30, 2018, the estimated fair values of our 1.875% exchangeable senior notes due 2021, or the 2021 Notes, and our 1.50% exchangeable senior notes due 2024, or the 2024 Notes, were approximately $619 million and $586 million, respectively. The fair values of the 2021 Notes and the 2024 Notes, which we refer to together as the Exchangeable Senior Notes, were estimated using quoted market prices obtained from brokers (Level 2). The estimated fair value of our borrowing under our term loan was approximately equal to its book value based on the borrowing rates currently available for variable rate loans (Level 2).

5. Derivative Instruments and Hedging Activities

We are exposed to certain risks arising from operating internationally, including fluctuations in interest rates on our outstanding term loan borrowings and fluctuations in foreign exchange rates primarily related to the translation of euro-denominated net monetary liabilities, including intercompany balances, held by subsidiaries with a U.S. dollar functional currency. We manage these exposures 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.

To achieve a desired mix of floating and fixed interest rates on our variable rate debt, we entered into interest rate swap agreements in March 2017 which are effective from March 3, 2017 until July 12, 2021. These agreements hedge contractual term loan interest rates. As of September 30, 2018 and December 31, 2017, the interest rate swap agreements had a notional amount of $300.0 million. As a result of these agreements, the interest rate on a portion of our term loan borrowings was fixed at 1.895%, plus the borrowing spread, until July 12, 2021.

The effective portion of changes in the fair value of derivatives designated as and that qualify as cash flow hedges is recorded in accumulated other comprehensive loss and is subsequently reclassified into earnings in the period that the hedged forecasted transaction affects earnings. The impact on accumulated other comprehensive loss and earnings from derivative instruments that qualified as cash flow hedges for the three and nine months ended September 30, 2018 and 2017 was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
Interest Rate Contracts:	**2018**	**2017**	**2018**	**2017**
Gain (loss) recognized in accumulated other comprehensive loss, net of tax	$ 876	$ (59)	$ 5,285	$ (2,234)
Loss (gain) reclassified from accumulated other comprehensive loss to interest expense, net of tax	(130)	451	19	1,278

Assuming no change in LIBOR-based interest rates from market rates as of September 30, 2018, $1.9 million of gains recognized in accumulated other comprehensive loss will be reclassified to earnings over the next 12 months.

We enter into foreign exchange forward contracts, with durations of up to 12 months, designed to limit the exposure to fluctuations in foreign exchange rates related to the translation of certain non-U.S. dollar denominated liabilities, including intercompany balances. Hedge accounting is not applied to these derivative instruments as gains and losses on these hedge transactions are designed to offset gains and losses on underlying balance sheet exposures. As of September 30, 2018 and December 31, 2017, the notional amount of foreign exchange contracts where hedge accounting is not applied was $210.1 million and $98.7 million, respectively. The foreign exchange loss in our condensed consolidated statements of income included losses of $2.4 million and $10.9 million for the three and nine months ended September 30, 2018, respectively, and gains of $8.0 million and $19.6 million for the three and nine months ended September 30, 2017, respectively, associated with foreign exchange contracts not designated as hedging instruments.

The cash flow effects of our derivative contracts for the nine months ended September 30, 2018 and 2017 are included within net cash provided by operating activities in the condensed consolidated statements of cash flows.

The following tables summarize the fair value of outstanding derivatives (in thousands):

	September 30, 2018			
	Asset Derivatives		Liability Derivatives	
	Balance Sheet Location	Fair Value	Balance Sheet Location	Fair Value
Derivatives designated as hedging instruments:				
Interest rate contracts	Other current assets	$ 2,150	Accrued liabilities	$ —
	Other non-current assets	5,674		
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	261	Accrued liabilities	1,258
Total fair value of derivative instruments		$ 8,085		$ 1,258

	December 31, 2017			
	Asset Derivatives		Liability Derivatives	
	Balance Sheet Location	Fair Value	Balance Sheet Location	Fair Value
Derivatives designated as hedging instruments:				
Interest rate contracts	Other non-current assets	$ 2,138	Accrued liabilities	$ 392
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	15,495	Accrued liabilities	5,017
Total fair value of derivative instruments		$ 17,633		$ 5,409

Although we do not offset derivative assets and liabilities within our condensed consolidated balance sheets, our International Swap and Derivatives Association agreements provide for net settlement of transactions that are due to or from the same counterparty upon early termination of the agreement due to an event of default or other termination event. The following tables summarize the potential effect on our condensed consolidated balance sheets of offsetting our interest rate contracts and foreign exchange forward contracts subject to such provisions (in thousands):

	September 30, 2018					
				Gross Amounts Not Offset in the Consolidated Balance Sheet		
Description	Gross Amounts of Recognized Assets/ Liabilities	Gross Amounts Offset in the Consolidated Balance Sheet	Net Amounts of Assets/ Liabilities Presented in the Consolidated Balance Sheet	Derivative Financial Instruments	Cash Collateral Received (Pledged)	Net Amount
Derivative assets	$ 1,957	$ —	$ 1,957	$ (457)	$ —	$ 1,500
Derivative liabilities	(457)	—	(457)	457	—	—

	December 31, 2017					
				Gross Amounts Not Offset in the Consolidated Balance Sheet		
Description	Gross Amounts of Recognized Assets/ Liabilities	Gross Amounts Offset in the Consolidated Balance Sheet	Net Amounts of Assets/ Liabilities Presented in the Consolidated Balance Sheet	Derivative Financial Instruments	Cash Collateral Received (Pledged)	Net Amount
Derivative assets	$ 1,639	$ —	$ 1,639	$ (875)	$ —	$ 764
Derivative liabilities	(875)	—	(875)	875	—	—

6. Inventories

Inventories consisted of the following (in thousands):

	September 30, 2018	December 31, 2017
Raw materials	$ 2,482	$ 3,542
Work in process	24,456	15,692
Finished goods	16,497	24,011
Total inventories	$ 43,435	$ 43,245

7. Goodwill and Intangible Assets

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

Balance at December 31, 2017	$ 947,537
Foreign exchange	(15,115)
Balance at September 30, 2018	$ 932,422

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

	September 30, 2018				December 31, 2017		
	Remaining Weighted-Average Useful Life (In years)	Gross Carrying Amount	Accumulated Amortization	Net Book Value	Gross Carrying Amount	Accumulated Amortization	Net Book Value
Acquired developed technologies	14.6	$3,122,811	$ (590,198)	$2,532,613	$3,392,832	$ (562,473)	$2,830,359
Priority review voucher		111,100	—	111,100	—	—	—
Manufacturing contracts	—	12,391	(12,391)	—	12,824	(12,634)	190
Trademarks	—	2,899	(2,899)	—	2,910	(2,910)	—
Total finite-lived intangible assets		3,249,201	(605,488)	2,643,713	3,408,566	(578,017)	2,830,549
Acquired IPR&D assets		143,568	—	143,568	148,578	—	148,578
Total intangible assets		$3,392,769	$ (605,488)	$2,787,281	$3,557,144	$ (578,017)	$2,979,127

The decrease in the gross carrying amount of intangible assets as of September 30, 2018 compared to December 31, 2017 reflects the sale of the Prialt acquired developed technology asset to TerSera in September 2018 and the negative impact of foreign currency translation adjustments, which was due to the weakening of the euro against the U.S. dollar, partially offset by our purchase of a rare pediatric disease priority review voucher, or PRV, from Spark Therapeutics, Inc. As we may use the PRV to obtain priority review by the FDA for one of our future regulatory submissions or may sell or transfer the PRV to a third party, we capitalized the acquisition cost, including direct transaction costs, as a finite-lived intangible asset upon closing of the transaction in May 2018.

The assumptions and estimates used to determine future cash flows and remaining useful lives of our intangible and other long-lived assets are complex and subjective. They can be affected by various factors, including external factors, such as industry and economic trends, and internal factors such as changes in our business strategy and our forecasts for specific product lines.

Based on acquired developed technology intangible assets recorded as of September 30, 2018, and assuming the underlying assets will not be impaired and that we will not change the expected lives of the assets, future amortization expenses were estimated as follows (in thousands):

Year Ending December 31,	Estimated Amortization Expense
2018 (remainder)	$ 46,802
2019	187,208
2020	185,969
2021	184,955
2022	184,246
Thereafter	1,743,433
Total	$ 2,532,613

8. Certain Balance Sheet Items

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

	September 30, 2018	December 31, 2017
Build-to-suit facility	$ 52,222	$ 51,721
Land and buildings	46,815	46,729
Construction-in-progress	46,058	21,738
Leasehold improvements	32,623	28,779
Manufacturing equipment and machinery	25,573	23,586
Computer software	19,135	19,969
Computer equipment	14,059	12,814
Furniture and fixtures	8,059	5,947
Subtotal	244,544	211,283
Less accumulated depreciation and amortization	(46,491)	(41,203)
Property, plant and equipment, net	$ 198,053	$ 170,080

Accrued liabilities consisted of the following (in thousands):

	September 30, 2018	December 31, 2017
Rebates and other sales deductions	$ 88,443	$ 81,368
Estimated loss contingency	57,753	—
Employee compensation and benefits	49,845	54,930
Clinical trial accruals	8,387	2,181
Selling and marketing accruals	5,837	3,189
Inventory-related accruals	3,290	3,002
Royalties	3,293	8,058
Accrued interest	2,678	7,297
Sales returns reserve	2,473	3,651
Professional fees	2,368	3,213
Derivative instrument liabilities	1,258	5,409
Other	31,828	26,481
Total accrued liabilities	$ 257,453	$ 198,779

9. Debt

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

	September 30, 2018	December 31, 2017
2021 Notes	$ 575,000	$ 575,000
Unamortized discount and debt issuance costs on 2021 Notes	(66,269)	(81,627)
2021 Notes, net	508,731	493,373
2024 Notes	575,000	575,000
Unamortized discount and debt issuance costs on 2024 Notes	(144,018)	(158,680)
2024 Notes, net	430,982	416,320
Term loan	654,256	671,345
Total debt	1,593,969	1,581,038
Less current portion	33,387	40,605
Total long-term debt	$ 1,560,582	$ 1,540,433

Amendment of Credit Facility

On June 18, 2015, Jazz Pharmaceuticals plc, as guarantor, and certain of our wholly owned subsidiaries, as borrowers, entered into a credit agreement, or the 2015 credit agreement, that provided for a $750.0 million principal amount term loan, which was drawn in full at closing, and a $750.0 million revolving credit facility, of which $160.0 million was drawn at closing and subsequently repaid. We used the proceeds from initial borrowings under the 2015 credit agreement to repay in full the $893.1 million principal amount of term loans outstanding under the credit agreement that we entered into in June 2012, as subsequently amended, which we refer to as the previous credit agreement, and to pay related fees and expenses. The previous credit agreement was terminated upon repayment of the term loans outstanding thereunder.

On July 12, 2016, we amended the 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 acquisition of Celator Pharmaceuticals, Inc., or Celator.

On June 7, 2018, we entered into a second amendment to the 2015 credit agreement to provide for a revolving credit facility of $1.6 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 $659.4 million principal amount was outstanding as of September 30, 2018. We refer to the 2015 credit agreement as amended by the first and second amendments as the amended credit agreement. We expect to use the proceeds from future loans under the revolving credit facility, if any, for permitted capital expenditures, permitted 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.

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 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.

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 September 30, 2018, we were in compliance with these financial covenants.

Exchangeable Senior Notes

The Exchangeable Senior Notes were issued by Jazz Investments I Limited, or the Issuer, a 100%-owned finance subsidiary of Jazz Pharmaceuticals plc. The Exchangeable Senior Notes are senior unsecured obligations of the Issuer and are fully and unconditionally guaranteed on a senior unsecured basis by Jazz Pharmaceuticals plc. No subsidiary of Jazz Pharmaceuticals plc guaranteed the Exchangeable Senior Notes. Subject to certain local law restrictions on payment of dividends, among other things, and potential negative tax consequences, we are not aware of any significant restrictions on the ability of Jazz Pharmaceuticals plc to obtain funds from the Issuer or Jazz Pharmaceuticals plc's other subsidiaries by dividend or loan, or any legal or economic restrictions on the ability of the Issuer or Jazz Pharmaceuticals plc's other subsidiaries to transfer funds to Jazz Pharmaceuticals plc in the form of cash dividends, loans or advances. There is no assurance that in the future such restrictions will not be adopted.

As of September 30, 2018, the carrying values of the equity component of the 2021 Notes and the 2024 Notes, net of equity issuance costs, were $126.9 million and $149.8 million, respectively.

Maturities

Scheduled maturities with respect to our long-term debt principal balances outstanding as of September 30, 2018 were as follows (in thousands):

Year Ending December 31,	Scheduled Long-Term Debt Maturities
2018 (remainder)	$ 8,346
2019	33,387
2020	33,387
2021	608,387
2022	33,387
Thereafter	1,092,494
Total	$ 1,809,388

10. Commitments and Contingencies

Indemnification

In the normal course of business, we enter into agreements that contain a variety of representations and warranties and provide for general indemnification, including indemnification associated with product liability or infringement of intellectual property rights. Our exposure under these agreements is unknown because it involves future claims that may be made but have not yet been made against us. To date, we have not paid any claims or been required to defend any action related to these indemnification obligations.

We have agreed to indemnify our executive officers, directors and certain other employees for losses and costs incurred in connection with certain events or occurrences, including advancing money to cover certain costs, subject to certain limitations. The maximum potential amount of future payments we could be required to make under the indemnification obligations is unlimited; however, we maintain insurance policies that may limit our exposure and may enable us to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits and other policy provisions, we believe the fair value of these indemnification obligations is not significant. Accordingly, we did not recognize any liabilities relating to these obligations as of September 30, 2018 and December 31, 2017. No assurances can be given that the covering insurers will not attempt to dispute the validity, applicability,

or amount of coverage without expensive litigation against these insurers, in which case we may incur substantial liabilities as a result of these indemnification obligations.

Lease and Other Commitments

Facility Leases. In January 2015, we entered into an agreement to lease office space located in Palo Alto, California in a building subsequently constructed by the landlord. The term of this lease is 12 years from the commencement date as defined in the lease agreement and we have an option to extend the term twice for a period of five years each. We are the deemed owner of the building based on applicable accounting guidance for build-to-suit leases. Accordingly, the landlord's costs of constructing the building were capitalized on our condensed consolidated balance sheets offset by a corresponding financing obligation. We began to occupy this office space in October 2017. As of September 30, 2018, the total amount of the related financing obligation was $62.9 million, which is classified within current liabilities and non-current liabilities on our condensed consolidated balance sheets.

In September 2017, we entered into an agreement to lease office space located in Palo Alto, California in a second building to be constructed by the same landlord. We expect to occupy this office space by the end of 2019. This lease has a term of 12 years from the commencement date as defined in the lease agreement and we have an option to extend the term of the lease twice for a period of 5 years each. We are the deemed owner of the building during the construction period based on applicable accounting guidance for build-to-suit leases. As of September 30, 2018, we recorded project construction costs of $43.7 million incurred by the landlord as construction-in-progress in property, plant and equipment, net and a corresponding financing obligation in other non-current liabilities on our condensed consolidated balance sheets. We will increase the asset and financing obligation as additional building costs are incurred by the landlord during the construction period.

Operating Leases. We have noncancelable operating leases for our office buildings and we are obligated to make payments under noncancelable operating leases for automobiles used by our sales force.

Other Commitments. As of September 30, 2018, we had $54.7 million of noncancelable purchase commitments due within one year, primarily related to agreements with third party manufacturers.

Legal Proceedings

Xyrem ANDA Litigation and Settlements. In December 2012, we received a notice of Paragraph IV Patent Certification, or Paragraph IV Certification, from Amneal Pharmaceuticals LLC, or Amneal, that it had submitted an ANDA to the FDA requesting approval to market a generic version of Xyrem. In January 2013, we filed a lawsuit against Amneal in the federal district court of New Jersey, or District Court, alleging that our patents covering Xyrem are infringed or will be infringed by Amneal's ANDA and seeking a permanent injunction to prevent Amneal from introducing a generic version of Xyrem that would infringe these patents. Additional patents covering Xyrem were issued after the date of the original lawsuit against Amneal, and lawsuits we brought against Amneal involving those patents were consolidated into a single case in the District Court.

In October 2018, we entered into a settlement agreement and related agreements resolving our patent infringement litigation against Amneal in the District Court, and the District Court subsequently approved an order dismissing the litigation. We previously settled lawsuits against the eight other companies that have sent us notices that they had filed ANDAs requesting approval to market a generic version of Xyrem. As a result, the settlement with Amneal represents settlement of all outstanding patent infringement litigation related to Xyrem. It is possible that additional companies may file ANDAs seeking to market a generic version of Xyrem or submit new drug applications referencing Xyrem, which could lead to additional patent litigation or challenges with respect to Xyrem.

The settlements with the nine ANDA filers are described below.

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 authorized generic version of Xyrem, or AG Product, in the U.S. beginning on January 1, 2023, or earlier under certain circumstances, including 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 an option to continue to sell the West-Ward AG Product for up to five years, and we are entitled to receive a meaningful royalty on net sales of the West-Ward AG Product, as well as payment for the supply of the West-Ward AG Product and reimbursement for a portion of the services costs associated with distribution of the West-Ward AG Product through the Xyrem REMS. We also granted West-Ward a license under the Xyrem patents to launch its own generic sodium oxybate product as early as six months after it has the right to sell the AG Product, but if it elects to sell its own generic sodium oxybate product, West-Ward will not be able to continue to sell the West-Ward AG Product.

In our settlements with Amneal, Lupin Inc., or Lupin, and Par Pharmaceutical, Inc., or Par, we granted each of them 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. Such circumstances include events related to 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 not infringed, or are invalid and/or unenforceable. The volume of each of Amneal's, Lupin's and Par's AG Products is limited to an annual amount equal to a low single-digit percentage of Xyrem sales volume during the calendar year preceding the entry date of such party's AG Product, and each party's right to sell its AG Product ends on December 31, 2025. We also granted each of Amneal, Lupin and Par a license under the Xyrem patents to launch its own generic sodium oxybate product under its ANDA (assuming FDA approval of its ANDA is obtained or maintained) on or after December 31, 2025, or earlier under certain circumstances. Such circumstances include events related to launch of a generic sodium oxybate product by West-Ward or another company under its ANDA, 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 such party will not be entitled to market its AG Product and its own generic sodium oxybate product simultaneously. We are entitled to receive a meaningful royalty on net sales of each of Amneal's, Lupin's and Par's AG Products, as well as payment for the supply of each party's AG Product and reimbursement for a portion of the services costs associated with distribution of each party's AG Product through the Xyrem REMS.

In our settlements with each of the other five ANDA filers, we granted each a license under the Xyrem patents to launch its own generic sodium oxybate product under its ANDA (assuming FDA approval of its ANDA is obtained or maintained) on or after December 31, 2025, or earlier under certain circumstances. Such circumstances include the launch by West-Ward or another company of a generic sodium oxybate product. The specific terms of all of the settlement agreements are confidential.

Xyrem Post-Grant Patent Review Matters. In January 2015, certain of the ANDA filers filed petitions for inter partes review, or IPR, with respect to the validity of six of our seven patents associated with the Xyrem REMS, or REMS patents. The Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office instituted IPR trials with respect to certain of these petitions. In July 2016, the PTAB issued final decisions that the claims of the six REMS patents are unpatentable. In March 2017, the PTAB issued a final decision that three claims of a seventh REMS patent are unpatentable. On July 13, 2018, the United States Court of Appeals for the Federal Circuit upheld the July 2016 and March 2017 PTAB decisions on appeal, and as a result, we will not be able to enforce claims the PTAB found unpatentable. We cannot predict whether new parties will petition for post-grant patent review in the future, the outcome of any future IPR or other proceeding or the impact any IPR or other proceeding might have on any future ANDA or other patent litigation proceedings or other aspects of our Xyrem business.

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

Other Contingencies

In May and October 2016 and in February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients, and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. Other companies have disclosed similar subpoenas and continuing inquiries. We have a comprehensive program intended to ensure our compliance with applicable legal and regulatory requirements for pharmaceutical companies, including guidelines established by the Office of Inspector General of the U.S. Department of Health and Human Services regarding patient assistance programs, and we have been cooperating with the government's investigation. We have engaged in discussions with the U.S. Department of Justice, or DOJ, about a possible resolution, and 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. During the nine months ended September 30, 2018, we recorded $57.8 million related to this matter, including related interest, within accrued liabilities on our condensed consolidated balance sheet with the related expense included in selling, general and administrative expenses on our condensed consolidated statement of income. Material issues remain subject to further negotiation and approval by us and the DOJ before the proposed settlement can be finalized. 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. Any such settlement is also likely to involve entry into a corporate integrity agreement, which would impose costs and burdens on the operation of our business. If we do not reach a final settlement, 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, and we would expect to incur significant costs in connection with such enforcement action, regardless of the outcome.

11. Shareholders' Equity

The following tables present a reconciliation of our beginning and ending balances in shareholders' equity for the nine months ended September 30, 2018 and 2017 (in thousands):

	Total Shareholders' Equity
Shareholders' equity at January 1, 2018	$ 2,713,097
Effect of adoption of new accounting standards	(298)
Issuance of ordinary shares in conjunction with employee equity incentive and purchase plans	84,056
Employee withholding taxes related to share-based awards	(17,192)
Share-based compensation	75,682
Shares repurchased	(77,015)
Other comprehensive loss	(38,641)
Net income	287,628
Shareholders' equity at September 30, 2018	$ 3,027,317

	Total Shareholders' Equity
Shareholders' equity at January 1, 2017	$ 1,877,339
Issuance of 2024 Notes	149,767
Issuance of ordinary shares in conjunction with employee equity incentive and purchase plans	22,793
Employee withholding taxes related to share-based awards	(17,909)
Share-based compensation	79,745
Shares repurchased	(56,425)
Other comprehensive income	158,346
Net income	255,641
Shareholders' equity at September 30, 2017	$ 2,469,297

Share Repurchase Program

In November 2016, our board of directors authorized a share repurchase program pursuant to which we are authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300 million, exclusive of any brokerage commissions. In the nine months ended September 30, 2018, we spent a total of $77.0 million to purchase 0.5 million of our ordinary shares under the share repurchase program at an average total purchase price, including commissions, of $154.03 per share. As of September 30, 2018, the remaining amount authorized under the share repurchase program was $105.7 million.

In November 2018, our board of directors increased the existing share repurchase program authorization by an aggregate purchase price of $320 million, exclusive of any brokerage commissions.

Accumulated Other Comprehensive Loss

The components of accumulated other comprehensive loss as of September 30, 2018 and December 31, 2017 were as follows (in thousands):

	Net Unrealized Gain From Hedging Activities	Foreign Currency Translation Adjustments	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2017	$ 1,482	$ (142,360)	$ (140,878)
Effect of adoption of ASU No. 2017-12	53	—	53
Balance at January 1, 2018	1,535	(142,360)	(140,825)
Other comprehensive income (loss) before reclassifications	5,285	(43,945)	(38,660)
Amounts reclassified from accumulated other comprehensive loss	19	—	19
Other comprehensive income (loss), net	5,304	(43,945)	(38,641)
Balance at September 30, 2018	$ 6,839	$ (186,305)	$ (179,466)

During the nine months ended September 30, 2018, other comprehensive loss reflects foreign currency translation adjustments, primarily due to the weakening of the euro against the U.S. dollar, and the net unrealized gain on derivatives that qualify as cash flow hedges.

12. Net Income per Ordinary Share

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Numerator:				
Net income	$ 149,316	$ 63,526	$ 287,628	$ 255,641
Denominator:				
Weighted-average ordinary shares used in per share calculations - basic	60,476	60,108	60,196	60,030
Dilutive effect of employee equity incentive and purchase plans	1,381	1,328	1,297	1,330
Weighted-average ordinary shares used in per share calculations - diluted	61,857	61,436	61,493	61,360
Net income per ordinary share:				
Basic	$ 2.47	$ 1.06	$ 4.78	$ 4.26
Diluted	$ 2.41	$ 1.03	$ 4.68	$ 4.17

Potentially dilutive ordinary shares from our employee equity incentive and purchase plans and the Exchangeable Senior Notes are determined by applying the treasury stock method to the assumed exercise of share options, the assumed vesting of outstanding restricted stock units, or RSUs, the assumed issuance of ordinary shares under our employee stock purchase plan, or ESPP, and the assumed issuance of ordinary shares upon exchange of the Exchangeable Senior Notes. The potential issue of ordinary shares issuable upon exchange of the Exchangeable Senior Notes had no effect on diluted net income per ordinary share because the average price of our ordinary shares for the three and nine months ended September 30, 2018 and 2017 did not exceed the effective exchange prices per ordinary share of the Exchangeable Senior Notes.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Exchangeable Senior Notes	5,504	3,958	5,504	3,238
Options to purchase ordinary shares and RSUs	2,230	2,998	2,959	3,175
Ordinary shares under ESPP	14	16	16	9

13. Revenues

The following table presents a summary of total revenues (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Xyrem	$ 357,251	$ 303,870	$ 1,030,036	$ 874,222
Erwinaze/Erwinase	41,134	49,173	150,474	149,585
Defitelio/defibrotide	36,177	31,213	111,736	97,351
Vyxeos	21,038	9,719	75,217	9,719
Prialt	5,792	7,930	20,839	21,303
Other	3,805	6,066	13,837	19,124
Product sales, net	465,197	407,971	1,402,139	1,171,304
Royalties and contract revenues	4,176	3,884	12,326	10,990
Total revenues	$ 469,373	$ 411,855	$ 1,414,465	$ 1,182,294

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
United States	$ 429,729	$ 372,846	$ 1,290,775	$ 1,068,716
Europe	30,816	30,297	94,165	89,027
All other	8,828	8,712	29,525	24,551
Total revenues	$ 469,373	$ 411,855	$ 1,414,465	$ 1,182,294

The following table presents a summary of the percentage of total revenues from customers that represented more than 10% of our total revenues:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Express Scripts	76%	74%	73%	74%
McKesson	15%	14%	18%	14%

Financing and payment

Our payment terms vary by the type and location of our customer but payment is generally required in a term ranging from 30 to 45 days.

Contract Liabilities - Deferred Revenue

The deferred revenue balance as of September 30, 2018 primarily related to deferred upfront fees received from Nippon Shinyaku Co., Ltd., or Nippon Shinyaku, in connection with two license, development and commercialization agreements granting Nippon Shinyaku exclusive rights to develop and commercialize each of Defitelio and Vyxeos in Japan. We recognized contract revenues of $1.9 million and $5.6 million during the three and nine months ended September 30, 2018,

respectively, relating to these upfront payments. The deferred revenue balances are being recognized over an average of four years representing the period we expect to perform our research and developments obligations under each agreement.

The following table presents a reconciliation of our beginning and ending balances in contract liabilities from contracts with customers for the nine months ended September 30, 2018 (in thousands):

	Contract Liabilities
Balance as of December 31, 2017	$ 24,733
Effect of adoption of ASU 2014-09	(2,240)
Amount recognized within royalties and contract revenues	(5,624)
Balance as of September 30, 2018	$ 16,869

14. Share-Based Compensation

Share-based compensation expense related to share options, RSUs and grants under our ESPP was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Selling, general and administrative	$ 18,978	$ 20,903	$ 57,012	$ 61,582
Research and development	4,600	4,650	13,684	13,651
Cost of product sales	1,525	1,573	5,022	4,346
Total share-based compensation expense, pre-tax	25,103	27,126	75,718	79,579
Income tax benefit from share-based compensation expense	(3,552)	(6,354)	(12,066)	(23,816)
Total share-based compensation expense, net of tax	$ 21,551	$ 20,772	$ 63,652	$ 55,763

Share Options

The table below shows the number of shares underlying options granted to purchase our ordinary shares, the weighted-average assumptions used in the Black-Scholes option pricing model and the resulting weighted-average grant date fair value of share options granted:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Shares underlying options granted (in thousands)	117	87	1,349	1,343
Grant date fair value	$ 53.93	$ 45.87	$ 46.95	$ 42.69
Black-Scholes option pricing model assumption information:				
Volatility	32%	35%	35%	35%
Expected term (years)	4.5	4.3	4.5	4.3
Range of risk-free rates	2.7-2.8%	1.6-1.8%	2.2-2.8%	1.6-1.8%
Expected dividend yield	—%	—%	—%	—%

Restricted Stock Units

The table below shows the number of RSUs granted covering an equal number of our ordinary shares and the weighted-average grant date fair value of RSUs granted:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
RSUs granted (in thousands)	71	35	564	537
Grant date fair value	$ 174.73	$ 148.60	$ 145.59	$ 137.23

The fair value of RSUs is determined on the date of grant based on the market price of our ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, generally over four years.

As of September 30, 2018, compensation cost not yet recognized related to unvested share options and RSUs was $82.8 million and $102.7 million, respectively, which is expected to be recognized over a weighted-average period of 2.7 years and 2.6 years, respectively.

15. Income Taxes

Our income tax provision was $19.3 million and $75.0 million in the three and nine months ended September 30, 2018, respectively, compared to $1.2 million and $65.9 million for the same periods in 2017. The effective tax rates were 11.4% and 20.6% in the three and nine months ended September 30, 2018, respectively, compared to 1.9% and 20.5% for the same periods in 2017. The increase in the effective tax rate for the three months ended September 30, 2018 compared to the same period in 2017 was primarily due to the release of a valuation allowance held against certain foreign net operating losses in 2017 and the impacts of movements on unrecognized tax benefits, partially offset by a decrease in the U.S. corporate income tax rate. The effective tax rate for the nine months ended September 30, 2018 was in line with the same period in 2017. The effective tax rate for the three months ended September 30, 2018 was lower than the Irish statutory rate of 12.5% primarily due to the release of reserves related to unrecognized tax benefits upon the expiration of a statute of limitations. The effective tax rate for the nine months ended September 30, 2018 was higher than the Irish statutory rate of 12.5% primarily due to income taxable at a rate higher than the Irish statutory rate, various expenses not deductible for income tax purposes and unrecognized tax benefits. 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.

