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 June 30, 2019

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 D04 E5W7
011-353-1-634-7800
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value $0.0001 per share	JAZZ	The Nasdaq Stock Market LLC

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 July 31, 2019, 56,621,139 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 JUNE 30, 2019

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We own or have rights to various copyrights, trademarks, and trade names used in our business in the U.S. and/or other countries, including the following: Jazz Pharmaceuticals®, Xyrem® (sodium oxybate) oral solution, Erwinaze® (asparaginase *Erwinia chrysanthemi*), Erwinase®, Defitelio® (defibrotide sodium), Defitelio® (defibrotide), CombiPlex®, Vyxeos® (daunorubicin and cytarabine) liposome for injection, Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion, Sunosi™ (solriamfetol) and FazaClo® (clozapine, USP). This report also includes trademarks, service marks and trade names of other companies. Trademarks, service marks and trade names appearing in this 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)

	June 30, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 637,739	$ 309,622
Investments	245,000	515,000
Accounts receivable, net of allowances	311,249	263,838
Inventories	68,999	52,956
Prepaid expenses	31,712	25,017
Other current assets	75,367	67,572
Total current assets	1,370,066	1,234,005
Property, plant and equipment, net	127,183	200,358
Operating lease assets	144,746	—
Intangible assets, net	2,687,941	2,731,334
Goodwill	924,990	927,630
Deferred tax assets, net	184,383	57,879
Deferred financing costs	8,517	9,589
Other non-current assets	40,835	42,696
Total assets	$ 5,488,661	$ 5,203,491
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 82,222	$ 40,602
Accrued liabilities	218,751	264,887
Current portion of long-term debt	33,387	33,387
Income taxes payable	30,413	1,197
Deferred revenue	4,720	5,414
Total current liabilities	369,493	345,487
Deferred revenue, non-current	7,221	9,581
Long-term debt, less current portion	1,567,842	1,563,025
Operating lease liabilities, less current portion	156,289	—
Deferred tax liabilities, net	283,669	309,097
Other non-current liabilities	120,713	218,879
Commitments and contingencies (Note 11)		
Shareholders' equity:		
Ordinary shares	6	6
Non-voting euro deferred shares	55	55
Capital redemption reserve	472	472
Additional paid-in capital	2,171,458	2,113,630
Accumulated other comprehensive loss	(210,436)	(197,791)
Retained earnings	1,021,879	841,050
Total shareholders' equity	2,983,434	2,757,422
Total liabilities and shareholders' equity	$ 5,488,661	$ 5,203,491

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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Revenues:				
Product sales, net	$ 523,423	$ 496,095	$ 1,026,754	$ 936,942
Royalties and contract revenues	10,710	4,384	15,565	8,150
Total revenues	534,133	500,479	1,042,319	945,092
Operating expenses:				
Cost of product sales (excluding amortization of intangible assets)	27,676	34,714	61,182	68,633
Selling, general and administrative	176,014	158,579	343,961	365,792
Research and development	62,384	56,132	122,489	118,799
Intangible asset amortization	61,576	54,959	118,461	107,966
Impairment charges	—	42,896	—	42,896
Acquired in-process research and development	2,200	—	58,200	—
Total operating expenses	329,850	347,280	704,293	704,086
Income from operations	204,283	153,199	338,026	241,006
Interest expense, net	(18,234)	(19,646)	(36,156)	(40,251)
Foreign exchange loss	(1,933)	(2,697)	(2,544)	(4,425)
Loss on extinguishment and modification of debt	—	(1,425)	—	(1,425)
Income before income tax provision (benefit) and equity in loss of investees	184,116	129,431	299,326	194,905
Income tax provision (benefit)	(78,650)	36,524	(49,534)	55,670
Equity in loss of investees	868	586	1,761	923
Net income	$ 261,898	$ 92,321	$ 347,099	$ 138,312
Net income per ordinary share:				
Basic	$ 4.62	$ 1.53	$ 6.09	$ 2.30
Diluted	$ 4.56	$ 1.50	$ 6.01	$ 2.26
Weighted-average ordinary shares used in per share calculations - basic	56,707	60,177	56,955	60,053
Weighted-average ordinary shares used in per share calculations - diluted	57,427	61,438	57,753	61,309

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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Net income	$ 261,898	$ 92,321	$ 347,099	$ 138,312
Other comprehensive income (loss):				
Foreign currency translation adjustments	13,319	(70,814)	(7,823)	(31,961)
Unrealized gain (loss) on hedging activities, net of income tax (benefit) provision of ($440), $193, ($689) and $651, respectively	(3,081)	1,354	(4,822)	4,558
Other comprehensive income (loss)	10,238	(69,460)	(12,645)	(27,403)
Total comprehensive income	$ 272,136	$ 22,861	$ 334,454	$ 110,909