Our net deferred tax liability primarily arose due to the acquisition of Celator. The balance is net of deferred tax assets which are comprised primarily of U.S. federal and state tax credits, U.S. federal and state and foreign net operating loss carryforwards and other temporary differences. We maintain a valuation allowance against certain foreign and U.S. federal and state deferred tax assets. Each reporting period, we evaluate the need for a valuation allowance on our deferred tax assets by jurisdiction and adjust our estimates as more information becomes available.

We are required to recognize the financial statement effects of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained upon examination. As a result, we have recorded an unrecognized tax benefit for certain tax benefits which we judge may not be sustained upon examination. Our most significant tax jurisdictions are Ireland, the U.S. (both at the federal level and in various state jurisdictions), Italy and France. These jurisdictions have statutes of limitations ranging from three to five years. However, in the U.S. (at the federal level and in most states), carryforward tax attributes that were generated in 2013 and earlier may still be adjusted upon examination by the tax authorities. Certain of our subsidiaries are currently under examination by the French tax authorities for the years ended December 31, 2012, 2013, 2015, 2016 and 2017. These examinations may lead to ordinary course adjustments or proposed adjustments to our taxes. 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 relating to certain transfer pricing adjustments. The notices provide for additional French tax of approximately $43 million, including interest and penalties through the date of the proposed assessment, translated at the foreign exchange rate at September 30, 2018. We disagree with the assessments and are contesting them vigorously.

During the three and nine months ended September 30, 2018, we recorded an income tax expense of $2.9 million as a provisional measurement period adjustment to the provisional estimates recorded as of December 31, 2017 in accordance with the SEC's Staff Accounting Bulletin No. 118, or SAB 118. The provisional measurement period adjustment was due to additional analysis on the one-time transition tax on deemed repatriated earnings of foreign subsidiaries. We will continue to analyze the impact of the U.S. Tax Cuts and Jobs Act of 2017 under SAB 118 and may record further adjustments to provisional amounts as our analyses are completed in the fourth quarter of 2018.

Item 2. 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 condensed consolidated financial statements and the notes to condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q. This discussion contains forward-looking statements that involve risks and uncertainties. When reviewing the discussion below, you should keep in mind the substantial risks and uncertainties that could impact our business. In particular, we encourage you to review the risks and uncertainties described in "Risk Factors" in Part II, Item 1A in this Quarterly Report on Form 10-Q. 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. Forward-looking statements are statements that attempt to forecast or anticipate future developments in our business, financial condition or results of operations. See the "Cautionary Note Regarding Forward-Looking Statements" that appears at the end of this discussion. These statements, like all statements in this report, speak only as of the date of this Quarterly Report on Form 10-Q (unless another date is indicated), and we undertake no obligation to update or revise these statements in light of future developments.

Overview

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

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

- **Xyrem® (sodium oxybate) oral solution**, the only product approved by the U.S. Food and Drug Administration, or FDA, and marketed in the U.S. for the treatment of both cataplexy and excessive daytime sleepiness, or EDS, in patients with narcolepsy;
- **Erwinaze® (asparaginase *Erwinia chrysanthemi*)**, a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia, or ALL, who have developed hypersensitivity to *E. coli*-derived asparaginase;
- **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.

Our strategy is to create shareholder value by:

- Growing sales of the existing products in our portfolio, including by identifying and investing in growth opportunities such as new treatment indications and new geographic markets;
- Acquiring or licensing rights to clinically meaningful and differentiated products on the market or product candidates at various stages of development; and
- Pursuing targeted development of post-discovery differentiated product candidates.

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

In the three and nine months ended September 30, 2018, our total net product sales increased by 14% and 20%, respectively, compared to the same periods in 2017, primarily due to an increase in Xyrem net product sales and net product sales of Vyxeos, which launched in the U.S. in August 2017. We expect total net product sales to increase in 2018 over 2017, primarily due to expected growth in sales of Xyrem, Vyxeos and Defitelio. Our ability to increase net product sales is subject to a number of risks and uncertainties as set forth below and under "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q. For additional information regarding our net product sales, see "—Results of Operations."

Significant Developments Affecting Our Business

In August 2018, we announced that the U.S. Centers for Medicare and Medicaid Services granted approval for a New Technology Add-on Payment for Vyxeos for the treatment of adults with newly diagnosed t-AML or AML-MRC.

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.

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 September 2018, Nippon Shinyaku Co., Ltd., or Nippon Shinyaku, announced that Japan's Ministry of Health, Labour and Welfare, or Ministry, granted orphan drug designation to NS-73 (defibrotide sodium) for the treatment of VOD following HSCT, and, in October 2018, Nippon Shinyaku announced that it had filed a new drug application, or NDA, for NS-73 to the Ministry.

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

On October 11, 2018, we entered into a settlement agreement and related agreements resolving our patent infringement litigation against Amneal Pharmaceuticals LLC, or Amneal. We had filed patent lawsuits against Amneal after it sent us a notice that it had filed an abbreviated new drug application, or ANDA, requesting approval to market a generic version of Xyrem. We previously settled lawsuits against the eight other ANDA filers. As a result, the settlement with Amneal represents settlement of all outstanding patent infringement litigation related to Xyrem.

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), or West-Ward, 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 (including Amneal) 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 (assuming FDA approval of its ANDA is obtained or maintained) 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 (assuming FDA approval of its ANDA is obtained or maintained) on or after December 31, 2025, or earlier under certain circumstances. We are entitled to receive a meaningful royalty on net sales of each of the AG Products, as well as payment for the supply of each party's AG Product and reimbursement for a portion of the services costs associated with distribution of each party's AG Product through the Xyrem risk evaluation and mitigation strategy, or REMS. For a further description of these settlement agreements, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

On October 26, 2018, the FDA approved our supplemental NDA, or sNDA, to revise the labeling for Xyrem to include an indication to treat cataplexy or EDS in pediatric narcolepsy patients ages seven and older. On October 25, 2018, the FDA confirmed that pediatric exclusivity has also been granted. As a result, each of our patents covering Xyrem will have an additional six months added to its expiration date. This six-month addition will also apply to any existing patent that covers a future oxybate product. The patent term additions do not affect the entry dates specified in the settlement agreements we have entered into with the ANDA filers.

Continued Emphasis on Research and Development

During the nine months ended September 30, 2018, we continued our focus on research and development activities, which currently include clinical development of new product candidates, activities related to line extensions and new indications for existing products and the generation of additional clinical data for existing products, all in our sleep and hematology/oncology therapeutic areas.

A summary of our ongoing development activities is provided below:

Project	Disease Area	Status
Sleep		
Solriamfetol (JZP-110)	EDS in obstructive sleep apnea, or OSA, and EDS in narcolepsy	NDA accepted for filing by FDA in first quarter of 2018 with a target action date under the Prescription Drug User Fee Act, or PDUFA, of December 20, 2018; preparing to submit a marketing authorization application to the European Medicines Agency in late 2018

Project	Disease Area	Status
Solriamfetol (JZP-110)	EDS in Parkinson's disease	Enrollment in Phase 2 trial completed in third quarter of 2018; top-line data expected early 2019
JZP-258 (oxybate; 90% sodium reduction)	EDS and cataplexy in narcolepsy	Expect top-line data in Phase 3 trial by second quarter of 2019
JZP-258	Idiopathic hypersomnia	Expect to commence patient enrollment in Phase 3 trial in fourth quarter of 2018
Oxybate once-nightly dosing	Narcolepsy	Program progressing; evaluation of several formulation options and technologies continues as part of once-nightly development process
Hematology/Oncology		
Vyxeos	Myelodysplastic syndrome	Preparing for Phase 2 trial with cooperative group with planned initiation in second quarter of 2019
Defibrotide	Prevention of VOD in high-risk patients following HSCT	First patient enrolled in Phase 3 trial in first quarter of 2017; interim analysis planned in 2019
Defibrotide	Prevention of acute Graft versus Host Disease following allogeneic HSCT	First patient enrolled in Phase 2 proof of concept trial in first quarter of 2018
Defibrotide	Transplant-associated thrombotic microangiopathy	Pivotal Phase 2 trial planned for 2019
Asparaginase	ALL and other hematological malignancies	Activities related to development of improved products, including a recombinant crisantaspase
CombiPlex combinations	Oncology/hematological disorders	Pre-clinical evaluation of oncology therapeutic combinations

In addition, we have entered into a number of licensing and collaboration agreements, including with:

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

For 2018 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, initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates. Our ability to continue to undertake our planned development activities, as well as the success of these activities, are subject to a number of risks and uncertainties, including the risk factors under the headings "Risks Related to Our Business" and "Risks Related to Our Industry" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Challenges, Risks and Trends Related to Our Lead Marketed Products and Product Candidates Submitted for Regulatory Approval

Xyrem. Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which accounted for 77% and 73% of our net product sales for the three and nine months ended September 30, 2018, respectively, and 74% of our net product sales for the year ended December 31, 2017. As a result, we continue to place a high priority on seeking to increase sales of Xyrem in its approved indications, while remaining focused on ensuring the safe and effective use of the product. We also focus on enhancing and enforcing our intellectual property rights related to Xyrem, and on product development efforts to develop product, service and safety improvements for patients.

Our future plans assume that sales of Xyrem will increase, but we cannot assure you that we can maintain sales of Xyrem at or near current levels, or that Xyrem sales will continue to grow. We have periodically increased the price of Xyrem, most recently in January 2018, and we cannot assure you that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes.

Our ability to maintain or increase Xyrem product sales is subject to risks and uncertainties, including those discussed in "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q, including those related to:

- the potential U.S. introduction of a generic version of Xyrem before the entry dates specified in our settlements with the ANDA filers, or on terms that are different from those contemplated by the settlement agreements, as further described below;
- the potential U.S. introduction of new products that compete with, or otherwise disrupt the market for, Xyrem in the treatment of cataplexy and/or EDS in narcolepsy;
- changes to or uncertainties around regulatory restrictions, including, among other things, changes to our Xyrem REMS, as further described below;
- potential challenges to our intellectual property around Xyrem, including the possibility of new ANDA or NDA filers or new post-grant patent review proceedings;
- any increase in pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors;
- changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing and REMS programs by government entities;
- operational disruptions at the Xyrem central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the FDA;
- any supply or manufacturing problems, including any problems with our sole source Xyrem 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;
- changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell Xyrem; and
- our U.S.-based API and Xyrem suppliers' ability to obtain sufficient quotas from the U.S. Drug Enforcement Administration, or DEA, to satisfy our needs for Xyrem.

Although Xyrem is protected by patents covering its manufacture, formulation, distribution system and method of use, nine companies have sent us notices that they had filed ANDAs 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. As described above under the heading "—Significant Developments Affecting our Business," we have settled all patent litigation against those nine ANDA filers. It is possible that other companies may in the future file ANDAs seeking to market a generic version of Xyrem or NDAs referencing Xyrem, which could lead to additional patent litigation or challenges with respect to Xyrem.

In July 2016, the Patent Trial and Appeal Board, or PTAB, issued final decisions that the claims of six patents associated with the Xyrem REMS are unpatentable. In March 2017, the PTAB issued a final decision that three claims of a seventh Xyrem patent associated with the Xyrem REMS are unpatentable. In July 2018, the United States Court of Appeals for the Federal Circuit upheld the July 2016 and March 2017 PTAB decisions on appeal, and as a result, we will not be able to enforce claims the PTAB found unpatentable.

For a further description of the PTAB proceedings and the settlement agreements relating to Xyrem, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

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, including as described above. For example, a company that has not settled ANDA litigation with us could obtain a final decision prior to January 1, 2023 that all unexpired claims of the Xyrem patents are invalid and/or unenforceable by prevailing against us in patent litigation or as a result of either an inter partes review, or IPR, challenge, which in turn could accelerate the launch dates for the AG Products and generic sodium oxybate products under our settlement agreements. Similarly, even in the absence of a final decision that all unexpired claims of the Xyrem patents are invalid and/or unenforceable, a company that has not settled ANDA litigation with us could obtain FDA approval for its generic sodium oxybate product and launch such product before the entry dates specified in our settlement agreements, if, for example, such company obtains a final determination that its product does not infringe our patents or if such company decides, before applicable patent litigation is concluded, to launch its product at risk of being held liable for damages for patent infringement.

Such a launch could accelerate the launch dates for the AG Products and generic sodium oxybate products under our settlement agreements, depending on the circumstances. In addition, a substantial reduction in Xyrem net sales could lead to acceleration of the launch date for West-Ward's AG Product, which in turn would accelerate the launch dates for the other settling ANDA filers' AG Products and generic sodium oxybate products.

In addition, Xyrem could also be subject to potential future competition from other products. Companies could develop and launch sodium oxybate or other products that are similar, but not identical, to Xyrem, such as an alternative formulation or an alternative delivery technology. For example, Avadel Pharmaceuticals plc, or Avadel, is using its proprietary technology for delivery of a sodium oxybate formulation to eliminate second nighttime dosing for narcolepsy patients. Avadel has stated that it is conducting a Phase 3 pivotal trial pursuant to an FDA-approved special protocol assessment, and has indicated that it intends to seek approval of its product candidate using a Section 505(b)(2) NDA approval pathway referencing Xyrem. We are also aware of products being developed by others for use as treatment options in cataplexy and/or EDS in patients with narcolepsy that have different safety profiles and mechanisms of action than Xyrem, including pitolisant, a product to treat adult patients with narcolepsy with or without cataplexy that received marketing approval in Europe in 2016. While pitolisant is currently not approved by the FDA for marketing in the U.S., the company that has exclusive U.S. commercialization rights to pitolisant established an expanded access program for the product and announced that the product has received Breakthrough Therapy and Fast Track designations from the FDA and that it is preparing an NDA submission for the product. If any company successfully develops, obtains FDA approval of and launches a product that is approved in the U.S. for the treatment of narcolepsy patients, it could result in a substantial reduction of Xyrem sales, which could have the additional impact of potentially triggering acceleration of market entry of AG Products or other generic sodium oxybate products under our ANDA litigation settlement agreements, as described elsewhere in this Quarterly Report on Form 10-Q. We expect that the launch of an AG Product or other generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, could have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects.

In February 2015, the FDA approved the Xyrem REMS, which requires, among other things, that Xyrem be distributed through a single pharmacy. In the FDA's letter approving the February 2015 Xyrem REMS, the FDA stated that (i) the approval action should not be construed or understood as agreement with what the FDA stated was our position that dispensing through a single pharmacy is the only way to ensure that the benefits of Xyrem outweigh its risks, and that the FDA has continuing concerns that limiting the distribution of Xyrem to one pharmacy imposes burdens on patient access and the healthcare delivery system, and (ii) as with all REMS, the FDA intends to evaluate the Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. In October 2018, in connection with the FDA's approval of our sNDA to revise the labeling for Xyrem to include an indication to treat cataplexy or EDS in pediatric narcolepsy patients ages seven and older, the FDA modified the February 2015 Xyrem REMS to add provisions and material for pediatric patients and caregivers, but did not modify the current operation of the Xyrem REMS. 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 indications or products, or whether FDA will approve modifications to the Xyrem REMS that we consider warranted in connection with the submission of applications for new oxybate indications or products. Any such modifications approved, required or rejected by the FDA could make it more difficult or expensive for us to distribute Xyrem, make distribution easier for sodium oxybate competitors, impair the safety profile of Xyrem, disrupt continuity of care for Xyrem patients and/or negatively affect sales of Xyrem.

In January 2017, the FDA approved West-Ward's ANDA and waived the shared REMS requirement, permitting West-Ward to use a separate REMS program from the Xyrem REMS, or the generic sodium oxybate REMS, for the generic sodium oxybate product, on the condition that the generic sodium oxybate REMS be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. This could potentially include future sodium oxybate products approved under a Section 505(b)(2) approval pathway. We cannot predict whether a company marketing a sodium oxybate product approved under Section 505(b)(2) would be required or permitted to distribute its product through the generic sodium oxybate REMS or a separate REMS.

We were not involved in the 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 could be distributed through multiple pharmacies, could increase the risks associated with sodium oxybate distribution. 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, public acceptance of Xyrem as a treatment for EDS and cataplexy in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, as patients, consumers and others may not differentiate generic sodium oxybate from Xyrem or differentiate between the different REMS programs, 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. We continue to evaluate potential challenges based on the FDA's waiver of the requirement for a single, shared system REMS in connection with the approvals of the ANDAs, including whether the FDA's waiver decision meets the conditions for such a waiver under applicable law. We cannot predict whether or when we may pursue any such challenges or whether any such challenges would be successful.

For further discussion regarding the risks associated with Xyrem, see the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales," "*We face substantial competition from other companies, including companies with greater resources, including larger sales organizations and more experience working with large and diverse product portfolios, than we have*" and "Risks Related to Our Intellectual Property" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

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 11% of our net product sales for the three and nine months ended September 30, 2018, respectively, and 12% for the year ended December 31, 2017. 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. A significant challenge to maintaining and potentially increasing sales is the limited supply of Erwinaze, which has resulted, and continues 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. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions throughout the fourth quarter of 2018 and during 2019. These supply disruptions have adversely impacted our ability to generate our previously anticipated level of sales of and revenues from Erwinaze in 2018, and we expect that they will continue to adversely impact our ability to generate sales of and revenues from Erwinaze in 2019.

In January 2017, the FDA issued a warning letter to PBL indicating that it was not satisfied with PBL's responses to the FDA Form 483 issued to PBL in March 2016 and citing significant violations of the FDA's current Good Manufacturing Practices, or 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. Following a site inspection of PBL by the UK Medicines and Healthcare Products Regulatory Agency, or 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. We cannot predict if or when PBL will correct the violations and deviations to the satisfaction of the FDA and MHRA or whether the FDA and MHRA will be satisfied with PBL's responses. Any failure by PBL to respond to the satisfaction of the FDA or MHRA could result in enforcement actions by the FDA or MHRA, including the FDA refusing admission of Erwinaze into the U.S. 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.

The current manufacturing capacity for Erwinaze is 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 certain 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 manufacturing capacity or otherwise 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 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 be further materially adversely affected.

In addition, our agreement with PBL, including our license, expires in December 2020, subject to five-year extensions unless terminated by either party in writing by December 31, 2018. The parties are in discussions regarding the agreement, but we cannot predict whether the term of the agreement will be extended or, if extended, the terms of any such extension. If the agreement is terminated and we do not enter into a new agreement with PBL, we will lose our license to sell Erwinaze in any market after December 2020, except under specified terms for a post-termination transition period. We cannot predict the

extent to which potential uncertainty related to our ongoing rights to Erwinaze will impact our sales of and revenues from Erwinaze.

Our ability to successfully maintain sales of Erwinaze is subject to a number of other challenges, including the development of new asparaginase treatments or treatment protocols and potential competition from future biosimilar products. For further discussion of these and other risks and uncertainties associated with Erwinaze, see the risk factors set forth in "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Defitelio/defibrotide. Sales of Defitelio/defibrotide were 8% of our net product sales for the three and nine months ended September 30, 2018 and for the year ended December 31, 2017. We seek to increase sales of Defitelio through selling and marketing activities. However, 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.

For further discussion of these and other risks and uncertainties associated with Defitelio, see the risk factors set forth in "Risks Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Vyxeos. In August 2017, the FDA approved our NDA for Vyxeos for the treatment of adults with newly-diagnosed t‑AML or AML-MRC. We launched and began selling Vyxeos in the U.S. in August 2017, and our commercial launch in the U.S. is still at an early stage. Sales of Vyxeos were 5% of our net product sales for the three and nine months ended September 30, 2018 and 2% of our net product sales for the year ended December 31, 2017. 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.

Our ability to realize the anticipated benefits from our investment in Vyxeos is subject to a number of additional risks and uncertainties, including potential delays or problems in the supply or manufacture of Vyxeos, 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 and potential competition from existing products and products in development. Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. There have 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. If we fail to obtain a sufficient supply of Vyxeos 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, and our business, financial condition, results of operations and growth prospects could be materially adversely affected. In any event, 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 further discussion of these and other risks and uncertainties associated with Vyxeos, see the risk factors set forth in "Risks Factors" in Part II, Item 1A of this Quarterly Report on Form 10‑Q.

Solriamfetol. In the fourth quarter of 2017, we submitted an NDA to the FDA to seek approval for solriamfetol in the treatment of EDS associated with OSA and EDS associated with narcolepsy. In the first quarter of 2018, the FDA accepted the NDA for filing with a standard review and set a target action date under PDUFA of December 20, 2018. We cannot predict whether our NDA will be approved by the FDA in a timely manner, or at all. Our ability to realize the anticipated benefits from an approved solriamfetol product and our investment in solriamfetol is subject to a number of risks and uncertainties, including, among other things, the outcome of DEA scheduling review, which will need to be completed after NDA approval, if any, but before commercial launch, market acceptance for an approved solriamfetol product, potential competition from other products in development and the availability of adequate pricing, coverage and reimbursement by government programs and third party payors. For further discussion of these and other risks and uncertainties associated with solriamfetol, see the risk factors set forth in "Risks Factors" Part II, Item 1A of this Annual Report on Form 10-Q.

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 2018 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.

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.

Several states have recently passed laws aimed at increasing transparency relating to drug pricing, and other states may do so in the future. Both the U.S. House of Representatives and the U.S. Senate have conducted several hearings with respect to pharmaceutical drug pricing practices, including in connection with the investigation of specific price increases by several pharmaceutical companies. Moreover, REMS and the improper use of REMS as a means of improperly blocking or delaying competition for branded pharmaceutical products have increasingly drawn public scrutiny from Congress, the Federal Trade Commission, or FTC, and the FDA. 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 through a REMS program. If we become the subject of any government investigation with respect to our drug pricing or other business practices, including as they relate to the Xyrem REMS, we could incur significant expense and could be distracted from operation of our business and execution of our strategy.

In May and October 2016 and in February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. Other companies have disclosed similar subpoenas and continuing inquiries. We have a comprehensive program intended to ensure our compliance with applicable legal and regulatory requirements for pharmaceutical companies, including guidelines established by the Office of Inspector General of the U.S. Department of Health and Human Services regarding patient assistance programs, and we have been cooperating with the government's investigation. We have engaged in discussions with the U.S. Department of Justice, or DOJ, about a possible resolution, and 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. Any such settlement is also likely to involve entry into a corporate integrity agreement, which would impose costs and burdens on the operation of our business. If we do not reach a final settlement, 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, and we would expect to incur significant costs in connection with such enforcement action, regardless of the outcome. For more information, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q and the risk factors under the headings "*Changes in healthcare law and implementing regulations, including those based on recently enacted legislation, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and these changes could have a material adverse effect on our business and financial condition*" and "*We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products*" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Other key challenges and risks that we face include risks and uncertainties related to:

- the challenges of protecting and enhancing our intellectual property rights;
- the challenges of achieving and maintaining commercial success of our products;
- delays or problems in the supply or manufacture of our products and product candidates, particularly with respect to certain products as to which we maintain limited inventories, our dependence on single source suppliers for most of our products, product candidates and APIs, and the requirement that we and our product suppliers be qualified by the FDA to manufacture product and comply with applicable manufacturing regulations;
- the need to obtain and maintain appropriate pricing and reimbursement for our products in an increasingly challenging environment due to, among other things, the attention being paid to healthcare cost containment and pharmaceutical pricing in the U.S. and worldwide, including the need to obtain and maintain reimbursement for Xyrem in the U.S. in an environment in which we are subject to increasingly restrictive conditions for reimbursement required by government programs and third party payors;
- our ability to identify and acquire, in-license or develop additional products or product candidates to grow our business;
- the challenges of compliance with the requirements of the FDA, the DEA and comparable non-U.S. regulatory agencies, including with respect to product labeling, requirements for distribution, obtaining sufficient DEA quotas

where needed, marketing and promotional activities, patient assistance programs, adverse event reporting and product recalls or withdrawals;

- the difficulty and uncertainty of pharmaceutical product development, including the timing thereof, and the uncertainty of clinical success, such as the risk that results from preclinical studies and/or early clinical trials may not be predictive of results obtained in later and larger clinical trials planned or anticipated to be conducted for our product candidates;
- the inherent uncertainty associated with the regulatory approval process, especially as we continue to increase investment in our product pipeline development projects and undertake multiple planned regulatory submissions for our product candidates;
- 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; and
- possible restrictions on our ability and flexibility to pursue certain future opportunities as a result of our substantial outstanding debt obligations.

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 II, Item 1A of this Quarterly Report on Form 10-Q.

Results of Operations

The following table presents our revenues and expenses (in thousands, except percentages):

	Three Months Ended September 30,		Increase/	Nine Months Ended September 30,		Increase/
	2018	2017	(Decrease)	2018	2017	(Decrease)
Product sales, net	$ 465,197	$ 407,971	14 %	$ 1,402,139	$ 1,171,304	20 %
Royalties and contract revenues	4,176	3,884	8 %	12,326	10,990	12 %
Cost of product sales (excluding amortization of intangible assets)	26,574	31,203	(15)%	95,207	84,940	12 %
Selling, general and administrative	155,873	124,523	25 %	521,665	401,106	30 %
Research and development	51,160	47,362	8 %	169,959	132,447	28 %
Intangible asset amortization	46,989	47,313	(1)%	154,955	99,164	56 %
Impairment charges	—	—	N/A(1)	42,896	—	N/A(1)
Acquired in-process research and development	—	75,000	N/A(1)	—	77,000	N/A(1)
Interest expense, net	18,920	19,192	(1)%	59,171	56,330	5 %
Foreign exchange loss	756	2,224	(66)%	5,181	9,115	(43)%
Loss on extinguishment and modification of debt	—	—	N/A(1)	1,425	—	N/A(1)
Income tax provision	19,348	1,239	1,462 %	75,018	65,914	14 %
Equity in loss of investees	437	273	60 %	1,360	637	114 %

(1) Comparison to prior period not meaningful.

Revenues

The following table presents our product sales, royalties and contract revenues, and total revenues (in thousands, except percentages):

	Three Months Ended September 30,		Increase/	Nine Months Ended September 30,		Increase/
	2018	2017	(Decrease)	2018	2017	(Decrease)
Xyrem	$ 357,251	$ 303,870	18 %	$ 1,030,036	$ 874,222	18 %
Erwinaze/Erwinase	41,134	49,173	(16)%	150,474	149,585	1 %
Defitelio/defibrotide	36,177	31,213	16 %	111,736	97,351	15 %
Vyxeos	21,038	9,719	116 %	75,217	9,719	674 %
Prialt	5,792	7,930	(27)%	20,839	21,303	(2)%
Other	3,805	6,066	(37)%	13,837	19,124	(28)%
Product sales, net	465,197	407,971	14 %	1,402,139	1,171,304	20 %
Royalties and contract revenues	4,176	3,884	8 %	12,326	10,990	12 %
Total revenues	$ 469,373	$ 411,855	14 %	$ 1,414,465	$ 1,182,294	20 %

Product Sales, Net

Xyrem product sales increased in the three and nine months ended September 30, 2018 compared to the same periods in 2017 due to an increase in sales volume and a higher average net selling price. Xyrem product sales volume increased by 9% in both the three and nine months ended September 30, 2018 compared to the same periods in 2017 primarily driven by an increase in the average number of patients on Xyrem. Price increases were instituted in January 2018 and July 2017. Erwinaze/Erwinase product sales decreased in the three months ended September 30, 2018 compared to the same period in 2017 primarily due to restricted supply. Erwinaze/Erwinase net product sales for the nine months ended September 30, 2018 were consistent with the same period in 2017. Ongoing supply challenges at the manufacturer have resulted in fluctuations in inventory and continue to negatively impact our ability to supply the market. We are experiencing supply disruptions globally and expect further supply disruptions throughout the fourth quarter of 2018 and during 2019. Defitelio/defibrotide product sales increased in the three and nine months ended September 30, 2018 compared to the same periods in 2017 primarily due to higher volumes and, to a lesser extent, the positive impact of foreign exchange rates. Vyxeos product sales increased in the three and nine months ended September 30, 2018 compared to the same periods in 2017 following the launch in the U.S. in August 2017. Prialt product sales decreased in the three and nine months ended September 30, 2018 compared to the same periods in 2017. We completed the sale of our rights to Prialt to TerSera in September 2018. Other product sales decreased in the three and nine months ended September 30, 2018 compared to the same periods in 2017 primarily due to a decrease in sales of our psychiatry products due to generic competition. We expect total product sales will increase in 2018 over 2017, primarily due to anticipated growth in sales of Xyrem, Vyxeos and Defitelio.

Royalties and Contract Revenues

Royalties and contract revenues increased in the three and nine months ended September 30, 2018 compared to the same periods in 2017 primarily due to higher contract revenues from out-licensing agreements. We expect royalties and contract revenues to increase in 2018 compared to 2017 due to higher contract revenue from out-licensing agreements.

Cost of Product Sales

Cost of product sales decreased in the three months ended September 30, 2018 compared to the same period in 2017 primarily due to lower royalty expenses. Cost of product sales increased in the nine months ended September 30, 2018 compared to the same period in 2017 primarily due to an increase in net product sales. Gross margin as a percentage of net product sales was 94.3% and 93.2% in the three and nine months ended September 30, 2018, respectively, compared to 92.4% and 92.7% for the same periods in 2017. The increase in the gross margin percentage in the three and nine months ended September 30, 2018 was primarily due to change in product mix. We do not expect our gross margin as a percentage of net product sales to change materially in 2018 compared to 2017.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased in the three months ended September 30, 2018 compared to the same period in 2017 primarily due to higher marketing and promotional expenses primarily driven by promotional costs for the

potential U.S. commercial launch of solriamfetol and for the rolling launch of Vyxeos in the EU, as well as an increase in compensation-related expenses driven by higher headcount. Selling, general and administrative expenses increased in the nine months ended September 30, 2018 compared to the same period in 2017 primarily due to an accrued estimated loss contingency, including related interest, of $57.8 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 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q. Selling, general and administrative expenses for the nine months ended September 30, 2018 also included higher marketing and promotional expenses primarily due to marketing and promotional costs for the potential U.S. commercial launch of solriamfetol and for the rolling launch of Vyxeos in the EU, and an increase in compensation-related expenses driven by higher headcount, compared to the same period in 2017. We expect selling, general and administrative expenses in 2018 to increase compared to 2017, primarily due to an estimated loss contingency, an increase in compensation-related expenses and other expenses resulting from the expansion and support of our business and an increase in expenses related to the preparation for the potential U.S. commercial launch of solriamfetol and the continuation of the commercial launch of Vyxeos in the U.S. and the EU.