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

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

	Ordinary Shares		Non-voting Euro Deferred		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2018	57,504	$ 6	4,000	$ 55	$ 472	$ 2,113,630	$ (197,791)	$ 841,050	$2,757,422
Cumulative effect adjustment from adoption of new accounting standards	—	—	—	—	—	—	—	4,848	4,848
Issuance of ordinary shares in conjunction with exercise of share options	54	—	—	—	—	3,057	—	—	3,057
Issuance of ordinary shares in conjunction with vesting of restricted stock units	203	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(13,810)	—	—	(13,810)
Share-based compensation	—	—	—	—	—	27,861	—	—	27,861
Shares repurchased	(858)	—	—	—	—	—	—	(111,249)	(111,249)
Other comprehensive loss	—	—	—	—	—	—	(22,883)	—	(22,883)
Net income	—	—	—	—	—	—	—	85,201	85,201
Balance at March 31, 2019	56,903	$ 6	4,000	$ 55	$ 472	$ 2,130,738	$ (220,674)	$ 819,850	$2,730,447
Issuance of ordinary shares in conjunction with exercise of share options	98	—	—	—	—	7,033	—	—	7,033
Issuance of ordinary shares under employee stock purchase plan	57	—	—	—	—	6,032	—	—	6,032
Issuance of ordinary shares in conjunction with vesting of restricted stock units	15	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(1,003)	—	—	(1,003)
Share-based compensation	—	—	—	—	—	28,658	—	—	28,658
Shares repurchased	(447)	—	—	—	—	—	—	(59,869)	(59,869)
Other comprehensive income	—	—	—	—	—	—	10,238	—	10,238
Net income	—	—	—	—	—	—	—	261,898	261,898
Balance at June 30, 2019	56,626	$ 6	4,000	$ 55	$ 472	$ 2,171,458	$ (210,436)	$1,021,879	$2,983,434

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

	Ordinary Shares		Non-voting Euro Deferred		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2017	59,898	$ 6	4,000	$ 55	$ 472	$ 1,935,486	$ (140,878)	$ 917,956	$2,713,097
Cumulative effect adjustment from adoption of new accounting standards	—	—	—	—	—	—	53	(351)	(298)
Issuance of ordinary shares in conjunction with exercise of share options	133	—	—	—	—	10,588	—	—	10,588
Issuance of ordinary shares in conjunction with vesting of restricted stock units	195	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(14,594)	—	—	(14,594)
Share-based compensation	—	—	—	—	—	24,276	—	—	24,276
Shares repurchased	(237)	—	—	—	—	—	—	(34,546)	(34,546)
Other comprehensive income	—	—	—	—	—	—	42,057	—	42,057
Net income	—	—	—	—	—	—	—	45,991	45,991
Balance at March 31, 2018	59,989	$ 6	4,000	$ 55	$ 472	$ 1,955,756	$ (98,768)	$ 929,050	$2,786,571
Issuance of ordinary shares in conjunction with exercise of share options	457	—	—	—	—	51,023	—	—	51,023
Issuance of ordinary shares under employee stock purchase plan	59	—	—	—	—	5,447	—	—	5,447
Issuance of ordinary shares in conjunction with vesting of restricted stock units	16	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(1,429)	—	—	(1,429)
Share-based compensation	—	—	—	—	—	26,294	—	—	26,294
Shares repurchased	(135)	—	—	—	—	—	—	(21,015)	(21,015)
Other comprehensive loss	—	—	—	—	—	—	(69,460)	—	(69,460)
Net income	—	—	—	—	—	—	—	92,321	92,321
Balance at June 30, 2018	60,386	$ 6	4,000	$ 55	$ 472	$ 2,037,091	$ (168,228)	$1,000,356	$2,869,752

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)

	Six Months Ended June 30,	
	2019	**2018**
Operating activities		
Net income	$ 347,099	$ 138,312
Adjustments to reconcile net income to net cash provided by operating activities:		
Intangible asset amortization	118,461	107,966
Share-based compensation	55,841	50,615
Impairment charges	—	42,896
Depreciation	6,894	7,457
Acquired in-process research and development	58,200	—
Loss on disposal of assets	7	115
Deferred tax benefit	(151,347)	(32,228)
Provision for losses on accounts receivable and inventory	2,403	2,670
Loss on extinguishment and modification of debt	—	1,425
Amortization of debt discount and deferred financing costs	22,584	21,504
Other non-cash transactions	(2,547)	10,996
Changes in assets and liabilities:		
Accounts receivable	(47,574)	(54,356)
Inventories	(18,562)	(8,938)
Prepaid expenses and other current assets	(15,929)	(5,268)
Other non-current assets	694	1,767
Operating lease assets	7,399	—
Accounts payable	(14,096)	7,371
Accrued liabilities	(59,031)	60,108
Income taxes payable	29,050	(3,285)
Deferred revenue	(3,054)	(3,749)
Other non-current liabilities	14,177	13,955
Operating lease liabilities, less current portion	431	—
Net cash provided by operating activities	351,100	359,333
Investing activities		
Proceeds from maturity of investments	630,000	385,000
Acquired in-process research and development	(58,200)	—
Purchases of property, plant and equipment	(21,911)	(11,281)
Acquisition of intangible assets	(25,500)	(111,102)
Acquisition of investments	(360,975)	(505,350)
Net cash provided by (used in) investing activities	163,414	(242,733)
Financing activities		
Proceeds from employee equity incentive and purchase plans	16,122	67,058
Payment of employee withholding taxes related to share-based awards	(14,813)	(16,023)
Repayments of long-term debt	(16,693)	(9,023)
Share repurchases	(171,118)	(55,561)
Proceeds from tenant improvement allowance on build-to-suit lease	—	1,253
Payment of debt modification costs	—	(6,406)
Net cash used in financing activities	(186,502)	(18,702)
Effect of exchange rates on cash and cash equivalents	105	1,148
Net increase in cash and cash equivalents	328,117	99,046
Cash and cash equivalents, at beginning of period	309,622	386,035
Cash and cash equivalents, at end of period	$ 637,739	$ 485,081