Research and Development Expenses

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Clinical studies and outside services	$ 26,501	$ 26,197	$ 86,889	$ 67,885
Personnel expenses	17,340	15,777	52,588	48,331
Milestone expense	—	—	11,000	—
Other	7,319	5,388	19,482	16,231
Total	$ 51,160	$ 47,362	$ 169,959	$ 132,447

Research and development expenses increased by $3.8 million and $37.5 million in the three and nine months ended September 30, 2018, respectively, compared to the same periods in 2017. Clinical studies and outside services costs for the three months ended September 30, 2018 were consistent with the same period in 2017. Clinical studies and outside services costs increased by $19.0 million in the nine months ended September 30, 2018 compared to the same period in 2017 primarily due to an increase in expenses related to our ongoing pre-clinical and clinical development programs, regulatory activities 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 $1.6 million and $4.3 million in the three and nine months ended September 30, 2018, respectively, compared to the same periods in 2017, primarily due to increased headcount in support of our development programs. Milestone expense of $11.0 million in the nine months ended September 30, 2018 related to milestone payments following FDA acceptance of our NDA for solriamfetol in March 2018.

For 2018 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, 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 II, Item 1A of this Quarterly Report on Form 10-Q.

Intangible Asset Amortization

Intangible asset amortization for the three months ended September 30, 2018 was consistent with the same period in 2017. Intangible asset amortization for the nine months ended September 30, 2018 increased by $55.8 million compared to the same period in 2017, primarily due to the commencement of amortization of the Vyxeos intangible asset upon FDA approval in August 2017. We expect intangible asset amortization to increase in 2018 compared to 2017 primarily due to the full year of amortization of the Vyxeos intangible asset.

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 the nine months ended September 30, 2018. The transaction closed on September 27, 2018.

Acquired In-Process Research and Development

Acquired in-process research and development, or IPR&D, expense in the three and nine months ended September 30, 2017 primarily related to an upfront payment of $75.0 million in connection with a collaboration and option agreement with ImmunoGen to acquire rights to opt into exclusive, worldwide licenses to develop and commercialize two early-stage, hematology-related ADC programs, as well as an additional program to be designated during the term of the agreement.

Interest Expense, Net

Interest expense, net for the three months ended September 30, 2018 was consistent with the same period in 2017. Interest expense, net increased by $2.8 million in the nine months ended September 30, 2018 compared to the same period in 2017, primarily due to interest expense on our 1.50% exchangeable senior notes due 2024, or the 2024 Notes, which were issued in August 2017, partially offset by higher interest income and a reduction in interest expense following repayment of our revolving credit facility in full in the third quarter of 2017. We expect interest expense, net will be higher in 2018 compared to 2017 primarily due to the amortization of the debt discount on the 2024 Notes, partially offset by higher interest income.

Foreign Exchange Loss

The foreign exchange loss 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 the nine months ended September 30, 2018, we recorded a loss of $1.4 million in connection with the 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.

Income Tax Provision

Our income tax provision was $19.3 million and $75.0 million in the three and nine months ended September 30, 2018, respectively, compared to $1.2 million and $65.9 million for the same periods in 2017. The effective tax rates were 11.4% and 20.6% in the three and nine months ended September 30, 2018, respectively, compared to 1.9% and 20.5% for the same periods in 2017. The increase in the effective tax rate for the three months ended September 30, 2018 compared to the same period in 2017 was primarily due to the release of a valuation allowance held against certain foreign net operating losses in 2017 and the impacts of movements on unrecognized tax benefits, partially offset by a decrease in the U.S. corporate income tax rate. The effective tax rate for the nine months ended September 30, 2018 was in line with the same period in 2017. The effective tax rate for the three months ended September 30, 2018 was lower than the Irish statutory rate of 12.5% primarily due to the release of reserves related to unrecognized tax benefits upon the expiration of a statute of limitations. The effective tax rate for the nine months ended September 30, 2018 was higher than the Irish statutory rate of 12.5% primarily due to income taxable at a rate higher than the Irish statutory rate, various expenses not deductible for income tax purposes and unrecognized tax benefits.

Equity in Loss of Investees

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

Liquidity and Capital Resources

As of September 30, 2018, we had cash, cash equivalents and investments of $1.1 billion, borrowing availability under our revolving credit facility of $1.6 billion and long-term debt principal balance of $1.8 billion. Our long-term debt included $659.4 million aggregate principal amount term loan, $575.0 million principal amount of our 1.875% exchangeable senior notes due 2021, or the 2021 Notes, and $575.0 million principal amount of the 2024 Notes. We generated cash flows from operations of $574.6 million during the nine months ended September 30, 2018, and we expect to continue to generate positive cash flows from operations during 2018.

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

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

In November 2016, our board of directors authorized a share repurchase program pursuant to which we are authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300 million, exclusive of any brokerage commissions. Under this program, which has no expiration date, we may repurchase ordinary shares from time to time on the open market. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the amended credit agreement, corporate and regulatory requirements and market conditions. In the nine months ended September 30, 2018, we spent a total of $77.0 million to purchase 0.5 million of our ordinary shares under the share repurchase program at an average total purchase price, including commissions, of $154.03 per share. As of September 30, 2018, the remaining amount authorized under the share repurchase program was $105.7 million.

In November 2018, our board of directors increased the existing share repurchase program authorization by an aggregate purchase price of $320 million, exclusive of any brokerage commissions.

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

	Nine Months Ended September 30,	
	2018	2017
Net cash provided by operating activities	$ 574,558	$ 488,528
Net cash used in investing activities	(428,229)	(237,072)
Net cash used in financing activities	(32,674)	(369,127)
Effect of exchange rates on cash and cash equivalents	(672)	4,323
Net increase (decrease) in cash and cash equivalents	$ 112,983	$ (113,348)

Net cash provided by operating activities of $574.6 million for the nine months ended September 30, 2018 related to net income of $287.6 million, adjusted for non-cash items of $286.7 million primarily related to intangible asset amortization, share-based compensation expense and impairment charges and a net cash inflow of $0.2 million related to changes in operating assets and liabilities. Net cash provided by operating activities of $488.5 million for the nine months ended September 30, 2017 related to net income of $255.6 million, adjusted for acquired IPR&D expense of $77.0 million and non-cash items of $170.6 million primarily related to intangible asset amortization and share-based compensation expense. This was partially offset by a net cash outflow of $14.7 million related to changes in operating assets and liabilities.

Net cash used in investing activities for the nine months ended September 30, 2018 primarily related to the net acquisition of investments of $350.0 million, acquisition of intangible assets of $111.1 million related to the purchase of a priority review voucher and purchases of property and equipment of $15.2 million, partially offset by net proceeds of $48.1 million from the sale of our rights to Prialt to TerSera. Net cash used in investing activities for the nine months ended September 30, 2017 primarily related to the net acquisition of investments of $140.0 million, upfront payments for acquired IPR&D of $77.0 million primarily related to a collaboration and option agreement with ImmunoGen and purchases of property and equipment of $20.1 million.

Net cash used in financing activities for the nine months ended September 30, 2018 primarily related to repurchase of ordinary shares under our share repurchase program of $77.0 million, repayment of our term loan principal of $17.4 million, payment of employee withholding taxes of $17.2 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 $84.1 million and proceeds from tenant improvement allowance on a build-to-suit lease of $1.3 million. Net cash used in financing activities for the nine months ended September 30, 2017 primarily related to repayment of borrowings under our prior revolving credit facility of $850.0 million, repurchase of ordinary shares under our share repurchase program of $56.4 million, repayment of our term loan principal of $27.1 million and payment of employee withholding taxes of $17.9 million related to share-based awards, partially offset by net proceeds from issuance of debt of $559.5 million and proceeds from employee equity incentive and purchase plans of $22.8 million.

Debt

The summary of our outstanding indebtedness under our financing arrangements is included in Note 9, Debt, of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q. As of September 30, 2018, no amounts were outstanding under our revolving credit facility. During the nine months ended September 30, 2018, there were no material changes to our Exchangeable Senior Notes as set forth in Note 11, Debt, of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2017. In June 2018, we entered into a second amendment of our 2015 credit agreement, which increased our revolving credit facility from $1.25 billion to $1.6 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. For more information, see Note 9, Debt, of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

Contractual Obligations

The table below presents a summary of our contractual obligations as of September 30, 2018 (in thousands):

Contractual Obligations (1)	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 years
Term loan - principal	$ 659,388	$ 33,387	$ 66,773	$ 559,228	$ —
Term loan - interest (2)	93,293	22,005	40,661	30,627	—
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)	19,000	4,056	8,122	6,822	—
Commitment to equity method investees	22,300	7,000	14,000	1,300	—
Purchase and other obligations (5)	152,366	54,746	39,782	41,168	16,670
Operating lease obligations (6)	41,410	8,508	12,097	10,652	10,153
Facility lease obligations (7)	191,518	9,215	29,239	31,020	122,044
Total	$ 2,413,369	$ 158,323	$ 824,487	$ 698,067	$ 732,492

(1) This table does not include potential future milestone payment or royalty obligations to third parties under asset purchase, product development, license and other agreements as the timing and likelihood of such milestone payments are not known, and, in the case of royalty obligations, as the amount of such obligations are not estimable. In 2014, we signed a definitive agreement with Aerial 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 $35.3 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 $87 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 September 30, 2018. The interest rate for our term loan borrowing was 3.62% as of September 30, 2018. Interest that is fixed, associated with our interest rate swaps, is calculated based on the fixed interest swap rate as of September 30, 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 September 30, 2018 until the respective final maturity dates of these notes.

(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 September 30, 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 $20 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. 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. 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 Estimates

To understand our financial statements, it is important to understand our critical accounting estimates. The preparation of our financial statements in conformity with U.S. generally accepted accounting principles, or U.S. GAAP, requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Significant estimates and assumptions are required in determining the amounts to be deducted from gross revenues, in particular estimates of government rebates, which include Medicaid and TRICARE rebates, and estimated product returns. Significant estimates and assumptions are also required to determine whether to capitalize intangible assets, the amortization periods for identifiable intangible assets, the potential impairment of goodwill and other intangible assets, income taxes and share-based compensation. Some of these judgments can be subjective and complex, and, consequently, actual results may differ from these estimates. For any given individual estimate or assumption we make, there may also be other estimates or assumptions that are reasonable. Although we believe our estimates and assumptions are reasonable, they are based upon information available at the time the estimates and assumptions were made.

Our critical accounting policies and significant estimates are detailed in our Annual Report on Form 10-K for the year ended December 31, 2017. Except for the revenue recognition policy that was updated as a result of adopting ASU No. 2014-09, "Revenue from Contracts with Customers", our critical accounting policies and significant estimates have not changed substantially from those previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2017.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Cautionary Note Regarding Forward-Looking Statements

This Quarterly Report on Form 10-Q 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 current plans, objectives, estimates, expectations and intentions and on information currently available to our management. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "propose," "intend," "continue," "potential," "possible," "foreseeable," "likely," "unforeseen" and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss many of these risks, uncertainties and other risk factors in greater detail under Part II, Item 1A of this Quarterly Report on Form 10-Q. 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 plans, objectives, estimates, expectations and intentions only as of the date of this filing. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results and the timing of events 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 undertake no obligation to update or supplement any forward-looking statements publicly, or to update or supplement 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.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

During the three and nine months ended September 30, 2018, there were no material changes to our market risk disclosures as set forth in Part II, Item 7A "Quantitative and Qualitative Disclosures About Market Risk" in our Annual Report on Form 10-K for the year ended December 31, 2017.

Item 4. 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 Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on their evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of September 30, 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 September 30, 2018, there have been 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.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings

The information required to be set forth under this Item 1 is incorporated by reference to Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

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 Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and accompanying notes.

Risks Related to Xyrem and the Significant Impact of Xyrem Sales

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

Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which accounted for 77% and 73% of our net product sales for the three and nine months ended September 30, 2018 and 74% of our net product sales for the year ended December 31, 2017. Our future plans assume that sales of Xyrem will increase, but we cannot assure you that we can maintain sales of Xyrem at or near current levels, or that Xyrem sales will continue to grow. We have periodically increased the price of Xyrem, most recently in January 2018, and we cannot assure you that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes.

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

- the potential U.S. introduction of a generic version of Xyrem 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, as further described below;
- the potential U.S. introduction of new products that compete with, or otherwise disrupt the market for, Xyrem in the treatment of cataplexy and/or excessive daytime sleepiness, or EDS, in narcolepsy;
- changes to or uncertainties around regulatory restrictions, including, among other things, changes to our Xyrem risk evaluation and mitigation strategy, or REMS, as further described below;
- potential 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;
- any increase in pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors;
- changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing and REMS programs by government entities;
- operational disruptions at the Xyrem central pharmacy or any failure to comply with our REMS obligations to the satisfaction of the U.S. Food and Drug Administration, or FDA;
- 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;
- changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell Xyrem; and
- our U.S.-based API and Xyrem suppliers' ability to obtain sufficient quotas from the U.S. Drug Enforcement Administration, or DEA, to satisfy our needs for Xyrem.

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

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

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

Although Xyrem is protected by patents covering its manufacture, formulation, distribution system and method of use, nine companies have sent us notices that they had filed ANDAs with the FDA seeking approval to market a generic version of Xyrem, and we filed patent lawsuits against each of them, asserting that such generic products would violate our patents covering Xyrem. We settled lawsuits against all nine ANDA filers, and the settlements are described below.

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 authorized generic version of Xyrem, or AG Product, in the U.S. beginning on January 1, 2023, or earlier under certain circumstances, including 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. 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 AG Product, but if it elects to continue to sell the AG Product, which it may do for up to a total of five years, West-Ward will not be able to 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 of them 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. Such circumstances include events related to 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 not infringed, or 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(assuming FDA approval of its ANDA is obtained or maintained) on or after December 31, 2025, or earlier under certain circumstances. Such circumstances include events related to launch of a generic sodium oxybate product by West-Ward or another company under its ANDA, 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 Amneal, Par and Lupin will have the option to elect to market its AG Product until December 31, 2025, but such party will not be entitled to market its AG Product and its own generic sodium oxybate product simultaneously. In our settlements with each of the other ANDA filers, we granted each a license to launch its own generic sodium oxybate product under its ANDA (assuming FDA approval of its ANDA is obtained or maintained) on or after December 31, 2025, or earlier under certain circumstances, including the launch by West-Ward or another company of a generic sodium oxybate product. In accordance with legal requirements, we have submitted our Xyrem settlement agreements to the U.S. Federal Trade Commission, or FTC, and the U.S. Department of Justice, or DOJ, for review.

For further description of these settlements and legal proceedings, see Note 10, Commitments and Contingencies-Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q and "Management's Discussion and Analysis of Financial Condition and Results of Operations—Challenges, Risks and Trends Related to Our Lead Marketed Products and Product Candidates Submitted for Regulatory Approval" included in Part I, Item 2 of this Quarterly Report on Form 10-Q. It is possible that additional companies may file ANDAs seeking to market a generic version of Xyrem or NDAs referencing Xyrem, which could lead to additional patent litigation or challenges with respect to Xyrem.

Certain ANDA filers filed petitions for inter partes review, or IPR, by the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO, with respect to the validity of certain distribution, method of use and formulation patents covering Xyrem. After reviewing these patents through the IPR proceedings, the PTAB determined that all of the claims of six patents associated with the Xyrem REMS, or REMS patents and three claims of a seventh REMS patent, are unpatentable. In July 2018, the United States Court of Appeals for the Federal Circuit, or the Federal Circuit, upheld these PTAB decisions on appeal, and as a result, we will not be able to enforce claims the PTAB found unpatentable. For further description of these legal proceedings, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q. We cannot predict whether new parties will petition for post-grant patent review in the future, the outcome of any future IPR or other proceeding or the impact any IPR or other proceeding might have on any future ANDA or other patent litigation proceedings or other aspects of our Xyrem business.

In January 2017, the FDA approved West-Ward's ANDA for a generic sodium oxybate product. The FDA's letter approving West-Ward's ANDA notes that, as the first ANDA applicant, West-Ward is eligible for 180 days of generic drug exclusivity. West-Ward's ANDA approval also includes a waiver that permits West-Ward to use a separate REMS program from the Xyrem REMS on the condition that the REMS approved with West-Ward's ANDA, or the generic sodium oxybate REMS, be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. In January 2017, the FDA 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 additional ANDAs that have been filed.

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, including as described above.

For example, a company that has not settled ANDA litigation with us could obtain a final decision prior to January 1, 2023 that all unexpired claims of the Xyrem patents are invalid and/or unenforceable by prevailing against us in patent litigation or as a result of an IPR challenge. In such event, West-Ward's AG Product launch date would be accelerated to approximately the date of that final decision, which would also accelerate the permitted launch of Par, Lupin and Amneal's AG Products and could accelerate the launch of other generic sodium oxybate products

Another circumstance that could accelerate the launch of an AG Product or a generic sodium oxybate product is market entry of another generic sodium oxybate product. For example, if a company that has not settled ANDA litigation with us obtains FDA approval for its generic sodium oxybate product and is able to distribute its product through an approved generic sodium oxybate REMS, such company could launch its generic product before the entry dates specified in our settlement agreements even in the absence of a final decision that all unexpired claims of the Xyrem patents are invalid and/or unenforceable, subject in some cases to West-Ward's 180-day exclusivity. Circumstances that could result in such a launch include, for example, a judicial determination that such company's product does not infringe our patents; a judicial determination that our Xyrem patents are valid and infringed but that an injunction against such company launching its product is not warranted; or a decision by such company, before applicable patent litigation is concluded, to launch its product 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) agreed with West-Ward. If a company launches a 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.

Another circumstance that could trigger acceleration of West-Ward's launch date for an AG Product, which would also lead to acceleration of Par, Lupin and Amneal's launch date 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 substantially erodes Xyrem net sales prior to January 1, 2023.

Other companies could also develop and launch sodium oxybate or other products that are similar, but not identical, to Xyrem, such as an alternative formulation or a different delivery technology, and seek approval in the U.S. through 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. Avadel Pharmaceuticals plc, or Avadel, a company that is using its proprietary technology for delivery of a sodium oxybate formulation to eliminate second nighttime dosing for narcolepsy patients, has stated that it is conducting a Phase 3 pivotal trial pursuant to an FDA-approved special protocol assessment, and has indicated that it intends to seek approval of its product candidate using a Section 505(b)(2) NDA approval pathway referencing Xyrem.

We are also aware of products being developed by others for use as treatment options in cataplexy and/or EDS in patients with narcolepsy that have different safety profiles and mechanisms of action than Xyrem, including pitolisant, a product to treat adult patients with narcolepsy with or without cataplexy that received marketing approval in Europe in 2016. While pitolisant is currently not approved by the FDA for marketing in the U.S., the company that has exclusive U.S. commercialization rights to pitolisant established an expanded access program for the product and announced that it has received Breakthrough Therapy and Fast Track designations from the FDA for its investigational product and that it is preparing an NDA submission for the product. The receipt of marketing approval and commercialization of products that may be approved in the U.S. for the treatment of narcolepsy patients could, depending on the targeted patient population, reduce Xyrem sales, which could have the additional effect of potentially triggering acceleration of market entry of AG Products or other generic sodium oxybate products under our ANDA litigation settlement agreements, as described above and elsewhere in this Quarterly Report on Form 10-Q.

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 where 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 accordance with the terms of our settlement agreements. Any ANDA holder launching any AG Product or another generic sodium oxybate product will establish the price of the AG Product and/or its own generic sodium oxybate product. However, generic competition often

results in decreases in the prices at which branded products can be sold, particularly when there is more than one generic product available.

We expect that the launch of any generic sodium oxybate product, including any AG Product, or the approval and launch of other products that compete with Xyrem, would be likely to have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects.

For further discussion regarding legal proceedings and settlement agreements related to Xyrem, the risks associated with our ANDA settlement agreements, the approval and tentative approval of ANDAs, 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 "Management's Discussion and Analysis of Financial Condition and Results of Operations—Challenges, Risks and Trends Related to Our Lead Marketed Products and Product Candidates Submitted for Regulatory Approval" included in Part I, Item 2 of this Quarterly Report on Form 10-Q, the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales," "Risks Related to Our Intellectual Property," and "*We face substantial competition from other companies, including companies with greater resources, including larger sales organizations and more experience working with large and diverse product portfolios, than we have*" in this Part II, Item 1A, and Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

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

The FDA requires that we maintain a REMS for Xyrem to help ensure the safe distribution of Xyrem and minimize the risk of misuse, abuse and diversion of sodium oxybate. In February 2015, the FDA approved the current Xyrem REMS, which requires, among other things, that Xyrem be distributed through a single pharmacy. In the FDA's February 2015 letter approving the Xyrem REMS, the FDA stated that (i) the approval action should not be construed or understood as agreement with what the FDA stated was our position that dispensing through a single pharmacy is the only way to ensure that the benefits of Xyrem outweigh its risks, and that the FDA has continuing concerns that limiting the distribution of Xyrem to one pharmacy imposes burdens on patient access and the healthcare delivery system, and (ii) as with all REMS, the FDA intends to evaluate the Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. In October 2018, in connection with the FDA's approval of our supplemental NDA, or sNDA, to revise the labeling for Xyrem to include an indication to treat cataplexy or EDS in pediatric narcolepsy patients ages seven and older, the FDA modified the February 2015 Xyrem REMS to add provisions and material for pediatric patients and caregivers, but did not modify the current operation of the Xyrem REMS. 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 indications or products, or whether FDA will approve modifications to the Xyrem REMS that we consider warranted in connection with the submission of applications for new oxybate indications or products. Any modifications approved, required or rejected by the FDA could make it more difficult or expensive for us to distribute Xyrem, make distribution easier for sodium oxybate competitors, impair the safety profile of Xyrem, disrupt continuity of care for Xyrem patients and/or negatively affect sales of Xyrem.

In August 2015, we implemented the Xyrem REMS, as approved by the FDA in February 2015, and we plan to implement the October 2018 modifications to the Xyrem REMS within 120 days of that approval. We have submitted and expect to continue to submit ongoing assessments as set forth in the FDA's Xyrem REMS approval letters. However, we cannot guarantee that our implementation and ongoing assessments will be satisfactory to the FDA or that the Xyrem REMS will satisfy the FDA's expectations in its evaluation of the Xyrem REMS on an ongoing basis. Any failure to comply with the REMS obligations, or 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 take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

While we have an exclusive agreement with Express Scripts Specialty Distribution Services, Inc., the central pharmacy for Xyrem, through June 2019 (subject to a one-year extension at our discretion unless either party provides 180 days' notice to the other of its intent to terminate the agreement), if the central pharmacy does not fulfill its contractual obligations to us, fails to meet the requirements of the Xyrem REMS applicable to the central pharmacy, provides timely notice that it wants to terminate our agreement, refuses or fails to adequately serve patients, or fails to promptly and adequately address operational challenges or challenges in implementing REMS modifications, whether expected or unexpected, the fulfillment of Xyrem prescriptions and our sales would be adversely affected. If we change to a new central pharmacy, new contracts might be required with government and other insurers who pay for Xyrem, and the terms of any new contracts could be less favorable to us than current agreements. In addition, any new central pharmacy would need to be registered with the DEA and certified and

would also need to implement the particular processes, procedures and activities necessary to distribute Xyrem under the Xyrem REMS. Transitioning to a new pharmacy could result in product shortages, which would negatively affect sales of Xyrem, result in additional costs and expenses for us and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Section 505-1(i)(1) of the FDCA generally provides that (i) an ANDA that references a drug subject to a REMS with elements to assure safe use, or ETASU, is required to have a REMS with the same elements as the reference listed drug, or RLD, and (ii) the ANDA drug and the RLD shall use a single shared system to assure safe use. However, the FDA may waive this requirement for a single shared system and approve an ANDA with a separate REMS with differing but comparable aspects of ETASU under certain circumstances. These requirements do not apply to an application submitted under Section 505(b)(2) of the FDCA, even if that application references a drug subject to a REMS with ETASU.

In January 2017, the FDA approved West-Ward's ANDA and waived the shared REMS requirement. The FDA's waiver of the shared REMS requirement permits West-Ward to use a separate REMS program from the Xyrem REMS, or the generic sodium oxybate REMS, for the generic sodium oxybate product, on the condition that the generic sodium oxybate REMS be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. This could potentially include future sodium oxybate products approved under a Section 505(b)(2) approval pathway. We cannot predict whether a company marketing a sodium oxybate product approved under Section 505(b)(2) would be required or permitted to distribute its product through the generic sodium oxybate REMS or a separate REMS. In connection with the waiver, FDA issued a statement that it considers the generic sodium oxybate REMS to have the same ETASU as the Xyrem REMS and operationalizes those elements in a comparable manner to achieve the same level of safety as the Xyrem REMS. We were not involved in development of the generic sodium oxybate REMS and were not consulted regarding any features of 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 could be distributed through multiple pharmacies, could increase the risks associated with sodium oxybate distribution. 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, public acceptance of Xyrem as a treatment for EDS and cataplexy in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, as patients, consumers and others may not differentiate generic sodium oxybate from Xyrem or differentiate between the different REMS programs, 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.

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

For further discussion regarding these matters, see the risk factors under the headings "*The launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem*" and "Risks Related to Our Intellectual Property" in this Part II, Item 1A.

REMS and the improper use of REMS as a means of improperly blocking or delaying competition for branded pharmaceutical products have increasingly drawn public scrutiny from Congress, the FTC and the FDA. 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 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 (including in light of the FDA's statement in the February 2015 Xyrem REMS approval letter that the Xyrem REMS could be used in an anticompetitive manner inconsistent with applicable provisions of the FDCA) or have engaged in other anticompetitive practices. The FDCA further states that a REMS ETASU shall not be used by an NDA holder to block or delay generic drugs or drugs covered by an application under Section 505(b)(2) from entering the market. Several of the ANDA applicants asserted that our REMS patents should not have been listed in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book, and that the Xyrem REMS is blocking competition. We cannot predict the outcome of any potential government investigation of these claims or the impact of any similar claims that may be made in the future.

The FDA has required that Xyrem's labeling include a boxed warning regarding the risk of central nervous system depression and misuse and abuse. A boxed warning is the strongest type of warning that the FDA can require for a drug product and warns prescribers that the drug carries a significant risk of serious or even life-threatening adverse effects. A boxed warning also means, among other things, that the product cannot be advertised through reminder ads, or ads that mention the pharmaceutical brand name but not the indication or medical condition it treats. Our Xyrem REMS includes unique features that provide more extensive information about adverse events, including deaths, than is generally available for other products that are not subject to similar REMS requirements. As required by the FDA and other regulatory agencies, the adverse event information that we collect for Xyrem is regularly reported to the FDA and could result in the FDA requiring changes to Xyrem labeling, including additional warnings or boxed warnings, or requiring us to take other actions that could have an adverse effect on patient and prescriber acceptance of Xyrem.

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

Risks Related to Our Business

While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products and, in the case of our product candidates, our ability to obtain regulatory approval in the U.S. and Europe and, if approved, to successfully launch and commercialize those product candidates. Our inability to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition to Xyrem, we are commercializing a portfolio of products, including our other lead marketed products, Erwinaze, Defitelio and Vyxeos, and we are making significant investments in solriamfetol and other product candidates that are currently not approved as marketed products in any jurisdiction.

Erwinaze

Erwinaze (called Erwinase in markets outside the U.S.), a biologic product, is used in conjunction with chemotherapy to treat patients with acute lymphoblastic leukemia, or ALL, with hypersensitivity to *E. coli*-derived asparaginase. Erwinaze was approved by the FDA under a biologics license application, or BLA, and was launched in the U.S. in November 2011. It is also being sold under marketing authorizations, named patient programs, temporary use authorizations or similar authorizations in multiple countries in Europe and elsewhere. Erwinaze is licensed from, and manufactured by, a single source, Porton Biopharma Limited, or PBL, a company that is wholly owned by the UK Department of Health and Social Care. Our agreement with PBL, including our license, expires in December 2020, subject to five-year extensions unless terminated by either party in writing by December 31, 2018. The parties are in discussions regarding the agreement, but we cannot predict whether the term of the agreement will be extended or, if extended, the terms of any such extension. If the agreement is terminated and we do not enter into a new agreement with PBL, we will lose our license to sell Erwinaze in any market after December 2020, except under specified terms for a post-termination transition period. We cannot predict the extent to which potential uncertainty related to our ongoing rights to Erwinaze will impact our sales of and revenues from Erwinaze.

A significant challenge to our ability to maintain and potentially increase sales is the limited supply of Erwinaze, which has resulted, and continues 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. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions throughout the fourth quarter of 2018 and during 2019. These supply disruptions have adversely impacted our ability to generate our previously anticipated level of sales of and revenues from Erwinaze in 2018, and we expect that they will continue to adversely impact our ability to generate sales of and revenues from Erwinaze in 2019. See the discussion regarding Erwinaze supply issues in the risk factor under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A. Our ability to maintain and successfully and sustainably grow sales of Erwinaze is also subject to a number of additional challenges, including the limited population of patients with ALL and the incidence of hypersensitivity reactions to *E. coli*-derived asparaginase within that population and our need to apply for and receive marketing authorizations, through the European Union's, or EU's, mutual recognition procedure or otherwise in certain additional countries if we decide to launch promotional efforts in those countries.

We also face numerous other risks that may impact Erwinaze sales, including regulatory risks, the development of new asparaginase treatments or treatment protocols that could reduce the rate of hypersensitivity in patients with ALL, the development of new treatment protocols for ALL that may not include asparaginase-containing regimens, difficulties with obtaining and maintaining favorable pricing and reimbursement arrangements, and potential competition from future biosimilar products. In addition, if we fail to comply with our obligations under our agreement with the licensor and supplier of Erwinaze or lose rights to Erwinaze, including if our agreement terminates at the end of its current term in December 2020, or if we otherwise fail to maintain or grow sales of Erwinaze, our growth prospects could be negatively affected.

Defitelio

We made a significant investment in Defitelio in 2014, adding the product to our portfolio as a result of our acquisition of Gentium S.r.l, which we refer to as the Gentium Acquisition, and then securing worldwide rights to the product by acquiring rights to defibrotide in the Americas in August 2014. We began to commercialize Defitelio in certain European countries in 2014. In March 2016, the FDA approved our NDA for Defitelio for the treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT. We launched Defitelio in the U.S. shortly after FDA approval.

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

- the continued acceptance of Defitelio in the U.S. by hospital pharmacy and therapeutics committees and the continued availability of 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;
- delays or problems in the supply or manufacture of the product;
- the limited size of the population of VOD patients who are indicated for treatment with Defitelio (particularly if changes in HSCT treatment protocols reduce the incidence of VOD diagnosis);
- our ability to meet the post-marketing commitments and requirements imposed by the FDA in connection with its approval of our NDA for Defitelio; and
- our ability to obtain marketing approval in other countries and to develop the product for additional indications.

The process of maintaining pricing and reimbursement approvals is complex and varies from country to country. Many European countries periodically review their reimbursement classes, which could have an adverse impact on the reimbursement status of Defitelio. 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 any of these events occurs, our anticipated revenue from Defitelio and our other products in the EU would be negatively affected. 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 Defitelio in the EU could be negatively affected. In addition, our ability to commercialize Defitelio successfully in the U.S. will depend on, among other things, the continued availability of adequate coverage or reimbursement by U.S. government programs and third party payors.

The European Commission, or EC, granted marketing authorization to Defitelio under "exceptional circumstances" because it was not possible to obtain complete information about the product due to the rarity of the disease and because ethical considerations prevented conducting a study directly comparing Defitelio with best supportive care or a placebo. A marketing authorization granted under exceptional circumstances is subject to approval conditions and an annual reassessment of the risk-benefit balance by European Medicines Agency, or EMA. As a result, if we fail to meet the approval condition for Defitelio established by the EC, which requires that we set up a patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use, or if it is determined that the balance of risks and benefits of using Defitelio changes materially, the EMA could vary, suspend or withdraw the marketing authorization for Defitelio. In addition, the FDA imposed several post-marketing commitments and requirements in connection with its approval of our NDA for Defitelio in March 2016, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. We may be unable to comply with these or other post-marketing obligations imposed as part of the marketing approvals for Defitelio. If we fail to meet any of these post-marketing obligations, our sales of and revenues from Defitelio could be materially adversely affected, and our future maintenance and potential growth of the market for this product may be limited.

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

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

Because VOD is an ultra-rare disease, we have experienced inter-quarter variability in our Defitelio sales, and our Defitelio sales will be difficult to predict from period to period. As a result, Defitelio sales results or trends in any period are not necessarily indicative of future performance. If sales of Defitelio do not reach the levels we expect, our anticipated revenue from Defitelio would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Vyxeos

We made a significant investment in Vyxeos through the acquisition of Celator Pharmaceuticals, Inc., which we refer to as the Celator Acquisition. Vyxeos is the first injectable fixed ratio, drug delivery combination oncology product based on our CombiPlex technology platform approved by the FDA and the EC. In August 2017, the FDA approved our NDA for Vyxeos 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 launched and began shipping Vyxeos in the U.S. in August 2017, and our U.S. commercial launch is still at an early stage. 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. In addition, we are seeking or plan to seek approval to market Vyxeos in additional countries.

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

- our ability to differentiate Vyxeos from other liposomal chemotherapies and generically available chemotherapy combinations with which physicians and treatment centers are more familiar;
- 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 need to establish pricing and reimbursement support for Vyxeos in the U.S., the EU and in other countries;
- the acceptance of Vyxeos in the U.S., the EU and other countries by hospital pharmacy and therapeutics committees and the availability of adequate coverage and reimbursement by government programs and third party payors;

- 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; and
- the limited size of the population of high-risk AML patients who may potentially be indicated for treatment with Vyxeos, particularly given the ongoing clinical trials by other companies with the same patient population.

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

In addition, the FDA imposed two 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. The marketing authorization in the EU for Vyxeos also requires us to comply with certain manufacturing-related post-approval commitments. In the event that we are unable to comply with these or other post-marketing obligations imposed as part of the marketing approval for Vyxeos in the U.S. or EU, our sales of and revenues from Vyxeos could be materially adversely affected, and our future maintenance and potential growth of the market for this product may be limited.

If we fail to maintain or increase revenue from sales of Erwinaze, Defitelio and Vyxeos, our business, financial condition, results of operations and growth prospects could be materially adversely affected. In addition to the specific risks described above, sales volumes and revenues from each of these products could be negatively affected by other risks and uncertainties described elsewhere in this Part II, Item 1A.

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

Solriamfetol

In 2017, we announced positive efficacy results from our two Phase 3 clinical trials of solriamfetol, a late-stage investigational compound being developed for potential treatment of EDS in patients with obstructive sleep apnea, or OSA, and from our Phase 3 clinical trial of solriamfetol in patients with narcolepsy. We submitted an NDA to the FDA in the fourth quarter of 2017 to seek approval for solriamfetol in the treatment of EDS associated with OSA and EDS associated with narcolepsy. In the first quarter of 2018, the FDA accepted the NDA for filing with a standard review and set a target action date under the Prescription Drug User Fee Act, or PDUFA, of December 20, 2018. We cannot predict whether our NDA will be approved by the FDA in a timely manner, or at all. Our ability to realize the anticipated benefits from an approved solriamfetol product is subject to a number of risks and uncertainties, including, among other things, the outcome of DEA scheduling review, which will need to be completed after NDA approval, if any, but before commercial launch, market acceptance for an approved solriamfetol product, potential competition from other products in development and the availability of adequate pricing, coverage and reimbursement by government programs and third party payors, as well as other risks and uncertainties described elsewhere in this Part II, Item 1A.

Other Product Candidates

In furtherance of our growth strategy, we have made significant investments in a number of other product candidates, including ongoing development activities for two other product candidates in our sleep therapeutic area.

Any failure or delay in completing necessary clinical trials and conducting other activities, including chemistry, manufacturing and controls, or CMC, activities, that are required to complete our planned regulatory submissions and obtain regulatory approvals could materially and adversely affect our business, financial condition, results of operations and growth prospects. See the discussion under the heading "*Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A for a discussion of risks related to our clinical trials of solriamfetol and other product candidates. See also the discussions under the headings "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects"* and "*The regulatory approval process is expensive, time-consuming and uncertain and may prevent us or our partners from obtaining approvals for the commercialization of some or all of our product candidates"* in this Part II, Item 1A.

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.

The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of process controls required to consistently produce the API and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. We and our 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. These difficulties can be heightened when we or our suppliers are required to produce finished product at commercial scale or to produce increased quantities to meet growing demand. In addition, we and our suppliers are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and other equivalent rules and regulations prescribed by non-U.S. regulatory authorities. We have cGMP responsibilities for the products we manufacture in our own facilities and also have oversight responsibilities for the manufacturing conducted by third party suppliers operating under contract with us. 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 Athlone, Ireland. We are using this facility for the manufacture of Xyrem and development-stage products, including JZP-507 and JZP-258, and we expect to manufacture these products commercially at our Athlone facility should these candidates receive regulatory approval. However, other than our Athlone facility and our 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 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. In part due to the limited market size for our products and product candidates, we have a single source of supply for most of our marketed products, product candidates and their APIs. These single source arrangements put us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties at our suppliers.

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

Sodium oxybate is a Schedule I controlled substance in the U.S. The DEA limits the quantity of 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 to manufacture and procure sodium oxybate in the U.S. Accordingly, we require DEA quotas for Siegfried in the U.S. to manufacture sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to procure the sodium oxybate from Siegfried to manufacture and supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, Siegfried and Patheon are required to request and justify allocation of sufficient annual DEA quotas, as well as any additional DEA quotas necessary if our commercial or clinical requirements exceed the allocated quotas throughout the year. For the last few years, our suppliers were allocated only a portion of the published annual aggregate quota for the API. If one or more ANDA filers were to begin manufacturing a generic sodium oxybate product, generic manufacturers would need to obtain a portion of the annual aggregate API quota, which could decrease the DEA quota allocation obtained on our behalf by Siegfried and Patheon. In the past, we have had to engage in lengthy efforts to obtain the needed quotas after the original annual quotas had first been allocated. If, in the future, we and our third party suppliers cannot obtain the quotas that are

needed on a timely basis, or at all, our business, financial condition, results of operations and growth prospects could be materially and adversely affected.

Erwinaze is licensed from, and manufactured for us by, a single source, PBL, a company that is wholly owned by the UK Department of Health and Social Care. The FDA's approval of the BLA for Erwinaze includes a number of post-marketing commitments related to the manufacture of Erwinaze by PBL. We cannot predict if or when PBL will comply with its manufacturing-related post-marketing commitments that are part of the BLA approval. In 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. We cannot predict if or when PBL will correct the violations and deviations to the satisfaction of the FDA or whether the FDA will be satisfied with PBL's response. Any failure to do so to the satisfaction of the FDA could result in the FDA refusing admission of Erwinaze into the U.S., as well as additional enforcement actions by the FDA and other regulatory entities.

In the United Kingdom, or UK, where PBL's manufacturing facilities are located, PBL is subject to similar inspections conducted by the UK Medicines and Healthcare Products Regulatory Agency, or MHRA. 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. We cannot predict if or when PBL will correct the violations and deviations to the satisfaction of MHRA or whether the MHRA will be satisfied with PBL's responses. Any failure by PBL to do so to the satisfaction of the MHRA could result in an enforcement action by 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 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; 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. In addition, if the FDA or any non-U.S. regulatory authority mandates any changes to the specifications for Erwinaze, we may face challenges having product produced to meet such specifications, and our supplier may increase its price to supply Erwinaze meeting such specifications, which may result in additional costs to us or a delay in supply and may decrease any profit we would otherwise achieve with Erwinaze.

The current manufacturing capacity for Erwinaze is 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 certain 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 manufacturing capacity or otherwise 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 quality, manufacturing or regulatory issues persist, under our agreement with PBL, we do not have the right to engage a backup supplier for Erwinaze except in very limited circumstances, such as following the termination of the agreement by us due to the uncured material breach or the cessation of manufacturing by our supplier. If we are required to engage a backup or alternative supplier, the transfer of technical expertise and manufacturing process to the backup or alternative supplier would be difficult, costly and time-consuming, might not be successful and would increase the likelihood of a delay or 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.

We are our sole supplier of, and we believe that we are currently the sole worldwide producer of, the defibrotide drug compound. We manufacture the defibrotide compound in a single facility located in Villa Guardia, near Como, Italy. Patheon currently processes the defibrotide compound into its finished vial form, and Patheon is the sole provider of our commercial and clinical supply of Defitelio. If Patheon does not or is not able to supply us with Defitelio for any reason, it may take time

and resources to implement and execute the necessary technology transfer to another processor, and such delay could negatively impact our anticipated revenues from Defitelio and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

In addition, the API in Defitelio is derived from porcine DNA. If our porcine DNA supplier experiences safety or other issues that impact its ability to supply porcine materials to us as needed, we may not be able to find alternative suppliers in a timely fashion, which could negatively impact our supply of Defitelio.

Vyxeos is manufactured using 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. Given that our Vyxeos launch is at an early stage, there is limited experience with this complex manufacturing process. Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. 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. If we fail to obtain a sufficient supply of Vyxeos 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, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

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 are unable to obtain a sufficient supply of Vyxeos in accordance with applicable specifications on a timely basis for any reason, we may not have sufficient product for our planned commercial and clinical uses and 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, which could limit our future maintenance and potential growth of the market for this product. See also the discussion under the heading "*While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products and, in the case of our product candidates, our ability to obtain regulatory approval in the U.S. and Europe and, if approved, to successfully launch and commercialize those product candidates. Our inability to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A.

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 has supplied us with both the API and finished product for our development activities involving solriamfetol, including our ongoing Phase 2 clinical trial. We expect that Siegfried will manufacture and supply solriamfetol drug product 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. 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.

JZP-258 and JZP-507 are currently manufactured at our Athlone facility, and we expect to manufacture these products commercially at our Athlone facility should we seek and receive regulatory approval. However, there can be no assurance that we or our suppliers will be able to produce sufficient supplies of our product candidates in a timely manner or in accordance with applicable specifications. In addition, to obtain FDA approval of any product candidate, we or our supplier or suppliers for that product must obtain approval by the FDA to manufacture and supply product, in some cases based on qualification data provided to the FDA as part of our NDA submission. Any delay in generating, or failure to generate, data required in connection with submission of the CMC portions of any NDA could negatively impact our ability to meet our anticipated submission dates, and therefore our anticipated timing for obtaining FDA approval, or our ability to obtain FDA approval at all. In addition, any failure of us or a supplier to obtain approval by the FDA to manufacture and supply product or any delay in receiving, or failure to receive, adequate supplies of a product on a timely basis or in accordance with applicable specifications could negatively impact our ability to successfully launch and commercialize products and generate sales of products at the levels we expect.

Failure by us or our third party suppliers to comply with regulatory requirements could adversely affect our or their ability to supply products or ingredients. All facilities and manufacturing techniques used for the manufacture of

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

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

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

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

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

If physicians do not prescribe our products, we cannot generate the revenues we anticipate from product sales. Market acceptance of any of our products by physicians, patients, third party payors and the medical community depends on:

- the clinical indications for which a product is approved 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;
- the severity of side effects;
- acceptance by physicians and patients of each product as a safe and effective treatment;
- the extent to which the product is approved for inclusion on formularies of hospitals and managed care organizations;
- the conditions for reimbursement required by, and appropriate pricing and availability of reimbursement from, third party payors;
- availability of sufficient product inventory to meet demand, particularly with respect to Erwinaze;
- physicians' decisions relating to treatment practices based on availability of product inventory, 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 gamma-hydroxybutyrate, or GHB, and its effects, including with respect to illegal use, overdoses, serious injury and death. Because sodium oxybate, the API in Xyrem, is a derivative of GHB, Xyrem sometimes also receives negative mention in publicity relating to GHB. Patients, physicians and regulators may therefore view Xyrem as the same as or similar to illicit GHB. In addition, there are regulators and some law enforcement agencies that oppose the prescription and use of Xyrem generally because of its connection to GHB. Xyrem's label includes information about adverse events from GHB. Moreover, a sodium oxybate distribution system that is less restrictive than the Xyrem REMS, such as the generic sodium oxybate REMS approved by the FDA in January 2017, may increase the risks associated with sodium oxybate distribution, as patients, consumers and others may not differentiate generic sodium oxybate from Xyrem or differentiate between the different REMS programs. Any negative outcomes, including but not limited to risks to the public, caused by or otherwise related to the separate generic sodium oxybate REMS could have a significant negative impact in terms of product liability, goodwill, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, any of which could have a material adverse effect on our Xyrem revenues.

In addition, we have periodically increased the price of Xyrem, most recently in January 2018, and may do so again in the future. We also have made and may in the future make similar price increases on our other products. Price increases on our products and negative publicity regarding pricing and price increases generally, whether on our products or products distributed by other pharmaceutical companies, could negatively affect market acceptance of our products. For additional discussion about payor acceptance, see the risk factor under the heading "*Access and adequate reimbursement coverage may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably*" in this Part II, Item 1A.

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

The commercial potential of our current products and any future products may be reduced or eliminated if our competitors develop or acquire and commercialize generic or branded products that are safer or more effective, have fewer side effects, are easier to administer or are less expensive than our products. The pharmaceutical industry is highly competitive and dominated by a number of large, established pharmaceutical companies, as well as specialty pharmaceutical companies that market products and develop product candidates in sleep, hematology/oncology, pain and other therapeutic areas. Many of our competitors, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources than we do. They can spend more on, and have more expertise in, research and development, regulatory, manufacturing, distribution and sales activities. As a result, our competitors may obtain FDA or other regulatory approvals for their product candidates more rapidly than we may and may market their products more effectively than we do. Smaller or earlier stage companies may also prove to be significant competitors, particularly through focused development programs and collaborative arrangements with large, established companies.

While Xyrem is the only product approved by the FDA and currently marketed in the U.S. for the treatment of both cataplexy and EDS in patients with narcolepsy, cataplexy is often treated with tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors, even though these products are not approved by the FDA for the treatment of cataplexy. Other treatments for EDS in patients with narcolepsy include stimulants and wakefulness promoting agents, such as Provigil® (modafinil) and Nuvigil® (armodafinil), as well as generic versions of Provigil, the only other products both approved by the FDA and currently marketed for the treatment of EDS in patients with narcolepsy. Provigil, its generic equivalents and Nuvigil are also approved for improving wakefulness in patients with EDS associated with treated OSA or shift work disorder.

We are also aware of products being developed by others for use as treatment options in cataplexy and/or EDS in patients with narcolepsy, including pitolisant, a product to treat adult patients with narcolepsy with or without cataplexy that received marketing approval in Europe in 2016. While pitolisant is currently not approved by the FDA for marketing in the U.S., the company that has exclusive U.S. commercialization rights to pitolisant established an expanded access program for the product and announced that the product has received Breakthrough Therapy and Fast Track designations from the FDA and that it is preparing an NDA submission for the product. The receipt of marketing approval and commercialization of pitolisant in the U.S. for the treatment of narcolepsy patients could, depending on the targeted patient population, negatively impact our ability to maintain and grow sales of Xyrem.

Nine companies filed ANDAs with the FDA seeking to market generic versions of Xyrem, and we have settled patent litigation against all nine companies. The FDA has approved or tentatively approved some of these ANDAs, and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs that have been filed. For a description of the settlement agreements and the risks related to the launch of a generic sodium oxybate product, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1

of this Quarterly Report on Form 10-Q, "Management's Discussion and Analysis of Financial Condition and Results of Operations—Challenges, Risks and Trends Related to Our Lead Marketed Products and Product Candidates Submitted for Regulatory Approval" included in Part I, Item 2 of this Quarterly Report on Form 10-Q, and the risk factor under the heading "*The launch of a generic version of Xyrem or other sodium oxybate products that compete with Xyrem would adversely affect sales of Xyrem.*"

Other companies could also develop products that are similar, but not identical, to Xyrem, such as an alternative formulation or an alternative delivery technology, and seek approval in the U.S. through a Section 505(b)(2) NDA approval pathway, which allows companies to seek approval of a product that is similar, but not identical, to a previously-approved brand-name product, and to rely to some degree on the previously-approved product's safety and efficacy data. For example, Avadel has stated that it is conducting a Phase 3 pivotal trial pursuant to an FDA-approved special protocol assessment, and has indicated that it intends to seek approval of its product candidate using a Section 505(b)(2) NDA approval pathway referencing Xyrem. If Avadel successfully develops, obtains FDA approval of and is able to launch this product candidate, Avadel's product may compete with Xyrem and could result in a substantial reduction of Xyrem sales, which could have the additional impact of potentially triggering acceleration of market entry of AG Products or other generic sodium oxybate products under our ANDA litigation settlement agreements.

We expect that the launch of an AG Product or other generic version of Xyrem, or the approval and launch of other products that compete with Xyrem, could have a material adverse effect on our sales of Xyrem and on our business, financial condition, results of operations and growth prospects. For further discussion regarding these and other risks and challenges we face with respect to Xyrem, see the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" and "Risks Related to Our Intellectual Property" in this Part II, Item 1A.

While there is currently no direct competition to Erwinaze to treat ALL patients with hypersensitivity to *E. coli*-derived asparaginase, other companies have developed or are developing new treatments for ALL, including new asparaginase treatments that could reduce the rate of hypersensitivity in patients with ALL, and new treatment protocols are being developed for ALL that may not include asparaginase-containing regimens. For example, a number of companies are developing new immunotherapy treatments for relapsed or refractory ALL patients, including one treatment that was recently approved. The development of these new treatments could negatively impact our ability to 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.

AML, the cancer indication for which we commercialize Vyxeos, has alternative established therapies. A key consideration in the treatment of AML patients is the patient's suitability for chemotherapy. The patient population studied in the Vyxeos Phase 3 clinical trial included AML patients deemed able to tolerate chemotherapy. The existing options for the treatment of newly-diagnosed t-AML patients who can tolerate chemotherapy 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 for use as treatment options for AML patients, such as targeted agents (e.g., FLT-3, IDH-1, IDH-2, CD-33 and CAR T‑cell), immunotherapies and agents disrupting leukemia cell survival. 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. 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, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In the fourth quarter of 2017, we submitted an NDA for solriamfetol to the FDA for the treatment of patients with EDS in narcolepsy and EDS in OSA. In the first quarter of 2018, the FDA accepted the NDA for filing with a standard review and set a target action date under PDUFA of December 20, 2018. If solriamfetol is approved, we expect that the product will be subject to scheduling review under the U.S. Controlled Substances Act, or CSA, before it can be commercially launched. Other treatments for excessive sleepiness 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 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.

Many of our competitors are able to deploy more personnel to market and sell their products than we do. We currently have a relatively small number of sales representatives compared with the number of sales representatives of most other pharmaceutical companies with marketed products. Each of our sales representatives is responsible for a territory of significant size. The continued growth of our current products and the launch of any future products may require expansion of our sales force and sales support organization, and we may need to commit significant additional funds, management and other resources to the growth of our sales organization. We may not be able to achieve any necessary growth in a timely or cost-effective

manner or realize a positive return on our investment, and we may not have the financial resources to achieve the necessary growth in a timely manner, or at all. In particular, we compete with a significant number of pharmaceutical and life sciences companies with extensive sales, marketing and promotional experience in hematology/oncology markets, and our failure to compete effectively in this area could negatively affect our sales of Erwinaze, Defitelio, Vyxeos and other products. We also have to compete with other pharmaceutical and life sciences companies to recruit, hire, train and retain sales and marketing personnel, and turnover in our sales force and marketing personnel could negatively affect sales of our products. If our specialty sales force and sales organization are not appropriately sized to adequately promote any current or potential future products, the commercial potential of our current products and any future products may be diminished.

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

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

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

We intend to grow our business over the long term by acquiring or in-licensing and developing additional products and product candidates that we believe have significant commercial potential. Future growth through acquisition or in-licensing will depend upon the availability of suitable products and product candidates for acquisition or in-licensing on acceptable prices, terms and conditions.

Even if appropriate opportunities are available, we may not be able to successfully identify them, or we may not have the financial resources necessary to pursue them. Other companies, many of which may have substantially greater financial, marketing and sales resources, compete with us for these opportunities. In order to compete successfully to acquire attractive products or product candidates in the current business climate, we may have to pay higher prices for assets than may have been paid historically, which may make it more difficult for us to realize an adequate return on any acquisition.

Even if we are able to successfully identify and acquire, in-license or develop additional products or product candidates, we cannot assure you that we will be able to successfully manage the risks associated with integrating any products or product candidates or the risks arising from anticipated and unanticipated problems in connection with an acquisition or in-licensing. We may not be able to realize the anticipated benefits of any acquisition or in-licensing for a variety of reasons, including if:

- we are unable to obtain and maintain adequate funding to complete the development of, obtain regulatory approval for and commercialize an acquired product candidate;
- a product candidate proves not to be safe or effective in later clinical trials;
- a product fails to reach its forecasted commercial potential as a result of pricing pressures 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;
- 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.

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

As a condition to regulatory approval, each product candidate must undergo extensive and expensive preclinical studies and clinical trials to demonstrate to a statistically significant degree that the product candidate is safe and effective. The results at any stage of the development process may lack the desired safety, efficacy or pharmacokinetic characteristics. Results of limited preclinical studies, including studies of our product candidates in animal models, may not predict the results of human clinical trials of those product candidates. Similarly, results from early clinical trials may not be predictive of results obtained in later and larger clinical trials, and product candidates in later clinical trials may fail to show the desired safety and efficacy despite having progressed successfully through initial clinical testing. In that case, the FDA or any equivalent non-U.S. regulatory agency may determine our data is not sufficiently compelling to warrant marketing approval and may require us to engage in additional clinical trials or provide further analysis which may be costly and time-consuming. A number of companies in the pharmaceutical industry, including us, have suffered significant setbacks in clinical trials, even in advanced clinical trials after showing positive results in preclinical studies or earlier clinical trials. If a product candidate fails at any stage of development and does not receive regulatory approval, we will not be able to commercialize it and receive any return on our investment in that product candidate.

The FDA accepted for filing with standard review our NDA for solriamfetol to the FDA in the first quarter of 2018. The NDA was submitted to the FDA based on positive results from two Phase 3 clinical trials, but if the FDA determines that our safety or efficacy data 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, in which event we would not receive any return on our investment.

Our development pipeline projects may not be successful, and any adverse events or other data generated during the course of studies related to our product candidates and/or studies 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 clinical trials for line extensions or the generation of additional clinical data could materially and adversely affect the maintenance and growth of the markets for the related marketed products, which could adversely affect our business, financial condition, results of operations and overall growth prospects.

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

- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;
- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidate for use in trials;
- delays or failures in reaching agreement on acceptable terms with prospective study sites;

- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board, 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;
- 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, including negative results from ongoing preclinical studies and clinical trials and adverse events associated with product candidates;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites;
- difficulty identifying or enrolling eligible patients, in some cases based on the number of clinical trials with enrollment criteria targeting the same patient population;
- failure of our third party clinical trial managers to satisfactorily perform their contractual duties, comply with regulations or meet expected deadlines; or
- insufficient funds to complete the trials.

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

We are headquartered in Dublin, Ireland and have multiple offices in the U.S., Canada, the UK, Italy and other countries in Europe. Our headcount has grown to approximately 1,290 as of November 2018. This includes employees in 14 countries in North America and Europe, a European commercial presence, a complex distribution network for products in Europe and additional territories, and manufacturing facilities in Italy and Ireland. In addition, we may expand our international operations into other countries in the future, either organically or by acquisition. While we have acquired significant management and other personnel with substantial international experience, conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

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

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

In addition, in June 2016, eligible members of the electorate in the UK decided by referendum to leave the EU. On March 29, 2017, the government of the UK initiated the formal procedure for withdrawal from the EU. We have a significant office in Oxford, England, which focuses on commercialization of our products outside of the U.S., among other activities. We do not know to what extent, or when, the UK's withdrawal from the EU or any other future changes to membership in the EU will impact our business, if at all. In particular, our ability to conduct international business out of the UK may be adversely affected. For a further discussion, see the risks under the heading "*The results of the UK's referendum on withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business*" in this Part II, Item 1A. 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 trade tensions. However, these tariffs and other trade restrictions could increase our cost of doing business, reduce our gross margins or otherwise negatively impact our financial results.

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

We rely on contract research organizations and other third parties, such as cooperative groups, to assist us in designing, coordinating, managing, monitoring and otherwise conducting clinical trials with our product candidates. We do not control these third parties, and, as a result, they may not treat our clinical studies as a high priority, or in the manner in which we would prefer, which could result in delays. We are responsible for confirming that each of these clinical trials is conducted in accordance with its general investigational plan and protocol, as well as good clinical practices, and for conducting, recording and reporting the results of clinical trials to ensure that the data and results are credible and accurate and that the trial participants are adequately protected. The FDA and non-U.S. regulatory agencies enforce good clinical practices through periodic inspections of trial sponsors, principal investigators and trial sites. If we, contract research organizations 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 or its non-U.S. counterparts may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA or non-U.S. regulatory agencies will determine that any of these clinical trials comply with good clinical practices. In addition, these 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 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 succeed in our efforts to create approved line extensions for certain of our existing products or generate additional useful clinical data in support of these products.

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

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

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

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

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

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, 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 confidential information. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result we manage a number of third party vendors who may or could have access to our confidential information. In addition, many of those third parties, in turn, subcontract or outsource some of their responsibilities to third parties. As a result, our information technology systems, including the functions of third parties that are involved or have access to those systems, are large and complex. The size and complexity of our information technology systems, and the large amounts of confidential information stored on those systems, make such systems potentially vulnerable

to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third party vendors, and/or business partners, or from cyber-attacks by malicious third parties. Attacks of this nature are increasing in their frequency, levels of 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 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 lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices to access confidential information increases the risk of security breaches. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business. 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.

The results of the UK's referendum on withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business.

On March 29, 2017, the government of the UK initiated the formal procedure for withdrawal from the EU. The procedure involves a two-year negotiation period in which the UK and the EU must conclude an agreement setting out the terms of the UK's withdrawal and the arrangements for the UK's future relationship with the EU. This negotiation period could be extended by a unanimous decision of the European Council in agreement with the UK.

The referendum has created significant uncertainty concerning the future relationship between the UK and the EU. This includes the laws and regulations that will apply as the UK determines which EU laws to replace or replicate in the event of a withdrawal. From a regulatory perspective, the UK's withdrawal could result in significant complexity and risks.

The UK referendum 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. They may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets.

We have a significant office in Oxford, England, which focuses on commercialization of our products outside of the U.S., among other activities. We do not know to what extent, or when, the UK's withdrawal from the EU or any other future changes to membership in the EU will impact our business, if at all. In particular, our ability to conduct international business out of the UK may be adversely affected. For a further discussion, see the risks under the headings "*We have substantially expanded our international footprint and operations, and we may expand further in the future, but we do not yet have substantial historical experience in international markets and may not achieve the results that we, our shareholders or analysts who cover our business expect*" and "*The regulatory approval process is expensive, time-consuming and uncertain and may prevent us or our partners from obtaining approvals for the commercialization of some or all of our product candidates*" in this Part II, Item 1A.

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

In certain European countries, reimbursement for products that have not yet received marketing authorization may be provided through national named patient programs. Erwinase, Defitelio and Vyxeos are available on a named patient basis in many countries where they are not commercially available. Such reimbursement may cease to be available if authorization for a named patient program expires or is terminated. While we generate revenue from the distribution of these products through named patient programs, we cannot predict whether historical revenues from these programs will continue, whether we will be able to continue to distribute our products on a named patient basis in these countries, whether we will be able to commercialize our products in countries where the products have historically been available on a named patient basis, or

whether commercial revenues will exceed revenues historically generated from sales on a named patient basis. Any failure to maintain revenues from sales of Erwinase and/or Defitelio on a named patient basis and/or to generate revenues from commercial sales of these products exceeding historical sales on a named patient basis could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Risks Related to Our Intellectual Property

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

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

The patent position of pharmaceutical companies can be highly uncertain and involve complex and often changing legal, regulatory and factual questions. We own a portfolio of U.S. and non-U.S. patents and patent applications and have licensed rights to a number of issued patents and patent applications that cover or relate to our products and product candidates, including Xyrem, Defitelio, 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, invalidated, held unenforceable or circumvented, potentially including by FDA approval of an ANDA or Section 505(b)(2) application that avoids infringement of our intellectual property.