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

Our lead marketed products are:

- **Sunosi™ (solriamfetol)**, our newest lead marketed product launched in July 2019 and approved in the U.S. to improve wakefulness in adult patients with excessive daytime sleepiness, or EDS, associated with narcolepsy or obstructive sleep apnea. We are also seeking approval for solriamfetol in Europe and submitted a marketing authorization application to the European Medicines Agency in the fourth quarter of 2018;
- **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 EDS in both adult and pediatric patients with narcolepsy;
- **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;
- **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; 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.

In March 2019, we announced positive top-line results from our Phase 3 study evaluating the efficacy and safety of JZP-258, an oxybate product candidate that contains 92% less sodium than Xyrem, for the treatment of cataplexy and EDS in adult patients with narcolepsy, and we expect to submit a new drug application, or NDA, for this product by as early as the end of 2019.

Our strategy to create shareholder value is focused on:

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

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 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, 2018.

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 six months ended June 30, 2019 are not necessarily indicative of the results to be expected for the year ending December 31, 2019, for any other interim period or for any future period.

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, 2018 with the exception of the accounting policy relating to operating leases and financing obligations which was updated as a result of adopting Accounting Standards Update No. 2016-02, "Leases", or ASU No. 2016-02.

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.

Leases

We determine if an arrangement is a lease at inception. Operating leases are included in operating lease assets, other current liabilities, and operating lease liabilities on our condensed consolidated balance sheets. Operating lease assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. In determining the net present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. The operating lease asset also includes any lease payments made and excludes lease incentives and initial direct costs incurred. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

We have lease agreements with lease and non-lease components, which are generally accounted for separately. For vehicle leases we account for the lease and non-lease components as a single lease component.

We have elected the short-term lease exemption and, therefore, do not recognize a right-of-use asset or corresponding liability for lease arrangements with an original term of 12 months or less.

Adoption of New Accounting Standards

In February 2016, the Financial Accounting Standards Board, or FASB, issued ASU No. 2016-02. Under the new guidance, lessees are 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. We adopted ASU No. 2016-02 on a modified retrospective basis applied to leases existing as of, or entered into after, January 1, 2019. We elected the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allowed us to carry forward the historical lease classification of those leases in place as of January 1, 2019.

The adoption of ASU No. 2016-02 resulted in the recognition of right-of-use assets and lease liabilities of $149.4 million and $162.9 million, respectively, on the consolidated balance sheet as of January 1, 2019, and the de-recognition of the build-to-suit assets and related financing obligations on the consolidated balance sheet as of December 31, 2018 of $95.4 million and $109.8 million, respectively, with the balance impacting retained earnings, deferred rent and deferred tax liabilities. The right-of-use assets and lease liabilities primarily relate to real estate leases. Refer to Note 10 for lease-related disclosures.

The cumulative effect of the changes made to our consolidated balance sheet as of January 1, 2019 for the adoption of the ASU No. 2016-02 was as follows (in thousands):

	Balance at December 31, 2018	Transition Adjustments	Balance at January 1, 2019
Assets:			
Property, plant and equipment, net	$ 200,358	$ (95,397)	$ 104,961
Operating lease assets	—	149,442	149,442
Liabilities:			
Accrued liabilities	264,887	8,165	273,052
Operating lease liabilities, less current portion	—	153,158	153,158
Deferred tax liabilities, net	309,097	1,489	310,586
Other non-current liabilities	218,879	(113,615)	105,264
Shareholders' Equity:			
Retained earnings	841,050	4,848	845,898

Significant Risks and Uncertainties

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

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

Concentrations of Risk

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

We manage our foreign currency transaction risk and interest rate risk within specified guidelines through the use of derivatives. All of our derivative instruments are utilized for risk management purposes, and we do not use derivatives for speculative trading purposes. As of June 30, 2019, we had foreign exchange forward contracts with notional amounts totaling $288.9 million. As of June 30, 2019, the outstanding foreign exchange forward contracts had a net asset fair value of $1.6 million. As of June 30, 2019, we had interest rate swap contracts with notional amounts totaling $300.0 million. These outstanding interest rate swap contracts had a net liability fair value of $1.4 million as of June 30, 2019. 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 June 30, 2019 and December 31, 2018, allowances on receivables were not material. As of June 30, 2019, two customers accounted for 88% of gross accounts receivable, Express Scripts Specialty Distribution Services, Inc. and its affiliates, or Express Scripts, the central pharmacy for Xyrem, which accounted for 78% of gross accounts receivable, and McKesson Corporation and affiliates, or McKesson, which accounted for 10% of gross accounts receivable. As of December 31, 2018, two customers accounted for 89% of gross accounts receivable, Express Scripts, which accounted for 74% 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 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 No. 2018-15, “Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer’s Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract”, which aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software. The standard is effective for us beginning January 1, 2020 and early adoption is permitted. The new guidance is not expected to have a material impact on our results of operations and financial position.