Although 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, and 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. In addition, notwithstanding our patents, it is possible that a company that has not settled ANDA litigation with us obtains and maintains FDA approval of an ANDA for a generic version of Xyrem or an NDA for another sodium oxybate product and introduces such product before the entry dates specified in our settlement agreements, including if such company obtains a final determination that its products do not infringe our patents or if such company decides, before applicable patent litigation is concluded, to launch a sodium oxybate product at risk of being held liable for damages for patent infringement. If a company launches a product in any of these scenarios, it could accelerate the launch dates for the AG Products and generic sodium oxybate products under our settlement agreements, depending on the circumstances. 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 Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q, "Management's Discussion and Analysis of Financial Condition and Results of Operations—Challenges, Risks and Trends Related to Our Lead Marketed Products and Product Candidates Submitted for Regulatory Approval" included in Part I, Item 2 of this Quarterly Report on Form 10-Q, and the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" 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 II, Item 1A.

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

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

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

We also rely on trade secrets and other unpatented proprietary information to protect our products and commercial position, particularly with respect to our products with limited or no patent protection, such as Erwinaze. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality agreements with our employees, consultants, advisors and partners. Nevertheless, our employees, consultants, advisors and partners may unintentionally or willfully disclose our proprietary information to competitors, and we may not have adequate remedies for such disclosures. In addition, if our employees, consultants, advisors or partners develop inventions or processes independently, or jointly with us, that may be applicable to our products, disputes may arise about ownership or proprietary rights to those inventions and processes. Such inventions and processes will not necessarily become our property, but may remain the property of those third parties or their employers. Enforcing a claim that a third party illegally obtained or is using any of our inventions or trade secrets is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside of the U.S. are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Failure to obtain or maintain patent and/or trade secret protection, for any reason, could have a material adverse effect on our business.

We have patents covering many of our products in Europe and other parts of the world where patent laws operate differently than in the U.S., and provide a different scope of protection for our products than in the U.S. 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. Xyrem's regulatory exclusivity expired in the EU, and we are aware that generic or hybrid generic applications have been submitted, and additional generic or hybrid generic applications may be submitted, to various EU regulatory authorities. We cannot predict whether we or our licensees will be able to enforce our European patents or any patents we may be granted in the future, or other intellectual property against generic or hybrid generic filers in the EU.

Certain of the products we sell have no patent protection and, as a result, potential competitors face fewer barriers in introducing competing products. We rely on trade secrets and other unpatented proprietary information to protect our commercial position with respect to such products, which we may be unable to do. In some instances, we also rely on regulatory exclusivity. For example, Erwinaze has no patent protection. In addition to protection using trade secrets, Erwinaze 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 precluded approval of another product with the same principal molecular structure for the same indication until November 2018. Erwinaze, as a biologic product approved under a BLA, is also subject to the U.S. Biologics Price Competition and Innovation Act, or BPCIA. We believe that Erwinaze is protected by exclusivity that prevents approval of a biosimilar in the U.S. through late 2023 under the BPCIA. However, the BPCIA may evolve over time based on FDA issuance of guidance documents, proposed regulations, and decisions in the course of considering specific applications. 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 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 BCPIA exclusivity period has expired, which would adversely affect sales of Erwinaze. In the EU, the regulatory data protection and thus regulatory exclusivity period for Erwinase has lapsed. This also means that any new marketing authorizations for Erwinase in other EU member states will not receive any regulatory data protection. If a biosimilar product to Erwinaze is approved as interchangeable to Erwinaze in the U.S. or in other countries where Erwinaze is sold, a significant percentage of the prescriptions that would have been written for Erwinaze may be filled with the biosimilar version, resulting in a loss in sales of

Erwinaze, and there may be a decrease in the price at which Erwinaze can be sold. Competition from a biosimilar product to Erwinaze could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

We have incurred and 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. The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions. We have filed multiple U.S. patent applications and non-U.S. counterparts, and may file additional U.S. and non-U.S. patent applications. There can be no assurance that any issued patents we own or control will provide sufficient protection to conduct our business as presently conducted or as proposed to be conducted. Moreover, for a variety of reasons, including the existence of relevant prior research performed and the existence of conflicting patent applications submitted in the same manner or similar fields, there can be no assurance that any patents will issue from the patent applications owned by us, or that we will remain free from infringement claims by third parties.

If we choose to go to court to stop a third party from infringing our patents, our licensed patents or our partners' patents, that third party has the right to ask the court or an administrative agency to rule that these patents are invalid and/or should not be enforced. These lawsuits and administrative proceedings are expensive and consume time and other resources, and we may not be successful in these proceedings or in stopping infringement. In addition, the IPR process under the Leahy-Smith America Invents Act permits any person, whether they are accused of infringing the patent at issue or not, to challenge the validity of certain patents. As a result, entities associated with hedge funds as well as ANDA filers have challenged valuable pharmaceutical patents through the IPR process. There is a risk that a court or the PTAB could decide that our patents are not valid or infringed, and that we do not have the right to stop a third party from using the patented subject matter, such as 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 a discussion regarding the risks associated with our settlement agreements with Xyrem ANDA filers, the potential launch of the 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 "Management's Discussion and Analysis of Financial Condition and Results of Operations—Challenges, Risks and Trends Related to Our Lead Marketed Products and Product Candidates Submitted for Regulatory Approval" included in Part I, Item 2 of this Quarterly Report on Form 10-Q, Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q and the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" and "*It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection"* in this Part II, Item 1A. We cannot assure you that lawsuits or proceedings we may file in the future, or our defense against any lawsuits or other proceedings that may be brought against us will be successful in stopping the infringement of our patents, that any such litigation or other proceedings will be cost-effective, or that any of them will have a satisfactory result for us.

Litigation involving patent matters is frequently settled between the parties, rather than continuing to a court ruling, 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 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 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. Our competitors may have filed, and may in the future file, patent applications covering subject matter similar to ours. Any such patent application may have priority over our or our licensors' patents or applications and could further require us to obtain rights to issued patents covering such subject matter. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our U.S. patent position with respect to such inventions. Patent interferences are limited or unavailable for patent applications filed after March 16, 2013.

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

In September 2016, Jazz Pharmaceuticals, Inc., our wholly owned subsidiary, submitted a Citizen Petition to the FDA requesting that, for safety reasons, the FDA refuse to approve any sodium oxybate ANDA with a proposed package insert or REMS that omits the portions of the Xyrem package insert and the Xyrem REMS that instruct prescribers on adjusting the dose of the product when it is co-administered with divalproex sodium (also known as valproate or valproic acid). Our Xyrem patents include three DDI patents covering these instructions on the Xyrem package insert and Xyrem REMS. In January 2017, the FDA granted the Citizen Petition with respect to the Xyrem package insert. The FDA concluded that it will not approve any sodium oxybate ANDA referencing Xyrem that does not include in its package insert the portions of the currently approved Xyrem package insert related to the DDI with divalproex sodium. 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 method of administration 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 any of our 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. For further discussion of these matters, see the risk factors under the headings "Risks Related to Xyrem and the Significant Impact of Xyrem Sales" and "Risks Related to Our Intellectual Property" in this Part II, Item 1A.

We also own method of use patents and trade secrets that cover elements of the Xyrem REMS, including patents that relate to the use of a single central pharmacy to distribute Xyrem. In July 2016, the PTAB issued final decisions that the claims of six of seven REMS patents are unpatentable. In March 2017, the PTAB issued a final decision that three claims of a seventh REMS patent are unpatentable. In July 2018, the Federal Circuit upheld these PTAB decisions on appeal, and as a result, we

will not be able to enforce claims the PTAB found unpatentable. For a description of these matters, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q. We cannot predict whether new parties will petition for post-grant patent review in the future, the outcome of any future IPR or other proceeding or the impact any IPR or other proceeding might have on any future ANDA or other patent litigation proceedings or other aspects of our Xyrem business.

In the FDA's February 2015 letter approving the Xyrem REMS, the FDA stated that (i) the approval action should not be construed or understood as agreement with what the FDA stated was our position that dispensing through a single pharmacy is the only way to ensure that the benefits of Xyrem outweigh its risks, and that the FDA has continuing concerns that limiting the distribution of Xyrem to one pharmacy imposes burdens on patient access and the healthcare delivery system, and (ii) as with all REMS, the FDA intends to evaluate the Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. In October 2018, in connection with the FDA's approval of our sNDA to revise the labeling for Xyrem to include an indication to treat cataplexy or EDS in pediatric narcolepsy patients ages seven and older, the FDA modified the February 2015 Xyrem REMS to add provisions and material for pediatric patients and caregivers, but did not modify the current operation of the Xyrem REMS. 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 indications or products, or whether FDA will approve modifications to the Xyrem REMS that we consider warranted in connection with the submission of applications for new oxybate indications or products.

Any modifications approved, required or rejected by the FDA could make it more difficult or expensive for us to distribute Xyrem, make distribution easier for sodium oxybate competitors, impair the safety profile of Xyrem, disrupt continuity of care for Xyrem patients and/or negatively affect sales of Xyrem. In particular, depending on the nature of any such modifications or additional requirements, the ability of our existing patents and other intellectual property to protect our Xyrem distribution system from sodium oxybate competitors may be reduced. In addition, the extent of protection provided by our patents and other intellectual property related to the distribution of Xyrem depends on the nature of the distribution system that may be used by any sodium oxybate competitor. If the generic sodium oxybate REMS that has been approved by the FDA in connection with its approval of West-Ward's ANDA or any other sodium oxybate REMS that may be approved by the FDA does not fall within the scope of any of the claims of our patents, those patents will not be a barrier to an ANDA filer's or other unlicensed sodium oxybate product manufacturer's entry into the market. We cannot be certain whether our existing patent claims, patents that may be granted in the future or other intellectual property will be construed to cover the generic sodium oxybate REMS or any other sodium oxybate REMS that may be approved by the FDA. The interpretation of intellectual property protections and the effect of these protections are extremely complex, and we cannot predict the impact of any of these matters on our business.

Risks Related to Our Industry

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

We are not permitted to market a pharmaceutical product in the U.S. or in the EU member states until we receive approval from the FDA, the EC or the competent authorities of the EU member states, as applicable. An application for marketing approval must contain information demonstrating the quality, safety and efficacy of the pharmaceutical product, including data from preclinical and clinical trials, information pertaining to the preparation and manufacture of the API, analytical methods, product formulation, details on the manufacture and stability of the finished pharmaceutical product and proposed product packaging and labeling. Submission of an application for marketing authorization does not assure approval for marketing in any jurisdiction, and we may encounter significant difficulties or costs in our efforts to obtain approval to market products. Moreover, the redemption of a rare pediatric disease priority review voucher, or PRV, for one of our future regulatory submissions to the FDA, such as the PRV that we purchased in May 2018, 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. Furthermore, any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. Any such limitations could reduce the size of the market for the product.

We submitted an NDA for solriamfetol to the FDA in the fourth quarter of 2017, and the FDA accepted the NDA for standard review with a target action date under PDUFA of December 20, 2018. However, the FDA does not always meet its PDUFA target action dates, and if the FDA fails to meet the PDUFA target action date for our solriamfetol NDA submission or fails to meet future PDUFA targeted action dates established for any of our product candidates, if any, the commercialization of the affected product candidate could be delayed or impaired. In any event, we cannot predict whether we will be able to obtain approval of our NDA for solriamfetol in the U.S. in a timely manner, or at all. If the applicable regulatory authority for such applications determines that our quality, safety or efficacy data do not warrant marketing approval, we could be required to conduct additional clinical trials, which could be costly and time-consuming and could delay the approval of our application, or

we may not be able to commercialize solriamfetol in the U.S. If we are unable to obtain regulatory approval of our product candidates, we will not be able to commercialize them and recoup our research and development costs. Any delay or failure in obtaining approval of a drug candidate, or receipt of approval for narrower indications than sought, can have a negative impact on our financial performance.

A central nervous system-acting drug such as solriamfetol may be subject to scheduling as a controlled substance under the CSA depending on the drug's potential for abuse. We expect that solriamfetol will be subject to scheduling review under the CSA before it can be commercially launched. Moreover, depending on its scheduling status, the manufacture, importation, exportation, domestic distribution, storage, sale and legitimate use of solriamfetol may be subject to a significant degree of regulation by the DEA.

If the FDA, the EC or the competent authorities of the EU member states determine that a REMS or the imposition of post-marketing obligations is necessary to ensure that the benefits of the drug outweigh the risks, we may be required to include a proposed REMS as part of an NDA or BLA or to propose post-marketing obligations to be included in the marketing authorization for our products in the EU. In non-EU countries, we may also be required to include a patient package insert or a medication guide to provide information to consumers about the product's risks and benefits, a plan for communication to healthcare providers, and restrictions on the product's distribution. For example, the FDA requires a REMS for Xyrem, discussed in detail in the risk factor under the heading "*The distribution and sale of Xyrem are subject to significant regulatory oversight and restrictions and the requirements of a risk evaluation and mitigation strategy, and these restrictions and requirements, as well as the potential impact of changes to these restrictions and requirements, subject us to increased risks and uncertainties, any of which could negatively impact sales of Xyrem*" in this Part II, Item 1A, and other products that we sell are or may become subject to a REMS specific to our product or shared with other products in the same class of drug. We cannot predict the impact that any new REMS requirements applicable to any of our products would have on our business.

The FDA approved the BLA for Erwinaze in the U.S. in November 2011, subject to certain post-marketing requirements, which have been completed, and compliance with multiple post-marketing commitments, including certain commitments that must be met by the product's manufacturer with respect to product manufacturing, which are outside of our control. While activities are underway to complete the post-marketing commitments, any inability to comply with regulatory requirements, including compliance with manufacturing-related post-marketing commitments that are part of the BLA approval, as well as other requirements monitored by the FDA, could adversely affect Erwinaze supply, particularly in light of the limited supply of Erwinaze, and could result in FDA approval being revoked, product release being delayed resulting in product shortage or product recalls, any of which could have a material adverse effect on our sales of and revenues from Erwinaze and further limit our future maintenance and potential growth of the market for this product. See also the discussion under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects.*" in this Part II, Item 1A.

As another example, the marketing authorization in the EU for Defitelio requires us to comply with a number of post-marketing obligations, including obligations relating to the establishment of a patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use. In January 2017, we enrolled the first patient in the Defitelio 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. The FDA imposed several post-marketing commitments and requirements in connection with its approval of our NDA for Defitelio in March 2016, including the requirement that we conduct a clinical trial, or the Defitelio post-marketing trial, to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. If we fail to complete any of these post-marketing obligations, including our failure to satisfactorily complete the Defitelio post-authorization study, the ongoing validity of the marketing authorization may be called into question, our sales of and revenues from Defitelio could be materially adversely affected and our future maintenance and potential growth of the market for this product may be limited.

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. This includes the laws and regulations that will apply as the UK determines which EU laws to replace or replicate in the event of a withdrawal. From a regulatory perspective, the UK's withdrawal could result in significant complexity and risks. A basic requirement related to the grant of a marketing authorization for a medicinal product in the EU is the requirement that the applicant is 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 an arguable risk that the scope of a marketing authorization for a medicinal product granted by the EC pursuant to the centralized procedure, or the competent authorities of other EU member states through the

decentralized or mutual recognition procedures, would not, in the future, include the UK. In these circumstances, an authorization granted by the UK's 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 certification issued by the UK competent authorities. Our capability to rely on these manufacturing sites for products intended for the EU market would also depend upon the exact terms of the UK's withdrawal. There is also the risk that if there are batch release and quality control testing sites for finished product only in the UK, manufacturers will need to move to batch release and testing sites in other EU member states.

Any such changes to the regulatory regime could have a material adverse effect on the pharmaceutical industry generally and on our ability to obtain approval for our product candidates or, if approved, to successfully commercialize our product candidates. For a further discussion, see the risks under the heading "*The results of the UK's referendum on withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business*" in this Part II, Item 1A.

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

The Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act of 2010, together, the Healthcare Reform Act, is a sweeping measure intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals, 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 Public Health Service's 340B drug pricing program, or 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.

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

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

Moreover, additional legislative changes to or regulatory changes under the Healthcare Reform Act remain possible and appear likely. In this regard, the U.S. Tax Cuts and Jobs Act of 2017, or U.S. Tax Act, signed into law in December 2017, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Healthcare Reform Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." The nature and extent of any additional legislative or regulatory changes to the Healthcare Reform Act are uncertain at this time. We expect that the Healthcare Reform Act, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of our existing products or to successfully commercialize our product candidates, if approved. In addition to the Healthcare Reform Act, there will continue to be proposals by legislators at both the federal and state levels, regulators and third party payors to keep healthcare costs down while expanding individual healthcare benefits.

Likewise, in the countries in the EU, legislators, policymakers and healthcare insurance funds continue to propose and implement cost-containing measures to keep healthcare costs down, due in part to the attention being paid to healthcare cost containment in the EU. Certain of these changes could impose limitations on the prices we will be able to charge for our products and any approved product candidates or the amounts of reimbursement available for these products from governmental agencies or third party payors, may increase the tax obligations on pharmaceutical companies such as ours, or may facilitate the introduction of generic competition with respect to our products. Further, an increasing number of EU member states and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere. In addition, the ongoing budgetary difficulties faced by a number of EU member states, including Greece and Spain, have led and may continue to lead to substantial delays in payment and payment partially with government bonds rather than cash for medicinal drug products, which could negatively impact our revenues and profitability. Moreover, in order to obtain reimbursement for our products in some countries, including some EU member states, we may be required to conduct clinical trials that compare the cost-effectiveness of our products to other available therapies. There can be no assurance that our products will obtain favorable reimbursement status in any country.

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

Patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. 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, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses and reduce the availability of foundation support for our patients who need assistance.

In May and October 2016 and February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. We have engaged with the DOJ about a possible resolution, and in the first quarter of 2018, we recorded a $57.0 million accrual related to this matter. For more information, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q and the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products*" in this Part II, Item 1A.

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

FDA and Equivalent Non-U.S. Regulatory Authorities

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

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

The FDA and the competent authorities of the EU member states on behalf of the EMA also periodically inspect our records related to safety reporting. Following such inspections, the FDA may issue notices on FDA Form 483 and warning letters that could cause us to modify certain activities. The EMA's Pharmacovigilance Risk Assessment Committee 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 withdrawn. An FDA Form 483 notice, if issued at the conclusion of an FDA inspection, can list conditions the FDA investigators believe may have violated relevant FDA regulations or guidance. Failure to adequately and promptly correct the observation(s) can result in further regulatory enforcement action. The failure to adequately address any matters identified by the FDA or other regulatory agencies in the future could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In addition, the failure by any of our suppliers to address or remediate issues observed in an inspection by a regulatory authority 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. See the discussion regarding our contract suppliers in the risk factor under the heading "*The loss of our single source suppliers, delays or problems in the supply of our products for commercial sale or our product candidates for use in our clinical trials, or our or our suppliers' failure to comply with manufacturing regulations, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A.

If we receive regulatory approvals to sell our products, the FDA, the EC, the competent authorities of the EU member states and other non-U.S. regulatory authorities where our products are approved may impose significant restrictions on the indicated uses or marketing of our products, or impose requirements for burdensome post-approval clinical studies or trials. The terms of any product approval, including labeling, may be more restrictive than we desire and could affect the commercial potential of the product. If we become aware of problems with any of our products in the U.S., the EU or elsewhere in the world or at our third party suppliers' facilities, a regulatory agency may impose restrictions on our products, our suppliers, our other partners or us. In such an instance, we could experience a significant drop in the sales of the affected products, our product revenues and reputation in the marketplace may suffer, and we could become the target of lawsuits.

EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post-authorization efficacy studies and post-authorization safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and

expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

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

The marketing authorization in the EU for Defitelio requires us to comply with a number of post-marketing obligations, including obligations relating to the establishment of a patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use. In January 2017, we enrolled the first patient in the Defitelio 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. The FDA imposed several post-marketing requirements and commitments in connection with its March 2016 approval of our NDA for Defitelio, including the requirement that we conduct the Defitelio post-marketing trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. Additionally, the FDA imposed two post-marketing requirements in connection with its approval of our NDA for Vyxeos in August 2017, 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. The marketing authorization in the EU for Vyxeos also requires us to comply with certain manufacturing-related post-approval commitments. If we fail to complete any of these post-marketing obligations for Defitelio or Vyxeos, including our failure to satisfactorily complete post-marketing studies and trials, the ongoing validity of the marketing authorizations may be called into question, our sales of and revenues from Defitelio and Vyxeos could be materially adversely affected and our future maintenance and potential growth of the markets for these products may be limited.

Erwinase and defibrotide are available on a named patient basis in many countries where they are not commercially available. If any such country's regulatory authorities determine that we are promoting Erwinase or defibrotide without proper authorization, we could be found to be in violation of pharmaceutical advertising laws or the regulations permitting sales under named patient programs. In that case, we may be subject to financial or other penalties.

The FDA, the competent authorities of the EU member states and other governmental authorities require advertising and promotional labeling to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. The FDA routinely provides its interpretations of that authority in informal communications and also in more formal communications such as untitled letters or warning letters, and although such communications may not be considered final agency decisions, companies may decide not to contest the agency's interpretations so as to avoid disputes with the FDA, even if they believe the claims to be truthful, not misleading and otherwise lawful. In recent years, certain courts have determined that the First Amendment of the U.S. Constitution permits communications regarding off-label uses of drug products, as long as such communications are truthful and not misleading. At the beginning of 2017, the FDA released proposed rule changes and draft guidance on the FDA's interpretation on the limitations of such speech. These cases and regulatory actions create additional uncertainty regarding the limits of permissible communication regarding our products.

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

Other U.S. 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, or DOC, the OIG and other regulatory bodies, as well as governmental authorities in those non-U.S. countries in which we commercialize our products. In addition to the FDCA, other federal, state and non-U.S. statutes and regulations govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including preclinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information, promotion, marketing, and pricing to government purchasers and government healthcare programs. Our partners, including our suppliers and distributors and the central pharmacy for Xyrem, a controlled substance under the CSA, are also subject to DEA and state regulations relating to manufacturing, storage, distribution and physician prescription procedures, including limitations on prescription refills and are required to maintain necessary DEA registrations and state licenses. The DEA periodically inspects facilities for compliance with its rules and regulations. Failure to comply with current and future regulations of the DEA, relevant state authorities or any comparable international requirements could lead to a variety of sanctions, including revocation or denial of renewal of DEA registrations, fines, injunctions, or civil or criminal penalties, could result in, among other things, additional operating costs to us or delays in shipments outside or into the U.S. and could have an adverse effect on our business and financial condition.

In addition, drug products may be subject to scheduling by the FDA as a controlled substance under the CSA, depending on the drug's potential for abuse. In this regard, we expect that solriamfetol will be subject to scheduling review under the CSA before it can be commercially launched. Controlled substances that are pharmaceutical products are subject to a high degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. The DEA limits the quantity of certain Schedule I controlled substances that may be produced or procured in the U.S. in any given calendar year through a quota system. Accordingly, we require DEA quotas for Siegfried in the U.S. to manufacture sodium oxybate, a Schedule I controlled substance, and for Patheon, our U.S.-based Xyrem supplier, to procure the sodium oxybate from Siegfried in order to manufacture and supply us with Xyrem. Because the DEA typically grants quotas on an annual basis, Siegfried and Patheon are required to request and justify allocation of sufficient annual DEA quotas as well as additional DEA quotas if our commercial or clinical requirements exceed the allocated quotas throughout the year. For the last few years, our suppliers were allocated only a portion of the published annual aggregate quota for the API. If one or more ANDA filers were to begin manufacturing a generic sodium oxybate product, generic manufacturers would need to obtain a portion of the annual aggregate API quota, which could decrease the DEA quota allocation obtained on our behalf by Siegfried and Patheon. In the past, we have also had to engage in lengthy efforts to obtain the needed quotas after the original annual quotas had first been allocated. If, in the future, our suppliers cannot obtain the quotas that are needed on a timely basis, or at all, our business, financial condition, results of operations and growth prospects could be materially and adversely affected.

The U.S. federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Liability may be established without a person or entity having actual knowledge of the federal anti-kickback statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and Medicare patients, prescribers, purchasers and formulary managers on the other. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common manufacturer business arrangements and activities from prosecution and administrative sanction, the exemptions and safe harbors are drawn narrowly, and practices or arrangements that involve remuneration may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection, and therefore would be subject to a facts and circumstances analysis to determine potential anti-kickback statute liability.

The False Claims Act prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of federal funds, or knowingly making, or causing to be made, a false statement to get a false claim paid. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the statute and to share in any monetary recovery. Many pharmaceutical and other healthcare companies have been investigated or subject to lawsuits by whistleblowers and have reached substantial financial settlements with the federal government under the False Claims Act for a variety of alleged improper marketing

activities, including providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees, grants, free travel, and other benefits to physicians to induce them to prescribe the company's products; and inflating prices reported to private price publication services, which are used to set drug reimbursement rates under government healthcare programs. In addition, 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.

In addition, the Physician Payment Sunshine Act, or Sunshine provisions, 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, and such scrutiny may negatively impact our ability to engage with physicians on matters of importance to us. In addition, if the data reflected in our reports are found to be in violation of any of the Sunshine provisions or any other U.S. federal, state or local laws or regulations that may apply, or if we otherwise fail to comply with the Sunshine provisions, we may be subject to significant civil, criminal and administrative penalties, damages or fines.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. A number of states require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states restrict when pharmaceutical companies may provide meals or gifts to prescribers or engage in other marketing-related activities. Other states and cities require identification or licensing of sales representatives. Other states restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Massachusetts and Nevada require pharmaceutical companies to implement compliance programs or marketing codes of conduct. Various state and federal regulatory and enforcement agencies continue to actively investigate violations of health care laws and regulations, and the U.S. Congress continues to strengthen the arsenal of enforcement tools. Most recently, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the federal anti-kickback statute.

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 by the federal government.

In May and October 2016 and in February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients, and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. Other companies have disclosed similar subpoenas and continuing inquiries.

We have been cooperating with the government's investigation, and we have engaged in discussions with the DOJ about a possible resolution. 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. Material issues remain subject to further negotiation and approval by us and the DOJ before the proposed settlement can be finalized. 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. Any such settlement is also likely to involve entry into a corporate integrity agreement, which would impose costs and burdens on the operation of our business. If we do not reach a final settlement, 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, and we would expect to incur significant costs in connection with such enforcement action, regardless of the outcome. We are unable to predict how long this investigation will continue, whether we will receive additional subpoenas in connection with this investigation, or its outcome, but we expect that we will continue to incur significant costs in connection with the investigation, regardless of the outcome.

We may also become subject to similar investigations by other state or federal governmental agencies or offices. Any additional investigations of our patient assistance programs or other business practices may result in damages, fines, penalties

or other criminal, civil or administrative sanctions or enforcement actions against us or 501(c)(3) organizations that we support. Such investigations may also result in negative publicity or other negative actions as to us or 501(c)(3) organizations that we support that could harm our reputation, impact our business practices, reduce demand for, or patient access to, 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. For more information, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q and the risk factor under the heading "*Changes in healthcare law and implementing regulations, including those based on recently enacted legislation, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and these changes could have a material adverse effect on our business and financial condition*" in this Part II, Item 1A.

Other Regulatory Authorities

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

Interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct in the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of the EU member states, as described below. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states, such as France, Belgium and Portugal, 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.

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. The FCPA and similar anti-corruption laws generally prohibit the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to non-U.S. government officials in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The UK Bribery Act prohibits giving, offering, or promising bribes to any person, including both 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 which 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 non-UK government officials and private persons, in another country by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Liability is strict, with no element of a corrupt state of mind, but having in place adequate procedures designed to prevent bribery is an available defense. Furthermore, under the UK Bribery Act there is no exception for facilitation payments. As described above, our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers may be subject to regulation under the FCPA. Recently the U.S. Securities and Exchange Commission, or SEC, and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. There is no certainty that all employees and third party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of suppliers and other third party agents, although we may be liable for their actions.

Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

We are also subject to laws and regulations governing data privacy and the protection of health-related and other personal information. These laws and regulations govern our processing of personal data, including the collection, access, use, analysis, modification, storage, transfer, security breach notification, destruction and disposal of personal data. We must comply with laws and regulations associated with the international transfer of personal data based on the location in which the personal data originates and the location in which it is processed. Although there are legal mechanisms to facilitate the transfer of personal data from the European Economic Area, or EEA, and Switzerland to the U.S., the decision of the European Court of Justice that invalidated the safe harbor framework on which we previously relied has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it was no longer possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the EU to entities in the U.S. In February 2016, the EC announced an agreement with the DOC to replace the invalidated safe harbor framework with a new EU-U.S. "Privacy Shield." On July 12, 2016, the EC adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the European Court of Justice in its recent ruling by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and FTC and making commitments on the part of public authorities regarding access to information.

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

The privacy and data security landscape is still in flux. In October 2016, an action for annulment of the EC decision on the adequacy of Privacy Shield was brought before the European Court of Justice by three French digital rights advocacy groups, La Quadrature du Net, French Data Network and the Fédération FDN. This case, Case T-738/16, is currently pending before the European Court of Justice. Should the European Court of Justice invalidate the Privacy Shield, it will no longer be possible to transfer data from the EU to entities in the U.S. under a Privacy Shield certification, in which case other legal mechanisms would need to be put in place.

Healthcare providers who prescribe our products and research institutions that we collaborate with are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA. Although we are not directly subject to HIPAA other than with respect to providing certain employee benefits, we 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.