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

2. Collaboration and License Agreement

On January 2, 2019, we entered into a strategic collaboration agreement with Codiak BioSciences, Inc., or Codiak, focused on the research, development and commercialization of exosome therapeutics to treat cancer. Codiak granted us an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize therapeutic candidates directed at five targets to be developed using Codiak's engEx™ precision engineering platform for exosome therapeutics.

Under the terms of the agreement, Codiak is responsible for the execution of preclinical and early clinical development of therapeutic candidates directed at all five targets through Phase 1/2 proof of concept studies. Following the conclusion of the applicable Phase 1/2 study, we will be responsible for future development, potential regulatory submissions and

commercialization for each product. Codiak has the option to participate in co-commercialization and cost/profit-sharing in the U.S. and Canada on up to two products.

As part of the agreement, we paid Codiak an upfront payment of $56.0 million in January 2019, which was recorded as acquired IPR&D expense in our condensed consolidated statements of income for the six months ended June 30, 2019. Codiak is eligible to receive up to $20 million in preclinical development milestone payments across all five programs. Codiak is also eligible to receive milestone payments totaling up to $200 million per target based on investigational new drug application acceptance, clinical and regulatory milestones, including approvals in the U.S., the European Union and Japan, and certain sales milestones. Codiak is also eligible to receive tiered royalties on net sales of each approved product.

3. Cash and Available-for-Sale Securities

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

	June 30, 2019					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 261,194	$ —	$ —	$ 261,194	$ 261,194	$ —
Time deposits	370,000	—	—	370,000	125,000	245,000
Money market funds	251,545	—	—	251,545	251,545	—
Totals	$ 882,739	$ —	$ —	$ 882,739	$ 637,739	$ 245,000

	December 31, 2018					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 215,606	$ —	$ —	$ 215,606	$ 215,606	$ —
Time deposits	515,000	—	—	515,000	—	515,000
Money market funds	94,016	—	—	94,016	94,016	—
Totals	$ 824,622	$ —	$ —	$ 824,622	$ 309,622	$ 515,000

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 June 30, 2019 and December 31, 2018 that were measured at fair value on a recurring basis and were categorized using the fair value hierarchy (in thousands):

	June 30, 2019			December 31, 2018		
	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	$ —	$ 370,000	$ 370,000	$ —	$ 515,000	$ 515,000
Money market funds	251,545	—	251,545	94,016	—	94,016
Interest rate contracts	—	13	13	—	4,070	4,070
Foreign exchange forward contracts	—	1,732	1,732	—	1,194	1,194
Totals	$ 251,545	$ 371,745	$ 623,290	$ 94,016	$ 520,264	$ 614,280
Liabilities:						
Interest rate contracts	$ —	$ 1,445	$ 1,445	$ —	$ —	$ —
Foreign exchange forward contracts	—	142	142	—	1,460	1,460
Totals	$ —	$ 1,587	$ 1,587	$ —	$ 1,460	$ 1,460

As of June 30, 2019, 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 and 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 2019 or 2018.

As of June 30, 2019, the carrying amount of investments measured using the measurement alternative for equity investments without a readily determinable fair value was $4.5 million. The carrying amount, which is recorded within other non-current assets, represents the purchase price paid in December 2018.

As of June 30, 2019, 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 $587 million and $567 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 until July 2021. These agreements hedge contractual term loan interest rates. As of June 30, 2019 and December 31, 2018, 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 six months ended June 30, 2019 and 2018 was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
Interest Rate Contracts:	**2019**	**2018**	**2019**	**2018**
Gain (loss) recognized in accumulated other comprehensive loss, net of tax	$ (2,698)	$ 1,372	$ (4,039)	$ 4,409
Loss (gain) reclassified from accumulated other comprehensive loss to interest expense, net of tax	(383)	(18)	(783)	149

Assuming no change in LIBOR-based interest rates from market rates as of June 30, 2019, $0.1 million of losses, net of tax, 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 June 30, 2019 and December 31, 2018, the notional amount of foreign exchange contracts where hedge accounting is not applied was $288.9 million and $271.5 million, respectively.