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. In this regard, we expect that there will continue to be new laws, regulations and industry standards relating to privacy and data security in the U.S., the EU and other jurisdictions, such as the EU General Data Protection Regulation, or GDPR, that became effective in May 2018, and the California Consumer Privacy Act of 2018 that will become effective beginning January 2020 and mirrors a number of the key provisions in the GDPR. Failure to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors, 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 to allow for the transfer of personal data from the EEA or Switzerland to the U.S. (or other countries not considered by the EC to provide an adequate level of data protection) are not considered adequate, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted if our ability to transfer personal data outside of the EEA or Switzerland is restricted, which could adversely impact our operating results. The GDPR introduced new data protection requirements in the EU relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the documentation we must retain, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of personal data. The GDPR has increased our responsibility and potential liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR. However, our ongoing efforts related to compliance with the GDPR may not be successful and could increase our cost of doing business. In addition, data protection authorities of the different EU member states may interpret the GDPR differently, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU.

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

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

Several aspects of our business may subject us to antitrust scrutiny by the FTC or to civil litigation alleging violation of the antitrust laws. For example, REMS and the improper use of REMS as a means of improperly blocking or delaying competition for branded pharmaceutical products have increasingly drawn public scrutiny from Congress, the FTC and the FDA. 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 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 (including in light of the FDA's statement in the February 2015 Xyrem REMS approval letter that the Xyrem REMS could be used in an anticompetitive manner inconsistent with applicable provisions of the FDCA) or have engaged in other anticompetitive practices. The FDCA further states that a REMS shall not be used by an NDA holder to block or delay generic drugs or drugs covered by an application under Section 505(b)(2), from entering the market. Several of the ANDA applicants have asserted that our REMS patents should not have been listed in the Orange Book, and that the Xyrem REMS is blocking competition.

Another area of potential antitrust scrutiny relates to the settlement of patent litigation with potential generic competitors. Parties to such settlement agreements in the U.S. are required by law to file the agreements with the FTC and the DOJ for review. Accordingly, we have submitted our Xyrem patent settlement agreements 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 certain branded and generic 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. 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. 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.

Compliance with U.S. federal and state, EU and EU member state national laws that apply to pharmaceutical manufacturers is difficult and time-consuming, and companies that violate these laws may face substantial penalties. The potential sanctions include civil monetary penalties, exclusion of a company's products from reimbursement under government programs, criminal fines and imprisonment. Because of the breadth of these laws and, in some cases, the lack of extensive legal guidance in the form of regulations or court decisions, it is possible that some of our business activities could be subject to challenge under one or more of these laws. If we or the other parties with whom we work fail to comply with applicable regulatory requirements, we or they could be subject to a range of regulatory actions that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business.

We manufacture certain APIs, including the defibrotide drug substance, at our manufacturing facilities in Italy. In addition, we have engaged a third party supplier to process defibrotide into the finished product in Italy. Our manufacturing facilities and those of our third party manufacturer are subject to continuing regulation by the Italian Health Authority and other Italian regulatory authorities with respect to the manufacturing of APIs and drug products, including the defibrotide drug substance and its finished form. These facilities are also subject to inspection by the competent authorities of the EU member states and regulation by the EMA. Following initial approval in a jurisdiction, the competent authorities will continue to inspect our manufacturing facilities and those of our third party supplier, in some cases, unannounced, to confirm ongoing compliance with cGMP. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures, and we and our third party suppliers will need to ensure that all of our processes, methods and equipment are compliant with cGMP. If these authorities determine that either our facilities or our third party supplier's facility in Italy do not meet the standards of compliance required under applicable regulations, they may deny approval to manufacture our products, require us to stop manufacturing our products, deny approval to the sale of our products or suspend the sale of our products.

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

We participate in and have certain price reporting obligations to the Medicaid Drug Rebate program, several state Medicaid supplemental rebate programs and other governmental pricing programs, and we have obligations to report average sales price under the Medicare program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results.

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

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service's 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities

include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The Healthcare Reform Act expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the Healthcare Reform Act or otherwise could affect our 340B ceiling price calculations and negatively impact our results of operations.

As required under the Healthcare Reform Act, the Health Resources and Services Administration, or HRSA, has updated the agreement that manufacturers must sign to participate in the 340B program to obligate a manufacturer to offer the 340B price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. The Healthcare Reform Act also obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340B program. On January 5, 2017, 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 overcharge covered entities. The effective date of the regulation has been delayed until July 1, 2019. Implementation of this final rule and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

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

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

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

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

We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our covered products on a Tricare Agreement in order for these products to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Access and adequate reimbursement coverage 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, and to attract commercialization partners for our products, depends in significant part on access, the availability of adequate financial coverage and reimbursement from third party payors, including governmental payors (such as the Medicare and Medicaid programs in the U.S.), managed care organizations and private health insurers. The process for determining whether a third party 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. Without third party payor support, patients may not be able to obtain prescribed medications due to an inability to afford the medication.

Third party payors are increasingly examining the cost effectiveness of pharmaceutical products, in addition to their safety and efficacy, when making coverage, pricing 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 price approvals, 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.

Third party payors' practices for establishing access and reimbursement coverage can be complex, time-consuming for patients and prescribing physicians and vary widely from payor to payor. 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. 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 may have a material effect on the overall level of reimbursement coverage for Xyrem. Increases in reimbursement-related activities have extended the time required to fill prescriptions and could continue to do so in the future. 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.

In addition, reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a significant impact on the prescribing physicians' willingness to prescribe our products. For example, the U.S. federal government follows a Medicare severity diagnosis-related group, or MS-DRG, payment system for certain inpatient hospital services provided under Medicare, which some states also use for Medicaid. The MS-DRG system entitles a hospital to a fixed reimbursement based on discharge diagnoses rather than actual costs incurred in providing inpatient treatment, thereby increasing the incentive for the facility to limit or control expenditures for many healthcare products. For our products used in the inpatient hospital setting, there may not be sufficient reimbursement under the relevant MS-DRG to fully cover the cost of our products. Any failure to cover our products appropriately could impact our ability to maximize revenues in the federal marketplace. A significant portion of our revenue from Erwinaze is obtained through government payors, including Medicaid, and any failure to qualify for reimbursement for Erwinaze under those programs, including as a result of legislative changes to these programs, would have a material adverse effect on revenues from Erwinaze.

Third party payors are also increasingly considering new metrics as the basis for reimbursement rates, such as average net sales price, average manufacturer price and actual acquisition cost. Certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates. CMS surveys and publishes retail community pharmacy acquisition cost information in the form of National Average Drug Acquisition Cost files to provide state Medicaid agencies with a basis of comparison for their own reimbursement and pricing methodologies and rates. It may be difficult to project the impact of these evolving reimbursement mechanics on the willingness of payors, including government payors, to cover our products.

Increasing consolidation among third party payors has led to fewer and larger third party payors with increased negotiating power. In particular, a small number of third party payors cover a significant portion of Xyrem patients. As a result, we may experience increasing pressure from third party payors to agree to discounts, rebates or other restrictive pricing terms for Xyrem. In the retail pharmacy sector, in which we expect that sales of an approved solriamfetol product would occur, a small number of third party payors and other third-party organizations known as pharmacy benefit managers, or PBMs, tasked with administrating prescription drug programs for large employers, health plans and government programs 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 the retail sector, if approved by the FDA, solriamfetol may face such conditions following its commercial launch, which could impact our other products. In highly competitive treatment markets, third party payors and PBMs may also exert negotiating leverage by requiring incremental rebates from manufacturers in order to maintain their formulary position.

If solriamfetol is approved by the FDA, the product will enter a competitive retail 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. As part of the overall trend toward cost containment, 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. 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 favorable formulary positions, access and reimbursement coverage for, solriamfetol. An inability to obtain favorable 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.

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes, and we expect there will continue to be legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably. Several states have recently passed laws aimed at increasing transparency relating to drug pricing, and other states may do so in the future. We anticipate that the U.S. Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies and reforms intended to curb healthcare costs, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U.S. These cost containment measures may include federal and state controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government health care programs; 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; changes in drug importation laws; expansion of use of managed care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person; and public funding for cost effectiveness research, which may be used by government and private third party payors to make coverage and payment decisions.

Much attention has been paid to legislation proposing federal rebates on Medicare Part D and Medicare Advantage utilization for drugs issued to certain groups of lower income beneficiaries and the desire to change the provisions that treat these dual-eligible patients differently from traditional Medicare patients. Any such changes could have a negative impact on revenues from sales of our products. Beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2027. These cuts reduce reimbursement payments related to our products, which could potentially negatively impact our revenue. Any failure to cover our products appropriately, in addition to legislative and regulatory changes and others that may occur in the future, could impact our ability to maximize revenues in the federal marketplace. A significant portion of our revenue from Erwinaze is obtained through government payors, including Medicaid, and any failure to qualify for reimbursement for Erwinaze under those programs, including as a result of legislative changes to these programs, would have a material adverse effect on revenues from Erwinaze. There also continue to be legislative proposals to amend U.S. laws to allow the importation into the U.S. of prescription drugs, which can be sold at prices that are regulated by the governments of various non-U.S. countries. The potential importation of prescription drugs could pose significant safety concerns for patients, increase the risk of counterfeit products becoming available in the market, and could also have a negative impact on prescription drug prices in the U.S.

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 2018, and we have made and may in the future make similar price increases on our other products. We cannot assure you that such price adjustments will not negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our products, which could negatively impact our sales volumes and revenue. We expect to continue to experience pricing pressure

in the U.S. in connection with the sale of our products due to third party payer actions, the increasing influence of health maintenance organizations, PBMs and managed healthcare generally, additional legislative proposals to curb healthcare costs and negative publicity regarding pricing and price increases generally, which could limit the prices that we charge for our products, including Xyrem, limit the commercial opportunities for our products and/or negatively impact revenues from sales of our products.

If we become the subject of any government investigation with respect to our drug pricing or other business practices, including as they relate to the Xyrem REMS, we could incur significant expense and could be distracted from operation of our business and execution of our strategy. Any such investigation could also result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In May and October 2016 and February 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of 501(c)(3) organizations that provide financial assistance to Medicare patients and, for Xyrem, documents concerning the provision of financial assistance to Medicare patients. For more information, see Note 10, Commitments and Contingencies—Legal Proceedings of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q and the risk factors under the headings "*Changes in healthcare law and implementing regulations, including those based on recently enacted legislation, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and these changes could have a material adverse effect on our business and financial condition*" and "*We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products*" in this Part II, 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. We cannot predict the outcome of any periodic reviews required to maintain pricing and reimbursement approvals across Europe. 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 Defitelio and our other 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. These EU member states include the UK, France, Germany, Ireland, Italy, Spain, and Sweden. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products, as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. Pursuant to Directive 2011/24/EU, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This could lead to harmonization between EU member states of the criteria taken into account in the conduct of HTA and their impact on pricing and reimbursement decisions. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product, however, still vary between EU member states and cannot be determined or anticipated in relation to our products at the present time. If we are unable to ultimately obtain favorable pricing and reimbursement approvals in countries that represent significant markets, especially where a country's reimbursed price influences other countries, our growth prospects in Europe could be negatively affected.

In the EU, our products are marketed through various channels and within different legal frameworks. In certain EU member states, reimbursement for unauthorized products may be provided through national named patient programs. Such reimbursement may no longer be available if authorization for named patient programs expire or are terminated or when marketing authorization is granted. In other EU member states, authorization and reimbursement policies may also delay commercialization of our products, or may adversely affect our ability to sell our products on a profitable basis. After initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple

factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or arbitrage between low-priced and high-priced member states. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted, could negatively affect our growth prospects in Europe.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Moreover, we cannot be sure that third party payor reimbursement amounts, or the lack of reimbursement, will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only at limited levels, we may not be able to effectively commercialize our products. Our business could be materially harmed if the Medicaid program, Medicare program or other third party payors in the U.S. or elsewhere were to deny reimbursement for our products, limit the indications for which our products will be reimbursed, or provide reimbursement only on unfavorable terms. Sales of our products depend on the availability and extent of access and reimbursement coverage from third party payors, but pricing and reimbursement pressures due to increasing media and government scrutiny of drug costs may affect our profitability.

Product liability and product recalls could harm our business.

The development, manufacture, testing, marketing and sale of pharmaceutical products are associated with significant risks of product liability claims or recalls. Side effects or adverse events known or reported to be associated with, or manufacturing defects in, the products sold by us could exacerbate a patient's condition, or could result in serious injury or impairments or even death. This could result in product liability claims and/or recalls of one or more of our products. Some of our products, including Xyrem and Prialt, have boxed warnings in their labels. In addition, in the EU, Defitelio's label includes an inverted black triangle that indicates the product is subject to additional monitoring to permit quick identification of new safety information, as a condition of authorization of Defitelio under "exceptional circumstances." In many countries, including in EU member states, national laws provide for strict (no-fault) liability which applies even where damages are caused both by a defect in a product and by the act or omission of a third party.

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

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

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

Product recalls may be issued at our discretion or at the discretion of our suppliers, government agencies and other entities that have regulatory authority for pharmaceutical sales. Any recall of our products could materially adversely affect our business by rendering us unable to sell that product for some time and by adversely affecting our reputation. A recall could also result in product liability claims by individuals and third party payors. In addition, product liability claims could result in an investigation of the safety or efficacy of our products, our manufacturing processes and facilities, or our marketing programs conducted by the FDA, the EMA, or the competent authorities of the EU member states. Such investigations could also potentially lead to a recall of our products or more serious enforcement actions, limitations on the 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 the relevant jurisdictions 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, 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. Our manufacturing activities in Italy and Ireland involve the controlled storage, use and disposal of chemicals and solvents. Even if our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by 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. 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 September 30, 2018, we had total indebtedness of approximately $1.8 billion, which included $659.4 million in outstanding term loan indebtedness under a secured credit agreement that we entered into in June 2015, 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.

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 cause to be delivered solely ordinary shares to settle such exchange, we will be required to make cash payments in respect of the Exchangeable Senior Notes being exchanged. In this regard, 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 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, our acquisition of EUSA Pharma Inc., the Gentium Acquisition and the Celator Acquisition. To continue to grow our business over the longer term, we will need to commit substantial additional resources to 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 generic or other 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 the acquisition or in-licensing and development of additional marketed products or product candidates that are in late-stage development. We cannot assure you that we will continue to identify attractive opportunities. Even if appropriate opportunities are available, in order to compete successfully to acquire attractive products or product candidates in the current business climate, we may have to pay higher prices for assets than may have been paid historically, and we may not have the financial resources necessary to pursue them. As a result, we may be unable to expand our business if we do not have sufficient capital or cannot borrow or raise additional capital on attractive terms. 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 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. We are able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, together with intra-group service and transfer pricing agreements, each on an arm's length basis. However, changes in tax laws in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the U.S. Internal Revenue Service, or the IRS, actively audit and otherwise challenge these types of arrangements, and have done so in the pharmaceutical industry. We are subject to reviews and audits by the IRS and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure and transfer pricing arrangements through an audit or lawsuit. 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 relating to certain transfer pricing adjustments. The notices provide for additional French tax of approximately $43 million, including interest and penalties, through the date of the proposed assessment translated at the foreign exchange rate at September 30, 2018. While we disagree with the assessments and are contesting them, responding to or defending against this and other challenges from taxing authorities could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We generally cannot predict whether taxing authorities will conduct an audit or file a lawsuit challenging our structure, the cost involved in responding to any such audit or lawsuit, or the outcome. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our products or seek to raise additional funds. Any of these actions could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, on December 22, 2017, the U.S. Tax Act was signed into law. The legislation significantly changes U.S. tax law by, among other things, lowering the corporate income tax rate from a maximum of 35% to a flat 21%, implementing a modified territorial tax system, imposing a one-time transition tax on deemed repatriated earnings of foreign subsidiaries and changing the rules which determine whether a foreign corporation is treated for U.S. tax purposes as a controlled foreign corporation, or CFC, for 2017 and onwards. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our ordinary shares is also uncertain and could be adverse. Among other things, changes to the rules for

determining CFC status 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 shares. Investors should consult their own advisers regarding the potential application of these rules to their investments in us.

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. For us to be treated as a foreign corporation for U.S. federal tax purposes under Section 7874 of the Code, either (1) the former stockholders of Jazz Pharmaceuticals, Inc. must have owned (within the meaning of Section 7874 of the Code) less than 80% (by both vote and value) of our ordinary shares by reason of holding shares in Jazz Pharmaceuticals, Inc. after the Azur Merger (the "ownership test"), or (2) we must have substantial business activities in Ireland after the Azur Merger (taking into account the activities of our expanded affiliated group). The Jazz Pharmaceuticals, Inc. stockholders owned less than 80% of our share capital immediately after the Azur Merger by reason of their ownership of shares of Jazz Pharmaceuticals, Inc. common stock. As a result, we believe that we should be treated as a foreign corporation for U.S. federal tax purposes under current law. It is possible that the IRS could disagree with the position that the ownership test is satisfied and assert that Section 7874 of the Code applies to treat us as a U.S. corporation following the Azur Merger. There is limited guidance regarding the Code Section 7874 provisions, including the application of the ownership test described above. The IRS continues to scrutinize transactions that are potentially subject to Section 7874, and has issued several sets of final and temporary regulations under Section 7874 since 2012. Most recently, in July 2018, the IRS issued regulations under Section 7874 that finalized, with few changes, guidance that the IRS had previously issued in temporary form in 2016. We do not expect these regulations to affect the U.S. tax consequences of the Azur Merger. Nevertheless, new statutory and/or regulatory provisions under Section 7874 of the Code or otherwise could be enacted that adversely affect our status as a foreign corporation for U.S. federal tax purposes, and any such provisions could have retroactive application to us, our shareholders, Jazz Pharmaceuticals, Inc. and/or the Azur Merger. For more information, see the risk factor under the heading "*Future changes to the tax laws under which we expect to be treated as a foreign corporation for U.S. federal tax purposes or to other tax laws relating to multinational corporations could adversely affect us,*" in this Part II, Item 1A.

Section 7874 of the Code limits our U.S. affiliates' ability to utilize their U.S. tax attributes to offset certain U.S. taxable income, if any, generated by certain taxable transactions.

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

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 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.

Our U.S. affiliates have a significant amount of NOLs. Our ability to use these NOLs to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the NOLs, and we cannot predict with certainty when, or whether, our U.S. affiliates will generate sufficient taxable income to use all of the NOLs. Under the newly enacted U.S. Tax Act, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, realization of NOLs to offset potential future taxable income and related income taxes that would otherwise be due is subject to annual limitations under the "ownership change" provisions of Sections 382 and 383 of the Code and similar state provisions, which may result in the expiration of additional NOLs before future utilization. In general, an "ownership change" occurs if, during a three-year rolling period, there is a change of 50% or more in the percentage ownership of a company by 5% shareholders (and certain persons

treated as 5% shareholders), as defined in the Code and the U.S. Treasury Department regulations, or Treasury Regulations, promulgated thereunder. In this regard, we currently estimate that, as a result of these ownership change provisions, we have an annual limitation on the utilization of certain NOLs and credits of $399.9 million, before tax effect, for 2018, $76.4 million, before tax effect, for 2019 and a combined total of $311.0 million, before tax effect, for 2020 to 2032.

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

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

As described above, under current law, we believe that we should be treated as a foreign corporation for U.S. federal tax purposes. However, changes to the Code or the Treasury Regulations or other IRS guidance promulgated thereunder, including under Section 7874 of the Code, could adversely affect our status as a foreign corporation for U.S. federal tax purposes or could otherwise affect our effective tax rate, and any such changes could have prospective or retroactive application. Any future tax reform related to U.S. corporate tax residence, if enacted, could adversely affect our effective tax rate and our results of operations and financial condition.

The U.S. Congress, the EU, the Organization for Economic Co-operation and Development, or OECD, and other government agencies in jurisdictions where we and our affiliates do business have also had an extended focus on issues related to the taxation of multinational corporations. One example is 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 recommendations. 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.

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 September 30, 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, we recognized an impairment charge of $42.9 million in our condensed consolidated statements of income for the nine months ended September 30, 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.

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, we cannot assure you 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.

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 $128.58 on November 7, 2017 during the period from September 30, 2017 through September 30, 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 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 Xyrem, Defitelio and Vyxeos. The risks and uncertainties associated with our ability to maintain or increase sales of Xyrem, Erwinaze, Defitelio and Vyxeos include those discussed elsewhere in these risk factors. In the past, following periods of volatility in the market or significant price decline, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

In addition, the market price of our ordinary shares may decline if the effects of our transactions, including the 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.

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

Sales of a substantial number of our ordinary shares in the public market, including sales by members of our management or board of directors, or the perception that these sales might occur, could depress the market price of our ordinary shares and could impair our ability to raise capital through the sale of additional equity or equity-related securities. As of October 31, 2018, we had 60,321,590 ordinary shares outstanding, all of which shares are eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale and other requirements under Rule 144. In addition, future issuances by us of our ordinary shares upon the exercise or settlement of equity-based awards and exchanges of the Exchangeable Senior Notes would dilute existing shareholders' ownership interests in our company, and any sales in the public market of these ordinary shares, or the perception that these sales might occur, could also adversely affect the market price of our ordinary shares.

Moreover, we have in the past and may in the future grant rights to some of our shareholders that require us to register the resale of our ordinary shares on behalf of these shareholders and/or facilitate offerings of ordinary shares held by these shareholders, including in connection with potential future acquisitions of additional products, product candidates or companies. We have also filed registration statements to register the sale of our ordinary shares reserved for issuance under our equity incentive and employee stock purchase plans, and we intend to file additional registration statements to register any shares automatically added each year to the share reserves under these plans.

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

It may not be possible to enforce court judgments obtained in the U.S. against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liability

provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U.S. currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish company, we are governed by the Irish Companies Act 2014, which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company are generally owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a U.S. jurisdiction.

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 or repeal our articles of association; and
- permit our board of directors to issue one or more series of preferred shares with rights and preferences, as our shareholders may determine by ordinary resolution.

In addition 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.

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.

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

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

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

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 Securities Exchange Act of 1934, as amended, during each fiscal month during the three-month period ended September 30, 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)
July 1 - July 31, 2018	—	$ —	—	$ 127,186,612
August 1 - August 31, 2018	48,000	$ 172.45	48,000	$ 118,919,875
September 1 - September 30, 2018	79,500	$ 165.75	79,500	$ 105,734,725
Total	127,500	$ 168.27	127,500	

(1) This table does not include ordinary shares that we withheld in order to satisfy minimum tax withholding requirements in connection with the vesting and release of restricted stock units.

(2) Average price paid per ordinary share includes brokerage commissions.

(3) The ordinary shares reported in the table above were purchased pursuant to our publicly announced share repurchase program. In November 2016, we announced that our board of directors authorized the use of up to $300 million to repurchase our ordinary shares. In November 2018, our board of directors increased the existing share repurchase program authorization by an aggregate purchase price of $320 million, exclusive of any brokerage commissions. This authorization has no expiration date.

(4) The dollar amount shown represents, as of the end of each period, the approximate dollar value of ordinary shares that may yet be purchased under our publicly announced share repurchase program, exclusive of any brokerage commissions. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under our credit agreement, corporate and regulatory requirements and market conditions, and may be modified, suspended or otherwise discontinued at any time without prior notice.

Item 6. Exhibits

Exhibit Number	Description of Document
2.1	Agreement and Plan of Merger and Reorganization, dated as of September 19, 2011, by and among Azur Pharma Limited (now Jazz Pharmaceuticals plc), Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500) filed with the SEC on September 19, 2011).
2.2	Letter Agreement, dated as of January 17, 2012, by and among Jazz Pharmaceuticals plc, Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated by reference to Exhibit 2.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
2.3	Agreement and Plan of Merger, dated as of April 26, 2012, by and among Jazz Pharmaceuticals plc, Jewel Merger Sub Inc., EUSA Pharma Inc., and Essex Woodlands Health Ventures, Inc., Mayflower L.P., and Bryan Morton, in their capacity as the representatives of the equity holders of EUSA Pharma Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on April 27, 2012).
2.4	Assignment, dated as of June 11, 2012, by and among Jazz Pharmaceuticals plc and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 2.1B in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 12, 2012).
2.5	Tender Offer Agreement, dated December 19, 2013, by and among Jazz Pharmaceuticals Public Limited Company, Jazz Pharmaceuticals Italy S.r.l. and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K/A (File No. 001-33500), as filed with the SEC on December 20, 2013).
2.6†	Asset Purchase Agreement, dated January 13, 2014, by and among Jazz Pharmaceuticals International III Limited, Aerial BioPharma, LLC and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 13, 2014).
2.7†	Assignment Agreement, dated July 1, 2014, by and among Jazz Pharmaceuticals International II Limited, Sigma-Tau Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 5, 2014).
2.8	Amended and Restated Agreement for the Acquisition of the Topaz Portfolio Business of Jazz Pharmaceuticals plc, dated March 20, 2015, between Jazz Pharmaceuticals plc and Essex Bidco Limited (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on March 23, 2015).
2.9	Agreement and Plan of Merger, dated as of May 27, 2016, by and among Jazz Pharmaceuticals plc, Plex Merger Sub, Inc., and Celator Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on May 31, 2016).
3.1	Amended and Restated Memorandum and Articles of Association of Jazz Pharmaceuticals plc, as amended on August 4, 2016 (incorporated herein by reference to Exhibit 3.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
4.1	Reference is made to Exhibit 3.1.
4.2A	Investor Rights Agreement, dated July 7, 2009, by and between Jazz Pharmaceuticals, Inc. and the other parties named therein (incorporated herein by reference to Exhibit 10.88 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on July 7, 2009).
4.2B	Assignment, Assumption and Amendment Agreement, dated as of January 18, 2012, by and among Jazz Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and the other parties named therein (incorporated herein by reference to Exhibit 4.7B in the Annual Report on Form 10-K (File No. 001-33500) for the year 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).
4.3A	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).
4.3B	Form of 1.875% Exchangeable Senior Note due 2021 (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).

4.4A	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. 001-033500), as filed with the SEC on August 23, 2017).
4.4B	Form of 1.50% Exchangeable Senior Note due 2024 (incorporated herein by reference to Exhibit 4.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on August 23, 2017).
10.1	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.
10.2+	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.
10.3+	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.
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1*	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

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+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for portions of this exhibit. Omitted portions have been filed separately with the SEC.

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

SIGNATURES

Pursuant to the requirements of 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: November 6, 2018

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)

Exhibit 10.1

SECOND AMENDMENT TO LEASE

THIS SECOND AMENDMENT TO LEASE (this "***Amendment***") is executed as of July 26, 2018 (the "***Effective Date***") by and between THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California ("***Landlord***"), and JAZZ PHARMACEUTICALS, INC., a Delaware corporation ("***Tenant***"), in the following factual context:

A. Landlord and Tenant are parties to that certain Lease dated as of January 7, 2015, as amended by that certain First Amendment to Lease dated January 29, 2018 (as amended, the "***Lease***"), pursuant to which Landlord leased to Tenant the building located on that certain real property commonly known as 3170 Porter Drive, Palo Alto, California. Capitalized terms used in this Amendment that are not otherwise defined herein shall have the meanings given such terms in the Lease.

B. Landlord and Tenant now desire to modify the Lease to memorialize the parties' agreement regarding the solar panel system that Landlord installed on the roof of the Building, and to further amend the Lease as provided in this Amendment.

NOW, THEREFORE, intending to be legally bound, the parties agree as follows:

1. Solar Panel System. The following provision is added as Section 9.10 to the Lease:

> "**9.10 Solar Panel System.** Landlord, at its sole expense, installed a solar panel system on the roof of the Building (and with the connections and other infrastructure relating thereto, collectively, the "***Solar Panel System***"). The Solar Panel System shall be considered a part of the Building Systems. Landlord shall be responsible for the repair, replacement and maintenance of the Solar Panel System as a part of the Building Systems in accordance with Section 9.1, and the cost of repair, replacement and maintenance of the Solar Panel System shall be included in Operating Expenses. Notwithstanding any contrary provision of this Lease, Landlord makes no representations or warranties whatsoever with respect to the condition of the Solar Panel System, including without limitation, the performance thereof or the capacity thereof."

2. Utility Costs. Section 9.4 of the Lease is hereby deleted in its entirety and replaced with the following:

> "**9.4 Utility Costs.** As of November 3 2017, Tenant assumed direct responsibility for the payment of all utility costs billed by the City, including the cost of all electric, gas, water, sewer and refuse services provided to the Property. Without limiting the foregoing, Tenant shall be responsible for the cost of all electricity not provided by the Solar Panel System. Tenant shall be entitled to the energy produced by the Solar Panel System, and shall have the right to take advantage of any programs offered by the City, if any, including the "Net Energy Metering" program. Landlord shall have no obligations with respect to any costs billed by the City to Tenant, or any City energy programs. Tenant shall also be responsible for arranging for hazardous waste collection, telephone and other electronic communications services at the Premises. Tenant shall pay, either through Operating Expenses or as a reimbursement to Landlord after invoicing, for the cost of any other utilities provided by Landlord. If Tenant is billed directly by Landlord for any Landlord-provided utilities, Tenant shall deliver payment to Landlord within thirty (30)

days after receipt of an invoice. Tenant shall provide monthly electricity and gas usage data for the Premises to Landlord for the period of time requested by Landlord (in electronic or paper format) or, at Landlord's option, provide any written authorization or other documentation required for Landlord to request information regarding Tenant's electricity and gas usage data with respect to the Premises directly from the City. Tenant acknowledges and consents to Landlord's use and disclosure of such information to the extent required to comply with Applicable Laws."

3. Base Rent. In consideration of Landlord's installation of the Solar Panel System, Landlord and Tenant hereby agree that as of March 1, 2018, the Base Rent initially payable by Tenant and identified in Article 1 of the Lease shall be increased to $5.55 per square foot of Rentable Area per calendar month, which shall be subject to an annual rent increase of three percent (3%) per year, in accordance with the terms and conditions of Section 6.1 of the Lease, as set forth on the attached Exhibit A. With the rent payment due on or before September 1, 2018 (the "***Rent True-up Date***"), Tenant shall make a true-up Base Rent payment in the amount of Twenty-Nine Thousand Five Hundred Eighty-Seven and 80/100s Dollars ($29,587.80), which is calculated as the difference between the Base Rent actually paid and the increased Base Rent between March 1, 2018 and the Rent True-up Date.

4. Access. The following provision is added to the end of Section 3.3:

Landlord and Tenant agree and acknowledge, as required by California Civil Code Section 1938, the following:

> "A Certified Access Specialist (CASp) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises."

Landlord and Tenant agree and acknowledge that Tenant shall be solely responsible for the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards identified by the CASp inspection.

5. Effect of Amendment. As amended by this Amendment, the Lease shall continue in full force and effect and in accordance with all of its terms. In the event of any conflict between the terms and conditions of the Lease and this Amendment, the terms and conditions of this Amendment shall prevail.

6. Governing Law. This Amendment shall be construed in accordance with and governed by the laws of the State of California.

7. Partial Invalidity. If any one or more of the provisions contained in this Amendment shall be invalid, illegal or unenforceable in any respect, the remaining provisions contained herein shall not be affected in any way thereby.

8. Counterparts. This Amendment may be executed in any number of counterparts, each of which shall be an original, but all of which, when taken together, shall constitute one and the same instrument. This Amendment may be executed and delivered by the exchange of facsimile, .pdf or other electronic image file copies of the executed counterpart signature pages, which shall be considered the equivalent of ink signature pages for all purposes.

[Signatures on following page]

IN WITNESS WHEREOF, the parties have executed this Second Amendment to Lease effective as of the Effective Date.

LANDLORD:
THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California

By: /s/ Desiree Trister

Name: Desiree Trister

Its: Director, Asset Management
Stanford Research Park

TENANT:
JAZZ PHARMACEUTICALS, INC., a Delaware corporation

By: /s/ Karen Wilson

Name: Karen Wilson

Its: SVP, Finance

Exhibit A

Base Rent Schedule

Period During Lease Term	Monthly Base Rent per sq. ft. of Rentable Area	Monthly Base Rent
10/15/2017 - 1/14/2018	$0.00 (due to free rent)	$0.00 (due to free rent)
1/15/2018 - 2/28/2018	$5.50	$542,443.00
3/1/2018-10/31/2018 ($0.05 per square foot increase begins)	$5.55	$547,374.30
11/1/2018 - 10/31/2019	$5.72	$563,795.53
11/1/2019 - 10/31/2020	$5.89	$580,709.39
11/1/2020 - 10/31/2021	$6.06	$598,130.68
11/1/2021 - 10/31/2022	$6.25	$616,074.60
11/1/2022 - 10/31/2023	$6.43	$634,556.83
11/1/2023 - 10/31/2024	$6.63	$653,593.54
11/1/2024 - 10/31/2025	$6.83	$673,201.35
11/1/2025 - 10/31/2026	$7.03	$693,397.39
11/1/2026 - 10/31/2027	$7.24	$714,199.31
11/1/2027 - 10/31/2028	$7.46	$735,625.29
11/1/2028 - 10/14/2029	$7.68	$757,694.05

Exhibit 10.2

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
2007 NON-EMPLOYEE DIRECTORS STOCK AWARD PLAN

NON-U.S. OPTION GRANT NOTICE

Jazz Pharmaceuticals plc (the "***Company***"), pursuant to its Amended and Restated 2007 Non-Employee Directors Stock Award Plan (the "***Plan***"), hereby grants to Optionholder an option to purchase the number of Ordinary Shares specified and on the terms set forth below. This option is subject to all of the terms and conditions as set forth in this Non-U.S. Option Grant Notice (the "***Grant Notice***") and in the Non-U.S. Option Agreement, including any country-specific Appendix (the "***Agreement***"), and the Plan, both of which are attached hereto and incorporated herein in their entirety.

Optionholder:	_____
Option #:	_____
Date of Grant:	_____
Vesting Commencement Date:	_____
Number of Ordinary Shares Subject to Option:	_____
Exercise Price (Per Ordinary Share):	_____
Total Exercise Price:	_____
Expiration Date:	_____

Type of Grant: Nonstatutory Stock Option

Vesting Schedule: Subject to Section 1 of the Agreement and any country-specific Appendix to the Agreement, this option will vest as follows: **[**_____**]**

Payment: By one or a combination of the following items (described in the Agreement):

☒ By cash or check
☒ Pursuant to a Regulation T Program if the Ordinary Shares are publicly traded
☐ By delivery of already-owned Ordinary Shares if the Ordinary Shares are publicly traded

Additional Terms/Acknowledgements: The undersigned Optionholder acknowledges receipt of, and understands and agrees to, this Grant Notice, the Agreement and the Plan. Optionholder further acknowledges that as of the Date of Grant, this Grant Notice, the Agreement and the Plan set forth the entire understanding between Optionholder and the Company regarding the acquisition of Ordinary Shares and supersede all prior oral and written agreements, promises and/or representations on that subject with the exception of (i) options previously granted and delivered to Optionholder under the Plan, (ii) any other specific written agreement between Optionholder and the Company

and (iii) any compensation recovery policy that is adopted by the Company or is otherwise required by applicable law. By accepting this option, Optionholder consents to receive Plan documents by electronic delivery and to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.

JAZZ PHARMACEUTICALS PLC	**OPTIONHOLDER**
By: _____	_____
Signature	Signature
Title: _____	
Date: _____	Date: _____

ATTACHMENTS: Non-U.S. Option Agreement and Amended and Restated 2007 Non-Employee Directors Stock Award Plan

* * * * *

Based on the form of Non-U.S. Option Grant Notice for the Amended and Restated 2007 Non-Employee Directors Stock Option Plan as approved by the Board of Directors of Jazz Pharmaceuticals plc on August 1, 2013.

ATTACHMENT I

NON-U.S. OPTION AGREEMENT

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
2007 NON-EMPLOYEE DIRECTORS STOCK AWARD PLAN

NON-U.S. OPTION AGREEMENT
(NONSTATUTORY STOCK OPTION)

Pursuant to your Non-U.S. Option Grant Notice (the "***Grant Notice***") and this Non-U.S. Option Agreement, including any country-specific Appendix (the "***Agreement***"), Jazz Pharmaceuticals plc (the "***Company***") has granted you an option under its Amended and Restated 2007 Non-Employee Directors Stock Award Plan (the "***Plan***") to purchase the number of Ordinary Shares indicated in your Grant Notice at the exercise price indicated in your Grant Notice. The option is granted to you effective as of the date of grant set forth in the Grant Notice (the "***Date of Grant***"). Except as otherwise explicitly provided in the Grant Notice or this Agreement, in the event of any conflict between the terms in the Grant Notice or this Agreement and the Plan, the terms of the Plan shall control. Capitalized terms not explicitly defined in the Grant Notice or this Agreement but defined in the Plan shall have the same definitions as in the Plan.

The details of your option, in addition to those set forth in the Grant Notice and the Plan, are as follows:

1. VESTING. Subject to Section 9 and the limitations contained herein, your option will vest as provided in your Grant Notice, provided that vesting will cease upon the termination of your Continuous Service.

Notwithstanding the foregoing, if you do not stand for reelection at an annual general meeting of the Company's shareholders (an "***Annual Meeting***") in the year in which your term expires or you otherwise resign effective at an Annual Meeting, and, in either case, your Continuous Service terminates at such Annual Meeting, then effective as of the date of such Annual Meeting, the unvested portion, if any, of your option shall become vested and exercisable with respect to the portion of your option that would have vested through the anniversary of the Vesting Commencement Date (as set forth in the Grant Notice) in the year of such Annual Meeting.

2. NUMBER OF SHARES AND EXERCISE PRICE. The number of Ordinary Shares subject to your option and your exercise price per Ordinary Share referenced in your Grant Notice may be adjusted from time to time for Capitalization Adjustments.

3. METHOD OF PAYMENT. You must pay the full amount of the exercise price for the Ordinary Shares you wish to exercise. You may pay the exercise price in cash or by check

(subject to Section 4) or in any other manner ***permitted by your Grant Notice,*** which may include one or more of the following:

(a) Provided that at the time of exercise the Ordinary Shares are publicly traded, pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of Ordinary Shares, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds. This manner of payment is also known as a "broker-assisted exercise," "same day sale," or "sell to cover."

(b) Provided that at the time of exercise the Ordinary Shares are publicly traded, by delivery to the Company (either by actual delivery or attestation) of already-owned Ordinary Shares that are owned free and clear of any liens, claims, encumbrances or security interests, and that are valued at Fair Market Value on the date of exercise. "Delivery" for these purposes, in the sole discretion of the Company at the time you exercise your option, will include delivery to the Company of your attestation of ownership of such Ordinary Shares in a form approved by the Company. You may not exercise your option by delivery to the Company of Ordinary Shares if doing so would violate the provisions of any law, regulation or agreement applicable to the, or restricting the redemption of, the Ordinary Shares.

4. PAYMENT OF PAR (NOMINAL) VALUE. To the extent that any Ordinary Shares issued upon exercise of your option are newly issued Ordinary Shares, you must pay in cash or by check an amount equal to the par value of such number of newly issued Ordinary Shares (rounded up to the nearest whole cent).

5. WHOLE SHARES. You may exercise your option only for whole Ordinary Shares.

6. SECURITIES LAW COMPLIANCE. Notwithstanding anything to the contrary contained herein, you may not exercise your option unless the Ordinary Shares issuable upon such exercise are then registered under the Securities Act or, if such Ordinary Shares are not then so registered, the Company has determined that such exercise and issuance would be exempt from the registration requirements of the Securities Act. The exercise of your option also must comply with other applicable laws and regulations governing your option, and you may not exercise your option if the Company determines that such exercise would not be in material compliance with such laws and regulations. The Company shall have no liability to you should your option expire unexercised as a result of the Company's determination that the exercise of your option does not comply with the applicable laws and regulations governing the option or that the exercise is not in material compliance with such laws and regulations.

7. TERM. You may not exercise your option before the commencement or after the expiration of its term. The term of your option commences on the Date of Grant and expires, subject to the provisions of Section 5(i) of the Plan, upon the earliest of the following:

(a) three (3) months after the termination of your Continuous Service for any reason other than your Disability or death or upon a Change in Control (except as otherwise provided in Section 7(c) below); *provided, however,* that if during any part of such three (3) month period

your option is not exercisable solely because of the condition set forth in the section above relating to "Securities Law Compliance," your option will not expire until the earlier of the Expiration Date or until it has been exercisable for an aggregate period of three (3) months after the termination of your Continuous Service;

(b) twelve (12) months after the termination of your Continuous Service due to your Disability (except as otherwise provided in Section 7(c) below);

(c) eighteen (18) months after your death if you die either during your Continuous Service or within three (3) months after your Continuous Service terminates for any reason other than death;

(d) twelve (12) months after the effective date of a Change in Control if your Continuous Service terminates as of, or within twelve (12) months following the Change in Control (except as otherwise provided in Section 7(c) above);

(e) the Expiration Date indicated in your Grant Notice; or

(f) the day before the tenth (10th) anniversary of the Date of Grant.

8. EXERCISE.

(a) You may exercise the vested portion of your option during its term by (i) delivering a Notice of Exercise (in a form designated by the Company) or completing such other documents and/or procedures designated by the Company for exercise and (ii) paying the exercise price and any applicable Tax-Related Items (defined below) to the Company's Secretary, stock plan administrator, or such other person as the Company may designate, together with such additional documents as the Company may then require.

(b) By exercising your option you agree that, as a condition to any exercise of your option, the Company may require you to enter into an arrangement providing for the payment by you to the Company of any Tax-Related Items arising by reason of (i) the exercise of your option or (ii) the disposition of Ordinary Shares acquired upon such exercise.

9. CHANGE IN CONTROL. If you are either (i) required to resign your position as a Non-Employee Director as a condition of a Change in Control, or (ii) removed from your position as a Non-Employee Director in connection with a Change in Control, your option shall become fully vested and exercisable immediately prior to the effectiveness of such resignation or removal (and contingent upon the effectiveness of such Change in Control).

10. TRANSFERABILITY. Your option is not transferable, except by will or by the laws of descent and distribution, and is exercisable during your life only by you.

11. OPTION NOT A SERVICE CONTRACT. Your option is not an employment or service contract, and nothing in your option shall be deemed to create in any way whatsoever any obligation on your part to continue providing services to the Company or an Affiliate, or of the Company or an Affiliate to continue your services and shall not in any way restrict the Company

or an Affiliate to terminate your Continuous Service. In addition, nothing in your option shall obligate the Company or an Affiliate, their respective shareholders, Boards of Directors, Officers or Employees to continue any relationship that you might have as a Director or Consultant for the Company or an Affiliate.

12. TAX WITHHOLDING OBLIGATIONS.

You acknowledge that, regardless of any action taken by the Company or, if different, your employer, if your employer is an Affiliate of the Company (the "***Employer***"), the ultimate liability for all income tax, social insurance, payroll tax, fringe benefits tax, payment on account or other tax-related items related to your participation in the Plan and legally applicable to you ("***Tax-Related Items***"), is and remains your responsibility and may exceed the amount actually withheld by the Company or the Employer. You further acknowledge that the Company and/or the Employer (i) make no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of the option, including, but not limited to, the grant, vesting or exercise of the option, the subsequent sale of Ordinary Shares acquired pursuant to such exercise and the receipt of any dividends; and (ii) do not commit to and are under no obligation to structure the terms of the grant or any aspect of the option to reduce or eliminate your liability for Tax-Related Items or achieve any particular tax result. Further, if you are subject to Tax-Related Items in more than one jurisdiction between the Date of Grant and the date of any relevant taxable or tax withholding event, as applicable, you acknowledge that the Company and/or the Employer (or former employer, as applicable) may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

Prior to the relevant taxable or tax withholding event, as applicable, you agree to make adequate arrangements satisfactory to the Company and/or the Employer to satisfy all Tax-Related Items.

In this regard, you authorize the Company and/or the Employer, or their respective agents, at their discretion, to satisfy the obligations with regard to all Tax-Related Items by (i) withholding from proceeds of the sale of Ordinary Shares acquired at exercise of the option either through a voluntary sale or through a mandatory sale arranged by the Company (on your behalf pursuant to this authorization) without further consent or (ii) withholding from any cash compensation paid to you by the Company and/or the Employer.

Depending on the withholding method, the Company may withhold or account for Tax-Related Items by considering applicable minimum statutory withholding amounts or other applicable withholding rates, including maximum applicable rates, in which case you will receive a refund of any over-withheld amount in cash and will have no entitlement to the Ordinary Share equivalent.

Finally, you agree to pay to the Company or the Employer any amount of Tax-Related Items that the Company or the Employer may be required to withhold or account for as a result of your participation in the Plan that cannot be satisfied by the means previously described. The Company may refuse to issue or deliver the Ordinary Shares or the proceeds of the sale of Ordinary Shares, if you fail to comply with your obligations in connection with the Tax-Related Items.

13. NATURE OF GRANT. In accepting the option, you acknowledge, understand and agree that:

(a) the Plan is established voluntarily by the Company, it is discretionary in nature, and may be amended, suspended or terminated by the Company at any time, to the extent permitted by the Plan;

(b) the grant of the option is voluntary and occasional and does not create any contractual or other right to receive future grants of options, or benefits in lieu of options, even if options have been granted in the past;

(c) all decisions with respect to future option or other grants, if any, will be at the sole discretion of the Company;

(d) you are voluntarily participating in the Plan;

(e) the future value of the Ordinary Shares underlying the option is unknown, indeterminable, and cannot be predicted with certainty;

(f) if the underlying Ordinary Shares do not increase in value, the option will have no value;

(g) if you exercise the option and acquire Ordinary Shares, the value of such Ordinary Shares may increase or decrease in value, even below the exercise price;

(h) no claim or entitlement to compensation or damages shall arise from forfeiture of the option resulting from the termination of your Continuous Service; and

(i) neither the Company nor any Affiliate shall be liable for any foreign exchange rate fluctuation between your local currency and the United States Dollar that may affect the value of the option or of any amounts due to you pursuant to the exercise of the option or the subsequent sale of any Ordinary Shares acquired upon exercise.

14. NO ADVICE REGARDING GRANT. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding your participation in the Plan, or your acquisition or sale of the underlying Ordinary Shares. You should consult with your own personal tax, legal and financial advisors regarding your participation in the Plan before taking any action related to the Plan.

15. DATA PRIVACY. The Company and any Affiliate may collect, use, process, transfer or disclose your Personal Information for the purpose of implementing, administering and managing your participation in the Plan, in accordance with the Company's privacy practices. For example, your Personal Information will be transferred to the Company's stock administration team located in the United States and may be directly or indirectly transferred to E*TRADE or any other third party stock plan service provider as may be selected by the Company, and any other third parties assisting the Company with the implementation, administration and management of the Plan.

For more information on the Company's privacy practices, log in to your E*TRADE account to view a copy of the Jazz Pharmaceuticals Privacy Notice.

16. GOVERNING LAW AND VENUE. The option grant and the provisions of this Agreement are governed by, and subject to, the laws of the State of Delaware, without regard to its conflict of law provisions.

For purposes of any action, lawsuit or other proceedings brought to enforce this Agreement, relating to it, or arising from it, the parties hereby submit to and consent to the sole and exclusive jurisdiction of the courts of Santa Clara County, California, or the federal courts for the United States for the Northern District of California, and no other courts, where this grant is made and/or to be performed.

17. LANGUAGE. If you have received this Agreement, or any other document related to the option and/or the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

18. SEVERABILITY. The provisions of this Agreement are severable and if any one or more provisions are determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

19. APPENDIX. Notwithstanding any provisions in this Agreement, the option grant shall be subject to any special terms and conditions set forth in any Appendix to this Agreement for your country. Moreover, if you relocate to one of the countries included in the Appendix, the special terms and conditions for such country will apply to you, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. The Appendix constitutes part of this Agreement.

20. NOTICES; ELECTRONIC DELIVERY. Any notices provided for in your option or the Plan will be given in writing (including electronically) and will be deemed effectively given upon receipt or, in the case of notices delivered by mail by the Company to you, fourteen (14) days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company. The Company may, in its sole discretion, decide to deliver any documents related to participation in the Plan and this option by electronic means or to request your consent to participate in the Plan by electronic means. By accepting this option, you consent to receive such documents by electronic delivery and to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.

21. GOVERNING PLAN DOCUMENT. Your option is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your option, and is further subject to all interpretations, amendments, rules and regulations, which may from time to time be promulgated and adopted pursuant to the Plan. Except as otherwise explicitly provided herein, in the event of any conflict between the provisions of your option and those of the Plan, the provisions of the Plan shall control.

22. AMENDMENT. Notwithstanding anything in the Plan to the contrary, the Board reserves the right to change, by written notice to you, the provisions of this Agreement in any way it may deem necessary or advisable for legal or administrative reasons, and to require you to sign any additional agreements or undertakings that may be necessary to accomplish the foregoing.

23. IMPOSITION OF OTHER REQUIREMENTS. The Company reserves the right to impose other requirements on your participation in the Plan, on the option and on any Ordinary Shares purchased upon exercise of the option, to the extent the Company determines it is necessary or advisable for legal or administrative reasons, and to require you to sign any additional agreements or undertakings that may be necessary to accomplish the foregoing.

24. WAIVER. You acknowledge that a waiver by the Company of breach of any provision of this Agreement shall not operate or be construed as a waiver of any other provision of this Agreement, or of any subsequent breach by you or any other Optionholder.

25. INSIDER TRADING / MARKET ABUSE LAWS. You may be subject to insider trading restrictions and/or market abuse laws based on the exchange on which the Ordinary Shares are listed and in applicable jurisdictions including the United States and your country or your broker's country, if different, which may affect your ability to accept, acquire, sell or otherwise dispose of Ordinary Shares, rights to Ordinary Shares (e.g., options) or rights linked to the value of Ordinary Shares under the Plan during such times as you are considered to have "inside information" regarding the Company (as defined by the laws in the applicable jurisdictions). Local insider trading laws and regulations may prohibit the cancellation or amendment of orders you placed before you possessed inside information. Furthermore, you could be prohibited from (a) disclosing the inside information to any third party and (b) "tipping" third parties or causing them otherwise to buy or sell securities (third parties include fellow directors). Any restrictions under these laws or regulations are separate from and in addition to any restrictions that may be imposed under the Company's insider trading policy as may be in effect from time to time. You acknowledge that it is your responsibility to comply with any applicable restrictions, and you should speak to your personal advisor on this matter.

26. FOREIGN ASSET/ACCOUNT, EXCHANGE CONTROL AND TAX REPORTING. You may be subject to foreign asset/account, exchange control and/or tax reporting requirements as a result of the acquisition, holding and/or transfer of Ordinary Shares or cash (including dividends and the proceeds arising from the sale of Ordinary Shares) derived from your participation in the Plan, to and/or from a brokerage/bank account or legal entity located outside your country. The applicable laws of your country may require that you report such accounts, assets, the balances therein, the value thereof and/or the transactions related thereto to the applicable authorities in such country. You acknowledge that you are responsible for ensuring compliance with any applicable foreign asset/account, exchange control and tax reporting requirements and should consult your personal legal advisor on this matter.

27. REPORTING OBLIGATION. If you are a director, shadow director or secretary of the Company or an Irish Affiliate, you must notify the Company or the Irish Affiliate in writing if you receive or dispose of an interest exceeding 1% of the Company (e.g., options, Ordinary Shares), or become aware of the event giving rise to the notification requirement, or if you become

a director or secretary if such an interest exceeding 1% of the Company exists at the time. This notification requirement also applies with respect to the interests of a spouse or minor children (whose interests will be attributed to the director, shadow director or secretary, as applicable).

* * * * *

By signing the Non-U.S. Option Grant Notice to which this Non-U.S. Option Agreement is attached, you shall be deemed to have signed and agreed to the terms and conditions of this Non-U.S. Option Agreement.

* * * * *

Based on the form of Non-U.S. Option Agreement for the Amended and Restated 2007 Non-Employee Directors Stock Option Plan as approved by the Board of Directors of Jazz Pharmaceuticals plc on 2 August 2018.

APPENDIX
TO THE
NON-U.S. OPTION AGREEMENT

TERMS AND CONDITIONS

This Appendix contains additional terms and conditions that govern the option granted under the Plan to you if you reside and/or work in one of the countries listed below. Certain capitalized terms used but not defined in this Appendix have the meanings set forth in the Plan, the Grant Notice and/or the Agreement.

If you are a citizen or resident of a country other than the one in which you are currently working, transfer employment after the option is granted, or are considered a resident of another country for local law purposes, the information contained herein may not be applicable to you and the Company shall, in its discretion, determine to what extent the terms and conditions contained herein shall apply to you.

NOTIFICATIONS

This Appendix contains information regarding exchange controls and certain other issues of which you should be aware with respect to participation in the Plan. The information is based on the securities, exchange control and other laws in effect in the respective countries as of June 2018. Such laws are often complex and change frequently. As a result, the Company strongly recommends that you not rely on the information in this Appendix as the only source of information relating to the consequences of your participation in the Plan because the information may be out of date at the time you exercise the option or sell Ordinary Shares acquired pursuant thereto.

The information contained herein is general in nature and may not apply to your particular situation, and the Company is not in a position to assure you of a particular result. Accordingly, you are advised to seek appropriate professional advice as to how the relevant laws in your country may apply to your situation.

IRELAND

There are no country-specific provisions.

SWITZERLAND

NOTIFICATIONS

Securities Law Notification. The grant of the options and the issuance of any Ordinary Shares is not intended to be a public offering in Switzerland. Neither this document nor any other materials relating to the options constitute a prospectus as such term is understood pursuant to article 652a of the Swiss Code of Obligations, and neither this document nor any other materials relating to the options may be publicly distributed nor otherwise made publicly available in Switzerland. Finally, neither this document nor any other offering or marketing material relating to the options have been

or will be filed with, or approved or supervised by, any Swiss regulatory authority (in particular, the Swiss Financial Market Supervisory Authority (FINMA)).

UNITED KINGDOM

There are no country-specific provisions.

Attachment II

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
2007 NON-EMPLOYEE DIRECTORS STOCK AWARD PLAN

Exhibit 10.3

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
2007 NON-EMPLOYEE DIRECTORS STOCK AWARD PLAN

NON-U.S. RESTRICTED STOCK UNIT AWARD GRANT NOTICE

Jazz Pharmaceuticals plc (the "***Company***"), pursuant to its Amended and Restated 2007 Non-Employee Directors Stock Award Plan (the "***Plan***"), hereby awards to Participant the number of restricted stock units ("***RSUs***") specified and on the terms set forth below (the "***Award***"). The Award is subject to all of the terms and conditions as set forth in this Non-U.S. Restricted Stock Unit Award Grant Notice (the "***Grant Notice***") and in the Non-U.S. Restricted Stock Unit Award Agreement, including any country-specific Appendix (the "***Agreement***"), and the Plan, both of which are attached hereto and incorporated herein in their entirety.

Participant:	_____
RSU #:	_____
Date of Grant:	_____
Vesting Commencement Date:	_____
Number of RSUs Subject to Award:	_____
Consideration:	Participant's Services (payment of par value of newly issued shares)

Vesting Schedule: Subject to Section 3 of the Agreement and any country-specific Appendix to the Agreement, the Award will vest as follows: [_____]

Issuance Schedule: One Ordinary Share will be issuable for each RSU which vests at the time set forth in Section 4 of the Agreement.

Additional Terms/Acknowledgements: The undersigned Participant acknowledges receipt of, and understands and agrees to, this Grant Notice, the Agreement and the Plan. Participant further acknowledges that as of the Date of Grant, this Grant Notice, the Agreement and the Plan set forth the entire understanding between Participant and the Company regarding the Award and supersede all prior oral and written agreements on that subject, with the exception of: (i) any written agreement between Participant and the Company that would provide for vesting acceleration of the Award upon the terms and conditions set forth therein and (ii) any compensation recovery policy that is adopted by the Company or is otherwise required by applicable law. By accepting this Award, Participant consents to receive Plan documents by electronic delivery and to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.

JAZZ PHARMACEUTICALS PLC

By: _____
Signature

Title: _____

Date: _____

PARTICIPANT

_____
Signature

Date: _____

ATTACHMENTS: Non-U.S. Restricted Stock Unit Award Agreement, Amended and Restated 2007 Non-Employee Directors Stock Award Plan

* * * * *

Based on the form of Non-U.S. Restricted Stock Unit Award Grant Notice for the Amended and Restated 2007 Non-Employee Directors Stock Award Plan as approved by the Board of Directors of Jazz Pharmaceuticals plc on 3 November 2016.

ATTACHMENT I

NON-U.S. RESTRICTED STOCK UNIT AWARD AGREEMENT

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
2007 NON-EMPLOYEE DIRECTORS STOCK AWARD PLAN

NON-U.S. RESTRICTED STOCK UNIT AWARD AGREEMENT

Pursuant to your Non-U.S. Restricted Stock Unit Award Grant Notice (the "***Grant Notice***") and this Non-U.S. Restricted Stock Unit Award Agreement, including any country-specific Appendix (the "***Agreement***"), and in consideration of your services, Jazz Pharmaceuticals plc (the "***Company***") has awarded you a Restricted Stock Unit Award (the "***Award***") under its Amended and Restated 2007 Non-Employee Directors Stock Award Plan (the "***Plan***") for the number of restricted stock units (the "***RSUs***") indicated in your Grant Notice. The Award is granted to you effective as of the date of grant set forth in the Grant Notice (the "***Date of Grant***"). Except as otherwise explicitly provided in the Grant Notice or this Agreement, in the event of any conflict between the terms in the Grant Notice or this Agreement and the Plan, the terms of the Plan shall control. Capitalized terms not explicitly defined in the Grant Notice or this Agreement but defined in the Plan shall have the same definitions as in the Plan.

The details of your Award, in addition to those set forth in the Grant Notice and the Plan, are as follows.

1. GRANT OF THE AWARD. This Award represents your right to be issued on a future date the number of Ordinary Shares that is equal to the number of RSUs indicated in the Grant Notice. As of the Date of Grant, the Company will credit to a bookkeeping account maintained by the Company for your benefit (the "***Account***") the number of RSUs subject to the Award. This Award was granted in consideration of your services to the Company. Except as otherwise provided herein, you will not be required to make any payment to the Company (other than past and future services to the Company) with respect to your receipt of the Award, the vesting of the RSUs or the delivery of the Ordinary Shares to be issued in respect of the Award; *provided, however*, that to the extent that any Ordinary Shares issued upon settlement of your Award are newly issued Ordinary Shares, a payment must be received by the Company of an amount equal to the par value of such number of newly issued Ordinary Shares (rounded up to the nearest whole cent) in cash, by check, bank draft or money order payable to the Company.

2. NUMBER OF RSUS AND ORDINARY SHARES.

(a) The number of RSUs subject to your Award may be adjusted from time to time for Capitalization Adjustments, as provided in the Plan.

(b) Any additional RSUs that become subject to the Award pursuant to this Section 2 shall be subject, in a manner determined by the Board, to the same forfeiture restrictions,

restrictions on transferability, and time and manner of delivery as applicable to the other RSUs covered by your Award.

(c) Notwithstanding the provisions of this Section 2, no fractional Ordinary Shares or rights for fractional Ordinary Shares shall be created pursuant to this Section 2. The Board shall, in its discretion, determine an equivalent benefit for any fractional Ordinary Shares or fractional Ordinary Shares that might be created by the adjustments referred to in this Section 2.

3. VESTING. Subject to Section 12 and the limitations contained herein, your Award will vest, if at all, in accordance with the vesting schedule provided in the Grant Notice, provided that vesting will cease upon the termination of your Continuous Service. Upon such termination of your Continuous Service, the RSUs credited to the Account that were not vested on the date of such termination will be forfeited at no cost to the Company and you will have no further right, title or interest in such RSUs or the Ordinary Shares to be issued in respect of such portion of the Award.