The foreign exchange loss in our condensed consolidated statements of income included the following gains and losses associated with foreign exchange contracts not designated as hedging instruments (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
Foreign Exchange Forward Contracts:	**2019**	**2018**	**2019**	**2018**
Gain (loss) recognized in foreign exchange loss	$ 121	$ (12,238)	$ (3,288)	$ (8,487)

The cash flow effects of our derivative contracts for the six months ended June 30, 2019 and 2018 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):

	June 30, 2019			
	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	$ 13	Accrued liabilities	$ 128
			Other non-current liabilities	1,317
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	1,732	Accrued liabilities	142
Total fair value of derivative instruments		$ 1,745		$ 1,587

	December 31, 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	$ 1,929	Accrued liabilities	$ —
	Other non-current assets	2,141		
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	1,194	Accrued liabilities	1,460
Total fair value of derivative instruments		$ 5,264		$ 1,460

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):

	June 30, 2019					
				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	$ 1,745	$ —	$ 1,745	$ (512)	$ —	$ 1,233
Derivative liabilities	(1,587)	—	(1,587)	512	—	(1,075)

	December 31, 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	$ 5,264	$ —	$ 5,264	$ (935)	$ —	$ 4,329
Derivative liabilities	(1,460)	—	(1,460)	935	—	(525)

6. Inventories

Inventories consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Raw materials	$ 14,893	$ 10,895
Work in process	29,185	20,743
Finished goods	24,921	21,318
Total inventories	$ 68,999	$ 52,956

7. Goodwill and Intangible Assets

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

Balance at December 31, 2018	$ 927,630
Foreign exchange	(2,640)
Balance at June 30, 2019	$ 924,990

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

	June 30, 2019				December 31, 2018		
	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	13.6	$ 3,184,381	$ (748,678)	$ 2,435,703	$ 3,110,641	$ (632,413)	$ 2,478,228
Priority review voucher		111,101	—	111,101	111,101	—	111,101
Manufacturing contracts	—	12,181	(12,181)	—	12,256	(12,256)	—
Trademarks	—	2,894	(2,894)	—	2,896	(2,896)	—
Total finite-lived intangible assets		3,310,557	(763,753)	2,546,804	3,236,894	(647,565)	2,589,329
Acquired IPR&D assets		141,137	—	141,137	142,005	—	142,005
Total intangible assets		$ 3,451,694	$ (763,753)	$ 2,687,941	$ 3,378,899	$ (647,565)	$ 2,731,334

The increase in the gross carrying amount of intangible assets as of June 30, 2019 compared to December 31, 2018 reflects the capitalization of milestone payments triggered by FDA approval of Sunosi in March 2019 and subsequent U.S. Drug Enforcement Agency scheduling in June 2019, partially offset by the negative impact of foreign currency translation adjustments due to the weakening of the euro against the U.S. dollar.

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. We reduced the estimated remaining useful life of the Erwinaze intangible asset due to the receipt of a contract termination notice from Porton Biopharma Limited in February 2019. The reduction in the estimated remaining useful life increased intangible asset amortization expense by $15.0 million and $25.2 million, reduced net income by $10.2 million and $17.1 million, and reduced basic and diluted net income per ordinary share by $0.18 and $0.30 during the three and six months ended June 30, 2019, respectively.

Based on acquired developed technology intangible assets recorded as of June 30, 2019, 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
2019 (remainder)	$ 126,961
2020	252,774
2021	205,135
2022	159,563
2023	159,563
Thereafter	1,531,707
Total	$ 2,435,703

8. Certain Balance Sheet Items

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

	June 30, 2019	December 31, 2018
Land and buildings	$ 46,636	$ 46,650
Construction-in-progress	33,483	51,243
Leasehold improvements	32,572	33,273
Manufacturing equipment and machinery	26,859	25,837
Computer software	18,193	19,062
Computer equipment	14,341	13,679
Furniture and fixtures	7,759	8,155
Build-to-suit facility	—	52,067
Subtotal	179,843	249,966
Less accumulated depreciation and amortization	(52,660)	(49,608)
Property, plant and equipment, net	$ 127,183	$ 200,358

The decrease in the carrying amount of construction-in-progress and build-to-suit facility assets as of June 30, 2019 compared to December 31, 2018 reflects the de-recognition of assets related to build-to-suit facility leases on adoption of ASU No. 2016-02.

Accrued liabilities consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Rebates and other sales deductions	$ 79,134	$ 86,495
Employee compensation and benefits	49,050	58,543
Clinical trial accruals	9,780	5,904
Current portion of operating lease liabilities	8,722	—
Accrued interest	7,531	7,407
Accrued construction-in-progress	7,669	1,065
Inventory-related accruals	7,130	8,753
Selling and marketing accruals	6,275	6,780
Royalties	5,101	2,679
Professional fees	4,083	2,333
Sales returns reserve	2,395	2,510
Derivative instrument liabilities	270	1,460
Accrued loss contingency	—	58,154
Other	31,611	22,804
Total accrued liabilities	$ 218,751	$ 264,887

9. Debt

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

	June 30, 2019	December 31, 2018
2021 Notes	$ 575,000	$ 575,000
Unamortized discount and debt issuance costs on 2021 Notes	(50,194)	(60,910)
2021 Notes, net	524,806	514,090
2024 Notes	575,000	575,000
Unamortized discount and debt issuance costs on 2024 Notes	(128,683)	(138,914)
2024 Notes, net	446,317	436,086
Term loan	630,106	646,236
Total debt	1,601,229	1,596,412
Less current portion	33,387	33,387
Total long-term debt	$ 1,567,842	$ 1,563,025