4. DATE OF ISSUANCE.

(a) To the extent your Award is exempt from application of Section 409A of the Code and any state or foreign law of similar effect (collectively "***Section 409A***"), the Company will deliver to you a number of Ordinary Shares equal to the number of vested RSUs subject to your Award, including any additional RSUs received pursuant to Section 2 above that relate to those vested RSUs on the applicable vesting date(s). However, if a scheduled delivery date falls on a date that is not a U.S. business day, such delivery date shall instead fall on the next following U.S. business day. Notwithstanding the foregoing, in the event that (i) you are subject to the Company's Policy Regarding Stock Trading by Executive Officers, Directors and Other Designated Employees (or any successor policy) (the "***Policy***"), the Company's Policy Against Trading on the Basis of Inside Information, or you are otherwise prohibited from selling Ordinary Shares in the open market and any Ordinary Shares covered by your Award are scheduled to be delivered on a day (the "***Original Distribution Date***") that does not occur during an open "window period" applicable to you or a day on which you are permitted to sell Ordinary Shares pursuant to a written plan that meets the requirements of Rule 10b5-1 under the Exchange Act, as determined by the Company in accordance with the Policy, or does not occur on a date when you are otherwise permitted to sell Ordinary Shares in the open market, and (ii) the Company elects not to satisfy any Tax-Related Items (defined below) by withholding Ordinary Shares from your distribution, then such Ordinary Shares shall not be delivered on such Original Distribution Date and shall instead be delivered on the first U.S. business day of the next occurring open "window period" applicable to you pursuant to the Policy (regardless of whether you are still providing Continuous Service at such time) or the next U.S. business day when you are not prohibited from selling Ordinary Shares in the open market, but in no event later than the fifteenth (15th) day of the third calendar month of the calendar year following the calendar year in which the Ordinary Shares covered by the Award vest. Delivery of the Ordinary Shares pursuant to the provisions of this Section 4(a) is intended to comply with the requirements for the short-term deferral exemption available under Treasury Regulations Section 1.409A-1(b)(4) and shall be construed and administered in such manner. The form of such delivery of the Ordinary Shares (*e.g.*, a share certificate or electronic entry evidencing such Ordinary Shares) shall be determined by the Company.

(b) The provisions of this Section 4(b) are intended to apply to the extent you are a U.S. taxpayer and your Award is subject to Section 409A because of the terms of a severance

arrangement or other agreement between you and the Company, if any, that provide for acceleration of vesting of your Award upon your termination or separation from service (as such term is defined in Section 409A(a)(2)(A)(i) of the Code (and without regard to any alternative definition thereunder)) ("***Separation from Service***") and such severance benefit does not satisfy the requirements for an exemption from application of Section 409A provided under Treasury Regulations Section 1.409A-1(b)(4) or 1.409A-1(b)(9) ("***Non-Exempt Severance Arrangement***"). If you are not a U.S. taxpayer, this Section 4(b) shall not apply to you. To the extent your Award is subject to and not exempt from application of Section 409A due to application of a Non-Exempt Severance Arrangement, the following provisions in this Section 4(b) shall supersede anything to the contrary in Section 4(a).

(i) If your Award vests in the ordinary course during your Continuous Service in accordance with the vesting schedule set forth in the Grant Notice, without accelerating vesting under the terms of a Non-Exempt Severance Arrangement, in no event will the Ordinary Shares be issued in respect of your Award any later than the later of: (A) December 31st of the calendar year that includes the applicable vesting date and (B) the 60th day that follows the applicable vesting date.

(ii) If vesting of your Award accelerates under the terms of a Non-Exempt Severance Arrangement in connection with your Separation from Service, and such vesting acceleration provisions were in effect as of the Date of Grant of your Award and, therefore, are part of the terms of your Award as of the Date of Grant, then the Ordinary Shares will be earlier issued in respect of your Award upon your Separation from Service in accordance with the terms of the Non-Exempt Severance Arrangement, but in no event later than the 60th day that follows the date of your Separation from Service. However, if at the time the Ordinary Shares would otherwise be issued you are subject to the distribution limitations contained in Section 409A applicable to "specified employees," as defined in Section 409A(a)(2)(B)(i) of the Code, such Ordinary Shares shall not be issued before the date that is six (6) months following the date of your Separation from Service, or, if earlier, the date of your death that occurs within such six (6) month period.

(iii) If vesting of your Award accelerates under the terms of a Non-Exempt Severance Arrangement in connection with your Separation from Service, and such vesting acceleration provisions were not in effect as of the Date of Grant of the Award and, therefore, are not a part of the terms of your Award on the Date of Grant, then such acceleration of vesting of your Award shall not accelerate the issuance date of the Ordinary Shares, but the Ordinary Shares shall instead be issued on the same schedule as set forth in the Grant Notice as if they had vested in the ordinary course during your Continuous Service, notwithstanding the vesting acceleration of the Award. Such issuance schedule is intended to satisfy the requirements of payment on a specified date or pursuant to a fixed schedule, as provided under Treasury Regulations Section 1.409A-3(a)(4).

(c) If you are a U.S. taxpayer and your Award is subject to and not exempt from Section 409A (a "***Non-Exempt Award***"), then the provisions in this Section 4(c) shall apply and supersede anything to the contrary that may be set forth in the Plan, the Grant Notice or in any other section of this Agreement with respect to the permitted treatment of your Non-Exempt Award:

(i) Any exercise by the Board of discretion to accelerate the vesting of your Non-Exempt Award shall not result in any acceleration of the scheduled issuance dates for the

Ordinary Shares in respect of the Non-Exempt Award unless earlier issuance of the Ordinary Shares upon the applicable vesting dates would be in compliance with the requirements of Section 409A.

(ii) The Company explicitly reserves the right to (A) earlier settle your Non-Exempt Award to the extent permitted and in compliance with the requirements of Section 409A, including pursuant to any of the exemptions available in Treasury Regulations Section 1.409A-3(j)(4)(ix) and (B) provide that you will receive a cash settlement equal to the Fair Market Value of the Ordinary Shares that would otherwise be issued to you, if applicable and in compliance with the requirements of Section 409A.

(iii) To the extent the terms of your Non-Exempt Award provide that it will be settled upon a Change in Control or Corporate Transaction, to the extent it is required for compliance with the requirements of Section 409A, the Change in Control or Corporate Transaction event triggering settlement must also constitute a change in the ownership or effective control of the Company, or in the ownership of a substantial portion of the Company's assets, Section 409A(a)(2)(A)(v) of the Code and Treasury Regulations Section 1.409A-3(i)(5) (a "***409A Change of Control***"). To the extent the terms of your Non-Exempt Award provide that it will be settled upon a termination of employment or termination of Continuous Service, to the extent it is required for compliance with the requirements of Section 409A, the termination event triggering settlement must also constitute a Separation from Service. However, if at the time the Ordinary Shares would otherwise be issued to you in connection with your Separation from Service, you are subject to the distribution limitations contained in Section 409A applicable to "specified employees," as defined in Section 409A(a)(2)(B)(i) of the Code, such Ordinary Shares shall not be issued before the date that is six (6) months following the date of your Separation from Service, or, if earlier, the date of your death that occurs within such six (6) month period.

(iv) The provisions in this Agreement for delivery of the Ordinary Shares in respect of the Non-Exempt Award are intended to comply with the requirements of Section 409A so that the delivery of the Ordinary Shares to you in respect of your Non-Exempt Award will not trigger the additional tax imposed under Section 409A, and any ambiguities herein will be so interpreted.

5. DIVIDENDS. You shall receive no benefit or adjustment to your Award with respect to any cash dividend, share dividend or other distribution that does not result from a Capitalization Adjustment as provided in the Plan; *provided, however*, that this sentence shall not apply with respect to any Ordinary Shares that are delivered to you in connection with your Award after such Ordinary Shares have been delivered to you.

6. SECURITIES LAW COMPLIANCE. You may not be issued any Ordinary Shares in respect of your Award unless either (i) the Ordinary Shares are registered under the Securities Act; or (ii) the Company has determined that such issuance would be exempt from the registration requirements of the Securities Act. Your Award also must comply with other applicable laws and regulations governing the Award, and you will not receive such Ordinary Shares if the Company determines that such receipt would not be in material compliance with such laws and regulations. The Company shall not be liable if Ordinary Shares cannot be issued to you as a consequence of the Company's determination that the issuance of Ordinary Shares does not comply with applicable laws and regulations governing the Award.

7. RESTRICTIVE LEGENDS. The Ordinary Shares issued in respect of your Award shall be endorsed with appropriate legends determined by the Company.

8. TRANSFER RESTRICTIONS. Your Award is not transferable, except by will or by the laws of descent and distribution. In addition to any other limitation on transfer created by applicable securities laws, you agree not to assign, hypothecate, donate, encumber or otherwise dispose of any interest in any of the Ordinary Shares subject to the Award until the Ordinary Shares are issued to you in accordance with Section 4 of this Agreement. After the Ordinary Shares have been issued to you, you are free to assign, hypothecate, donate, encumber or otherwise dispose of any interest in such Ordinary Shares provided that any such actions are in compliance with the provisions herein (including the country-specific Appendix hereto) and applicable securities laws.

9. AWARD NOT A SERVICE CONTRACT.

(a) Nothing in this Agreement (including, but not limited to, the vesting of your Award pursuant to the schedule set forth in Section 3 herein or the issuance of the Ordinary Shares in respect of your Award), the Plan or any covenant of good faith and fair dealing that may be found implicit in this Agreement or the Plan shall: (i) confer upon you any right to continue in the service of, or affiliation with, the Company or an Affiliate; (ii) constitute any promise or commitment by the Company or an Affiliate regarding the fact or nature of future positions, future work assignments, future compensation or any other term or condition of service or affiliation; (iii) confer any right or benefit under this Agreement or the Plan unless such right or benefit has specifically accrued under the terms of this Agreement or Plan; or (iv) deprive the Company or its Affiliates, as applicable, of the right to terminate your service without regard to any future vesting opportunity that you may have.

(b) By accepting this Award, you acknowledge and agree that the right to continue vesting in the Award pursuant to the schedule set forth in Section 3 is earned only by providing Continuous Service (not through the act of being elected to the Board, being granted this Award or any other award or benefit) and that the Company has the right to reorganize, sell, spin-out or otherwise restructure one or more of its businesses or Affiliates at any time or from time to time, as it deems appropriate (a "reorganization"). You further acknowledge and agree that such a reorganization could result in the termination of your Continuous Service and the loss of benefits available to you under this Agreement, including but not limited to, the termination of the right to continue vesting in the Award. You further acknowledge and agree that this Agreement, the Plan, the transactions contemplated hereunder and the vesting schedule set forth herein or any covenant of good faith and fair dealing that may be found implicit in any of them do not constitute an express or implied promise of continued engagement as a Non-Employee Director for the term of this Agreement, for any period, or at all, and shall not interfere in any way with your right or the right of the Company or its Affiliate, as applicable, to terminate your Continuous Service at any time.

10. UNSECURED OBLIGATION. Your Award is unfunded, and as a holder of a vested Award, you shall be considered an unsecured creditor of the Company with respect to the Company's obligation, if any, to issue Ordinary Shares pursuant to this Agreement. You shall not have voting or any other rights as a shareholder of the Company with respect to the Ordinary Shares to be issued pursuant to this Agreement until such Ordinary Shares are issued to you pursuant to Section 4 of this Agreement. Upon such issuance, you will obtain full voting and other rights as a shareholder of the Company. Nothing contained in this Agreement, and no action taken pursuant

to its provisions, shall create or be construed to create a trust of any kind or a fiduciary relationship between you and the Company or any other person.

11. TAX WITHHOLDING OBLIGATIONS.

(a) On or before the time you receive a distribution of the Ordinary Shares subject to your Award, or at any time thereafter as requested by the Company, you hereby authorize the Company to withhold from the Ordinary Shares issuable to you an amount sufficient to satisfy any income tax, social insurance, payroll tax, fringe benefits tax, payment on account or other tax-related items which arise in connection with your Award ("***Tax-Related Items***"), where the Fair Market Value of the Ordinary Shares is measured as of the date the Ordinary Shares are issued pursuant to Section 4. Additionally, the Company may, in its sole discretion, satisfy all or any portion of the Tax-Related Items obligation relating to your Award by any of the following means or by a combination of such means: (i) withholding from any compensation otherwise payable to you by the Company; (ii) causing you to tender a cash payment; or (iii) permitting or requiring you to enter into a "same day sale" commitment with a broker-dealer that is a member of the Financial Industry Regulatory Authority (a "***FINRA Dealer***") whereby you irrevocably elect to sell a portion of the Ordinary Shares to be delivered in connection with your Award to satisfy the Tax-Related Items and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the Tax-Related Items directly to the Company and/or its Affiliates. If the obligation for Tax-Related Items is satisfied by withholding from Ordinary Shares otherwise issuable to you, (i) the number of such Ordinary Shares so withheld shall not exceed the minimum statutory withholding rates in connection with the taxes composing the Tax Related-Items, and (ii) for tax purposes, you are deemed to have been issued the full number of Ordinary Shares subject to the vested RSUs, notwithstanding that a number of the Ordinary Shares are held back solely for the purpose of paying the Tax-Related Items. Furthermore, you acknowledge that the Company makes no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of the Award, including, but not limited to, the grant or vesting of the RSUs, the subsequent sale of Ordinary Shares acquired pursuant to such vesting and the receipt of any dividends, and does not commit to and is under no obligation to structure the terms of the grant or any aspect of the Award to reduce or eliminate your liability for Tax-Related Items or achieve any particular tax result. You further acknowledge that if you become subject to tax in more than one jurisdiction between the Date of Grant and the date of any relevant taxable event, the Company may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

(b) Unless the tax withholding obligations of the Company are satisfied, the Company shall have no obligation to deliver to you any Ordinary Shares.

(c) In the event the Company's obligation to withhold arises prior to the delivery to you of Ordinary Shares or it is determined after the delivery of Ordinary Shares to you that the amount of the Company's withholding obligation was greater than the amount withheld by the Company, you agree to indemnify and hold the Company harmless from any failure by the Company to withhold the proper amount.

12. CHANGE IN CONTROL. If you are either (i) required to resign your position as a Non-Employee Director as a condition of a Change in Control, or (ii) removed from your position as a Non-Employee Director in connection with a Change in Control, your Award shall become

fully vested immediately prior to the effectiveness of such resignation or removal (and contingent upon the effectiveness of such Change in Control).

13. PARACHUTE PAYMENTS.

(a) If you are a U.S. taxpayer and any payment or benefit you would receive from the Company or otherwise in connection with a Change in Control or other similar transaction ("***Payment***") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "***Excise Tax***"), then such Payment shall be equal to the Reduced Amount. The "Reduced Amount" shall be either (x) the largest portion of the Payment that would result in no portion of the Payment being subject to the Excise Tax, or (y) the largest portion, up to and including the total, of the Payment, whichever amount ((x) or (y)), after taking into account all applicable federal, state, foreign and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in payments or benefits constituting "parachute payments" is necessary so that the Payment equals the Reduced Amount, reduction shall occur in the manner that results in the greatest economic benefit for you.

(b) The independent registered public accounting firm engaged by the Company for general audit purposes as of the day prior to the effective date of the event described in Section 280G(b)(2)(A)(i) of the Code shall perform the foregoing calculations. If the independent registered public accounting firm so engaged by the Company is serving as accountant or auditor for the individual, entity or group effecting such Change in Control or similar transaction, the Company shall appoint a nationally recognized independent registered public accounting firm to make the determinations required hereunder. The Company shall bear all expenses with respect to the determinations by such independent registered public accounting firm required to be made hereunder.

(c) The independent registered public accounting firm engaged to make the determinations hereunder shall provide its calculations, together with detailed supporting documentation, to the Company and you within thirty (30) calendar days after the date on which your right to a Payment is triggered (if requested at that time by the Company or you) or such other time as reasonably requested by the Company or you. Any good faith determinations of the independent registered public accounting firm made hereunder shall be final, binding and conclusive upon the Company and you.

14. NATURE OF GRANT. In accepting the grant, you acknowledge, understand and agree that:

(a) the Plan is established voluntarily by the Company, it is discretionary in nature and it may be modified, amended, suspended or terminated by the Company at any time, to the extent permitted by the Plan;

(b) the Award grant is voluntary and occasional and does not create any contractual or other right to receive future grants of RSUs, or benefits in lieu of RSUs, even if RSUs have been granted in the past;

(c) all decisions with respect to future grants of RSUs or other grants, if any, will be at the sole discretion of the Company;

(d) you are voluntarily participating in the Plan;

(e) the future value of the underlying Ordinary Shares is unknown, indeterminable and cannot be predicted with certainty;

(f) no claim or entitlement to compensation or damages shall arise from forfeiture of the Award resulting from the termination of your Continuous Service; and

(g) neither the Company nor any Affiliate shall be liable for any foreign exchange rate fluctuation between your local currency and the United States Dollar that may affect the value of the Award or of any amounts due to you pursuant to the settlement of the Award or the subsequent sale of any Ordinary Shares acquired upon settlement.

15. NO ADVICE REGARDING GRANT. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding your participation in the Plan, or your acquisition or sale of the underlying Ordinary Shares. You should consult with your own personal tax, legal and financial advisors regarding your participation in the Plan before taking any action related to the Plan.

16. DATA PRIVACY. The Company and any Affiliate may collect, use, process, transfer or disclose your Personal Information for the purpose of implementing, administering and managing your participation in the Plan, in accordance with the Company's privacy practices. For example, your Personal Information will be transferred to the Company's stock administration team located in the United States and may be directly or indirectly transferred to E*TRADE or any other third party stock plan service provider as may be selected by the Company, and any other third parties assisting the Company with the implementation, administration and management of the Plan. For more information on the Company's privacy practices, log in to your E*TRADE account to view a copy of the Jazz Pharmaceuticals Privacy Notice.

17. GOVERNING LAW AND VENUE. The Award and the provisions of this Agreement are governed by, and subject to, the laws of the State of Delaware, without regard to the conflict of law provisions.

For purposes of any action, lawsuit or other proceedings brought to enforce this Agreement, relating to it, or arising from it, the parties hereby submit to and consent to the sole and exclusive jurisdiction of the courts of Santa Clara County, California, or the federal courts for the United States for the Northern District of California, and no other courts, where this grant is made and/or to be performed.

18. LANGUAGE. If you have received this Agreement or any other document related to the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

19. APPENDIX. Notwithstanding any provisions in this Agreement, the Award shall be subject to any special terms and conditions set forth in any Appendix to this Agreement for your

country. Moreover, if you relocate to one of the countries included in the Appendix, the special terms and conditions for such country will apply to you, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. The Appendix constitutes part of this Agreement.

20. NOTICES; ELECTRONIC DELIVERY. Any notices provided for in your Award or the Plan shall be given in writing (including electronically) and shall be deemed effectively given upon receipt or, in the case of notices delivered by the Company to you, fourteen (14) days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company. Notwithstanding the foregoing, the Company may, in its sole discretion, decide to deliver any documents related to participation in the Plan and this Award by electronic means or to request your consent to participate in the Plan by electronic means. By accepting this Award you consent to receive such documents by electronic delivery and, if requested, to agree to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.

21. HEADINGS. The headings of the Sections in this Agreement are inserted for convenience only and shall not be deemed to constitute a part of this Agreement or to affect the meaning of this Agreement.

22. AMENDMENT. Notwithstanding anything in the Plan to the contrary, the Board reserves the right to change, by written notice to you, the provisions of this Agreement in any way it may deem necessary or advisable for legal or administrative reasons, and to require you to sign any additional agreements or undertakings that may be necessary to accomplish the foregoing.

23. MISCELLANEOUS.

(a) All covenants and agreements hereunder shall inure to the benefit of, and be enforceable by the Company's successors and assigns, if any. Your rights and obligations under your Award may only be assigned with the prior written consent of the Company.

(b) You agree upon request to execute any further documents or instruments necessary or desirable in the sole determination of the Company to carry out the purposes or intent of your Award.

(c) You acknowledge and agree that you have reviewed your Award in its entirety, have had an opportunity to obtain the advice of counsel prior to executing and accepting your Award, and fully understand all provisions of your Award.

(d) All obligations of the Company under the Plan and this Agreement shall be binding on any successor to the Company, whether the existence of such successor is the result of a direct or indirect purchase, merger, consolidation, or otherwise, of all or substantially all of the business and/or assets of the Company.

24. GOVERNING PLAN DOCUMENT. Your Award is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your Award, and is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. Except as expressly provided in this Agreement, in

the event of any conflict between the provisions of your Award and those of the Plan, the provisions of the Plan shall control. In addition, your Award (and any compensation paid or Ordinary Shares issued under your Award) is subject to recoupment in accordance with the Dodd–Frank Wall Street Reform and Consumer Protection Act and any implementing regulations thereunder, any clawback policy adopted by the Company and any compensation recovery policy otherwise required by applicable law.

25. SEVERABILITY. If all or any part of this Agreement or the Plan is declared by any court or governmental authority to be unlawful or invalid, such unlawfulness or invalidity shall not invalidate any portion of this Agreement or the Plan not declared to be unlawful or invalid. Any Section of this Agreement (or part of such a Section) so declared to be unlawful or invalid shall, if possible, be construed in a manner which will give effect to the terms of such Section or part of a Section to the fullest extent possible while remaining lawful and valid.

26. OTHER DOCUMENTS. You hereby acknowledge receipt or the right to receive a document providing the information required by Rule 428(b)(1) promulgated under the Securities Act, which includes the Plan prospectus. In addition, you acknowledge receipt of the Company's policy permitting officers and directors to sell Ordinary Shares only during certain "window" periods and the Company's insider trading policy, in effect from time to time.

27. WAIVER. You acknowledge that a waiver by the Company of breach of any provision of this Agreement shall not operate or be construed as a waiver of any other provision of this Agreement, or of any subsequent breach by you or any other participant.

28. INSIDER TRADING / MARKET ABUSE LAWS. You may be subject to insider trading restrictions and/or market abuse laws based on the exchange on which the Ordinary Shares are listed and in applicable jurisdictions including the United States and your country or your broker's country, if different, which may affect your ability to accept, acquire, sell or otherwise dispose of Ordinary Shares, rights to Ordinary Shares (e.g., RSUs) or rights linked to the value of Ordinary Shares under the Plan during such times as you are considered to have "inside information" regarding the Company (as defined by the laws in the applicable jurisdictions). Local insider trading laws and regulations may prohibit the cancellation or amendment of orders you placed before you possessed inside information. Furthermore, you could be prohibited from (a) disclosing the inside information to any third party and (b) "tipping" third parties or causing them otherwise to buy or sell securities (third parties include fellow directors). Any restrictions under these laws or regulations are separate from and in addition to any restrictions that may be imposed under the Company's insider trading policy as may be in effect from time to time. You acknowledge that it is your responsibility to comply with any applicable restrictions, and you should speak to your personal advisor on this matter.

29. FOREIGN ASSET/ACCOUNT, EXCHANGE CONTROL AND TAX REPORTING. You may be subject to foreign asset/account, exchange control and/or tax reporting requirements as a result of the acquisition, holding and/or transfer of Ordinary Shares or cash (including dividends and the proceeds arising from the sale of Ordinary Shares) derived from your participation in the Plan, to and/or from a brokerage/bank account or legal entity located outside your country. The applicable laws of your country may require that you report such accounts, assets, the balances therein, the value thereof and/or the transactions related thereto to the applicable authorities in such country. You acknowledge that you are responsible for ensuring compliance

with any applicable foreign asset/account, exchange control and tax reporting requirements and should consult your personal legal advisor on this matter.

30. DIRECTOR NOTIFICATION OBLIGATION. If you are a director, shadow director or secretary of the Company or an Irish Affiliate, you must notify the Company or the Irish Affiliate in writing if you receive or dispose of an interest exceeding 1% of the Company (*e.g.,* RSUs, Ordinary Shares), or become aware of the event giving rise to the notification requirement, or if you become a director or secretary if such an interest exceeding 1% of the Company exists at the time. This notification requirement also applies with respect to the interests of a spouse or minor children (whose interests will be attributed to the director, shadow director or secretary, as applicable).

* * * * *

By signing the Non-U.S. Restricted Stock Unit Award Grant Notice to which this Non-U.S. Restricted Stock Unit Award Agreement is attached, you shall be deemed to have signed and agreed to the terms and conditions of this Non-U.S. Restricted Stock Unit Award Agreement.

* * * * *

Based on the form of Non-U.S. Restricted Stock Unit Award Agreement for the Amended and Restated 2007 Non-Employee Directors Stock Award Plan as approved by the Board of Directors of Jazz Pharmaceuticals plc on 2 August 2018.

APPENDIX

TO THE

NON-U.S. RESTRICTED STOCK UNIT AWARD AGREEMENT

TERMS AND CONDITIONS

This Appendix contains additional terms and conditions that govern the Award granted under the Plan to you if you reside and/or work in one of the countries listed below. Certain capitalized terms used but not defined in this Appendix have the meanings set forth in the Plan and/or the Agreement.

If you are a citizen or resident of a country other than the one in which you are currently working, transfer residency after the RSUs are granted, or are considered a resident of another country for local law purposes, the information contained herein may not be applicable to you, and the Company shall, in its discretion, determine to what extent the terms and conditions contained herein shall apply to you.

NOTIFICATIONS

This Appendix contains information regarding exchange controls and certain other issues of which you should be aware with respect to participation in the Plan. The information is based on the securities, exchange control, and other laws in effect in the respective countries as of June 2018. Such laws are often complex and change frequently. As a result, the Company strongly recommends that you not rely on the information in this Appendix as the only source of information relating to the consequences of your participation in the Plan because the information may be out of date at the time you vest in the RSUs or sell Ordinary Shares acquired pursuant thereto.

The information contained herein is general in nature and may not apply to your particular situation, and the Company is not in a position to assure you of a particular result. Accordingly, you are advised to seek appropriate professional advice as to how the relevant laws in your country may apply to your situation.

IRELAND

TERMS AND CONDITIONS

Vesting and Issuance. The following supplements Sections 3 and 4 of the Agreement:

Notwithstanding the vesting schedule provided in the Grant Notice and Section 4 (a) of the Agreement, (i) if any vesting date set forth in the Grant Notice ("***Vesting Date***") falls on a date when the Company determines that you are not permitted to sell Ordinary Shares in the open market for any reason, including under the Company's Policy Regarding Stock Trading by Executive Officers, Directors and Other Designated Employees (or any successor policy) or the Company's Policy Against Trading on the Basis of Inside Information (or any successor policy), and (ii) the Company elects not to satisfy any Tax-Related Items (defined in Section 11) by withholding Ordinary Shares, then such Vesting Date shall instead be the later of the next U.S. business day of the next occurring

open "window period" applicable to you or the next U.S. business day when the Company determines that you are not prohibited from selling Ordinary Shares in the open market (such later date, the "***Actual Vesting Date***").

Notwithstanding the foregoing and Section 3 of the Agreement: (i) if your Continuous Service terminates between the Vesting Date and the Actual Vesting Date, then the vesting of the Ordinary Shares subject to the Award originally scheduled to vest on the Vesting Date will cease and not vest upon termination of your Continuous Service, unless your Continuous Service terminates for a reason other than Cause, in which case they will instead vest in full on the first U.S. business day following the termination of your Continuous Service; and (ii) if you are a Non-Employee Director and you do not stand for reelection at an annual general meeting of the Company's shareholders (an "***Annual Meeting***") in the year in which your term expires or you otherwise resign effective at an Annual Meeting, and, in either case, your Continuous Service terminates at such Annual Meeting, then effective as of the date of such Annual Meeting, the unvested portion, if any, of the Award shall become vested with respect to the portion of the Award that would have vested on the anniversary of the Vesting Commencement Date in the year of such Annual Meeting.

For purposes of the foregoing, "Cause" means the occurrence of any of the following events that has a material negative impact on the business or reputation of the Company or an Affiliate: (i) your conviction for any criminal offence (other than an offence under any road traffic legislation for which a fine or non-custodial penalty is imposed) or any offence under any regulation or legislation relating to insider dealing, fraud or dishonesty; (ii) your attempted commission of, or participation in, a fraud or act of dishonesty against the Company or an Affiliate; (iii) your intentional, material violation of any contract or agreement between you and the Company or an Affiliate, or of any statutory duty owed to the Company or an Affiliate; (iv) your unauthorized use or disclosure of the Company's or an Affiliate's confidential information or trade secrets; or (v) your gross misconduct. The determination that a termination of your Continuous Service is either for Cause or without Cause shall be made by the Company in its sole discretion. Any determination by the Company that your Continuous Service was terminated with or without Cause for the purposes of this Agreement shall have no effect upon any determination of the rights or obligations of the Company or an Affiliate or you for any other purpose.

SWITZERLAND

NOTIFICATIONS

Securities Law Notification. The grant of the RSUs and the issuance of any Ordinary Shares is not intended to be a public offering in Switzerland. Neither this document nor any other materials relating to the RSUs constitute a prospectus as such term is understood pursuant to article 652a of the Swiss Code of Obligations, and neither this document nor any other materials relating to the RSUs may be publicly distributed nor otherwise made publicly available in Switzerland. Finally, neither this document nor any other offering or marketing material relating to the RSUs have been or will be filed with, or approved or supervised by, any Swiss regulatory authority (in particular, the Swiss Financial Market Supervisory Authority (FINMA)).

UNITED KINGDOM

TERMS AND CONDITIONS

Settlement in Ordinary Shares. Notwithstanding anything in the Plan or the Agreement to the contrary, the Award may only be settled by the delivery of Ordinary Shares.

ATTACHMENT II

JAZZ PHARMACEUTICALS PLC
AMENDED AND RESTATED
2007 NON-EMPLOYEE DIRECTORS STOCK AWARD PLAN

Exhibit 31.1

CERTIFICATION

I, Bruce C. Cozadd, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Jazz Pharmaceuticals public limited company;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 6, 2018

By: /s/ Bruce C. Cozadd

Bruce C. Cozadd
Chairman and Chief Executive Officer and Director

Exhibit 31.2

CERTIFICATION

I, Matthew P. Young, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Jazz Pharmaceuticals public limited company;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 6, 2018

By: /s/ Matthew P. Young

Matthew P. Young
Executive Vice President and Chief Financial Officer

Exhibit 32.1

CERTIFICATION[(1)]

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), Bruce C. Cozadd, Chief Executive Officer of Jazz Pharmaceuticals public limited company (the "Company"), and Matthew P. Young, Executive Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2018, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 6, 2018

/s/ Bruce C. Cozadd

Bruce C. Cozadd

Chairman and Chief Executive Officer and Director

/s/ Matthew P. Young

Matthew P. Young

Executive Vice President and Chief Financial Officer

(1) This certification accompanies the Quarterly Report on Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Jazz Pharmaceuticals public limited company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing. A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to Jazz Pharmaceuticals public limited company and will be retained by Jazz Pharmaceuticals public limited company and furnished to the Securities and Exchange Commission or its staff upon request.