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 June 30, 2019, 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 June 30, 2019 were as follows (in thousands):

Year Ending December 31,	Scheduled Long-Term Debt Maturities
2019 (remainder)	$ 16,693
2020	33,387
2021	608,387
2022	33,387
2023	517,493
Thereafter	575,000
Total	$ 1,784,347

10. Leases

The components of the lease expense for the three and six months ended June 30, 2019 were as follows (in thousands):

Lease Cost	Three Months Ended June 30, 2019	Six Months Ended June 30, 2019
Operating lease cost	$ 6,056	$ 11,926
Short-term lease cost	619	1,220
Variable lease cost	1	4
Sublease income	(158)	(320)
Net lease cost	$ 6,518	$ 12,830

Supplemental balance sheet information related to operating leases was as follows (in thousands):

Leases	Classification	June 30, 2019
Assets		
Operating lease assets	Operating lease assets	$ 144,746
Liabilities		
Current		
Operating lease liabilities	Accrued liabilities	8,722
Non-current		
Operating lease liabilities	Operating lease liabilities, less current portion	156,289
Total operating lease liabilities		$ 165,011

Lease Term and Discount Rate	June 30, 2019
Weighted-average remaining lease term - operating leases (years)	10.1
Weighted-average discount rate - operating leases	5.3%

Supplemental cash flow information related to operating leases was as follows (in thousands):

	Six Months Ended June 30, 2019
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash outflows from operating leases	$ 8,240
Non-cash operating activities:	
Right-of-use assets obtained in exchange for new operating lease liabilities (1)	152,142

(1) Includes the balances recognized on January 1, 2019 on adoption of ASU No. 2016-02.

Maturities of operating lease liabilities were as follows (in thousands):

Year Ending December 31,	Operating leases
2019 (remainder)	$ 6,716
2020	21,050
2021	20,923
2022	20,889
2023	21,066
Thereafter	128,223
Total lease payments	$ 218,867
Less imputed interest	(53,856)
Present value of lease liabilities	$ 165,011

11. Commitments and Contingencies

Indemnification

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

We have agreed to indemnify our executive officers, directors and certain other employees for losses and costs incurred in connection with certain events or occurrences, including advancing money to cover certain costs, subject to certain limitations. The maximum potential amount of future payments we could be required to make under the indemnification obligations is unlimited; however, we maintain insurance policies that may limit our exposure and may enable us to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits and other policy provisions, we believe the fair value of these indemnification obligations is not significant. Accordingly, we did not recognize any liabilities relating to these obligations as of June 30, 2019 and December 31, 2018. 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

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. Refer to Note 10 for details of the maturity of our operating lease liabilities.

Other Commitments. As of June 30, 2019, we had $69.6 million of noncancelable purchase commitments due within one year, primarily related to agreements with third party manufacturers.

Legal Proceedings

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 charitable organizations that provide financial assistance to Medicare patients. In April 2018, we reached an agreement in principle with the U.S. Department of Justice, or DOJ, on terms for a civil settlement of potential claims by the DOJ in the amount of $57.0 million plus interest to accrue at the statutory rate of 2.75%, subject to negotiation of a definitive settlement agreement and other contingencies. On April 4, 2019, we finalized the settlement agreement with the DOJ and the Office of Inspector General of the U.S. Department of Health and Human Services,

and we entered into a corporate integrity agreement requiring us to maintain our ongoing corporate compliance program and obligating us to implement or continue, as applicable, a set of defined corporate integrity activities for a period of five years from the effective date of the corporate integrity agreement. During 2018, we recorded $58.2 million related to this matter, including related interest, within selling, general and administrative expenses on our consolidated statement of income. During the six months ended June 30, 2019, we recorded an additional $0.4 million of interest related to this matter. The settlement amount was paid in April 2019. Under the settlement agreement, we are released from any civil or administrative monetary claim arising from allegations relating to our conduct between 2011 and May 2014 in supporting a charitable foundation that provided financial assistance to Medicare patients. The settlement agreement is not an admission of any wrongdoing or liability by us but a settlement of claims. In the event of a breach of the corporate integrity agreement, we could become liable for payment of certain stipulated penalties or could be excluded from participation in federal health programs.

12. Shareholders' Equity

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 $300.0 million, exclusive of any brokerage commissions. In November and December 2018, our board of directors increased the existing share repurchase program authorization by $320.0 million and $400.0 million, respectively, thereby increasing the total amount authorized to $1.02 billion. Under this program, which has no expiration date, we may repurchase ordinary shares from time to time on the open market. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the amended credit agreement, corporate and regulatory requirements and market conditions. The share repurchase program may be modified, suspended or discontinued at any time without prior notice. In the six months ended June 30, 2019, we spent a total of $171.1 million to purchase 1.3 million of our ordinary shares under the share repurchase program at an average total purchase price, including commissions, of $131.17 per share. All ordinary shares repurchased were canceled. As of June 30, 2019, the remaining amount authorized under the share repurchase program was $208.0 million.

Accumulated Other Comprehensive Loss

The components of accumulated other comprehensive loss as of June 30, 2019 and December 31, 2018 were as follows (in thousands):

	Net Unrealized Gain (Loss) From Hedging Activities	Foreign Currency Translation Adjustments	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2018	$ 3,557	$ (201,348)	$ (197,791)
Other comprehensive loss before reclassifications	(4,039)	(7,823)	(11,862)
Amounts reclassified from accumulated other comprehensive loss	(783)	—	(783)
Other comprehensive loss, net	(4,822)	(7,823)	(12,645)
Balance at June 30, 2019	$ (1,265)	$ (209,171)	$ (210,436)

During the six months ended June 30, 2019, 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 loss on derivatives that qualify as cash flow hedges.

13. 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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Numerator:				
Net income	$ 261,898	$ 92,321	$ 347,099	$ 138,312
Denominator:				
Weighted-average ordinary shares used in per share calculations - basic	56,707	60,177	56,955	60,053
Dilutive effect of employee equity incentive and purchase plans	720	1,261	798	1,256
Weighted-average ordinary shares used in per share calculations - diluted	57,427	61,438	57,753	61,309
Net income per ordinary share:				
Basic	$ 4.62	$ 1.53	$ 6.09	$ 2.30
Diluted	$ 4.56	$ 1.50	$ 6.01	$ 2.26

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 six months ended June 30, 2019 and 2018 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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Exchangeable Senior Notes	5,504	5,504	5,504	5,504
Options, RSUs and ESPP	5,202	3,374	5,095	3,340

14. Revenues

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Xyrem	$ 413,212	$ 356,008	$ 781,529	$ 672,785
Erwinaze/Erwinase	27,622	58,713	88,521	109,340
Defitelio/defibrotide	46,055	40,498	87,555	75,559
Vyxeos	31,362	27,951	60,305	54,179
Other	5,172	12,925	8,844	25,079
Product sales, net	523,423	496,095	1,026,754	936,942
Royalties and contract revenues	10,710	4,384	15,565	8,150
Total revenues	$ 534,133	$ 500,479	$ 1,042,319	$ 945,092

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
United States	$ 480,932	$ 455,359	$ 943,794	$ 861,046
Europe	36,518	35,018	71,919	63,349
All other	16,683	10,102	26,606	20,697
Total revenues	$ 534,133	$ 500,479	$ 1,042,319	$ 945,092

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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Express Scripts	77%	71%	75%	71%
McKesson	12%	20%	15%	20%

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 June 30, 2019 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 $1.2 million and $3.1 million during the three and six months ended June 30, 2019, respectively, relating to these upfront payments. The deferred revenue balances are being recognized over an average of four years representing the period over which 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 six months ended June 30, 2019 (in thousands):

	Contract Liabilities
Balance as of December 31, 2018	$ 14,995
Amount recognized within royalties and contract revenues	(3,054)
Balance as of June 30, 2019	$ 11,941

15. 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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Selling, general and administrative	$ 20,685	$ 19,800	$ 41,055	$ 38,034
Research and development	5,896	4,709	11,419	9,084
Cost of product sales	1,708	1,803	3,367	3,497
Total share-based compensation expense, pre-tax	28,289	26,312	55,841	50,615
Income tax benefit from share-based compensation expense	(4,473)	(4,846)	(8,140)	(8,514)
Total share-based compensation expense, net of tax	$ 23,816	$ 21,466	$ 47,701	$ 42,101

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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Shares underlying options granted (in thousands)	102	80	1,399	1,232
Grant date fair value	$ 38.95	$ 49.28	$ 42.56	$ 46.28
Black-Scholes option pricing model assumption information:				
Volatility	31%	34%	32%	35%
Expected term (years)	4.5	4.5	4.5	4.5
Range of risk-free rates	1.8-2.3%	2.5-2.7%	1.8-2.5%	2.2-2.7%
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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
RSUs granted (in thousands)	42	32	561	493
Grant date fair value	$ 132.73	$ 152.36	$ 138.87	$ 141.36

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 June 30, 2019, compensation cost not yet recognized related to unvested share options and RSUs was $98.7 million and $124.0 million, respectively, which is expected to be recognized over a weighted-average period of 2.8 years.

16. Income Taxes

Our income tax benefit was $78.7 million and $49.5 million in the three and six months ended June 30, 2019, respectively, compared to an income tax provision of $36.5 million and $55.7 million for the same periods in 2018. The effective tax rate was (42.7)% and (16.5)% in the three and six months ended June 30, 2019, respectively, compared to 28.2% and 28.6% for the same periods in 2018. The income tax benefit for the three and six months ended June 30, 2019 includes a discrete tax benefit of $112.3 million resulting from an intra-entity intellectual property asset transfer. The tax benefit, which represents a deferred future benefit, was recorded as a deferred tax asset. The decrease in the effective tax rates for the three and six months ended June 30, 2019 compared to the same periods in 2018 was primarily due to the impact of the intra-entity intellectual property asset transfer. Excluding this effect, the decrease in the effective tax rate for the three months ended June 30, 2019 compared to the same period in 2018 was primarily due to the impairment charge recognized on the Prialt assets held for sale in 2018, and the decrease in the effective tax rate for the six months ended June 30, 2019 compared to the same period in 2018 was primarily due to the impairment charge recognized on the Prialt assets held for sale and the impact of the loss contingency expense in 2018. The effective tax rates for the three and six months ended June 30, 2019 were lower than the Irish statutory rate of 12.5% primarily due to the impact of the intra-entity intellectual property asset transfer. 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 Pharmaceuticals, Inc. 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 and the U.S. (both at the federal level and in various state jurisdictions). In Ireland, we are no longer subject to income tax audits by taxing authorities for the years prior to 2013. The U.S. jurisdictions generally have statutes of limitations three to four years from the later of the return due date or the date when the return was filed. However, in the U.S. (at the federal level and in most states), carryforward tax attributes that were generated in 2014 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, and in December 2018, we received a proposed tax assessment notice for 2015, relating to certain transfer pricing adjustments. The notices provide for additional French tax of approximately $43 million for 2012 and 2013 and approximately $4 million for 2015, including interest and penalties through the respective dates of the proposed assessments, translated at the foreign exchange rate at June 30, 2019. We disagree with the assessments and are contesting them vigorously.

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

Our lead marketed products are:

- **Sunosi™ (solriamfetol)**, our newest lead marketed product launched in July 2019 and approved in the U.S. to improve wakefulness in adult patients with excessive daytime sleepiness, or EDS, associated with narcolepsy or obstructive sleep apnea, or OSA. We are also seeking approval for solriamfetol in Europe and submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, in the fourth quarter of 2018;
- **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 EDS in both adult and pediatric patients with narcolepsy;
- **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;
- **Erwinaze® (asparaginase *Erwinia chrysanthemi*)**, a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia, or ALL, who have developed hypersensitivity to *E. coli*-derived asparaginase; and
- **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 to create shareholder value is focused on:

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

In the three and six months ended June 30, 2019, our total net product sales increased by 6% and 10%, compared to the same periods in 2018, primarily due to an increase in Xyrem net product sales. We expect total net product sales to increase in 2019 over 2018, primarily due to expected growth in sales of Xyrem, Defitelio and Vyxeos. 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 April 2019, we finalized a settlement agreement with the U.S. Department of Justice, or DOJ, and the Office of Inspector General of the Department of Health and Human Services, or OIG, and we entered into a corporate integrity agreement requiring us to maintain our ongoing corporate compliance program and obligating us to implement or continue, as applicable, a set of defined corporate integrity activities for a period of five years from the effective date of the corporate integrity agreement. For more information, see Note 11, Commitments and Contingencies—Other Contingencies of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

In June 2019, the U.S. Drug Enforcement Agency, or DEA, designated Sunosi as a Schedule IV controlled substance, and, in July 2019, Sunosi was launched in the U.S.

In June 2019, our partner, Nippon Shinyaku Co., Ltd, announced that Japan's Ministry of Health, Labour and Welfare approved the marketing authorization of Defitelio® injection 200mg (defibrotide sodium) for the treatment of sinusoidal obstruction syndrome/hepatic VOD.

In June 2019, we received notice from ImmunoGen, Inc., or ImmunoGen, that, as a result of portfolio prioritization and restructuring initiatives, ImmunoGen will be discontinuing development of its IMGN779 antibody-drug conjugate, or ADC, product candidate, for which we possess opt-in rights, as well as the programs from which a third opt-in candidate was to be selected. IMGN632, a CD123-targeted ADC product candidate for which we possess opt-in rights, remains under development by ImmunoGen.

In July 2019, we acquired from Redx Pharma plc, or Redx, a pan-RAF inhibitor program for the potential treatment of RAF and RAS mutant tumors. Under the terms of our agreement with Redx, we paid Redx $3.5 million at closing and Redx is eligible to receive up to $203 million in development, regulatory and commercial milestone payments from us, as well as incremental tiered royalties in mid-single digit percentage based on any future net sales.

Continued Emphasis on Research and Development

During the six months ended June 30, 2019, we continued our focus on research and development activities, all in our sleep and hematology/oncology therapeutic areas.

Our recent research and development activities included the following developments:

- In July 2019, we announced that we are pursuing development activities for solriamfetol for the potential treatment of EDS in patients with major depressive disorder, or MDD; and
- In August 2019, we announced that, based on the results of a Phase 1 clinical trial, we plan to commence a single-arm, pivotal Phase 2/3 clinical trial of JZP-458, a recombinant crisantaspase product candidate, for the potential treatment of ALL and lymphoblastic lymphoma, or LBL, by the end of 2019.

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

Sleep

Product Candidates	Description
Submitted for Regulatory Approval	
Solriamfetol in the European Union, or EU	EDS in OSA and EDS in narcolepsy
Phase 3	
JZP-258 (oxybate; 92% sodium reduction)	Cataplexy and EDS in narcolepsy
JZP-258 (oxybate; 92% sodium reduction)	Idiopathic hypersomnia
Preclinical	
Oxybate once-nightly formulation	Narcolepsy

Hematology/Oncology

Product Candidates	Description
Phase 3	
Defitelio	Prevention of VOD in high-risk patients following HSCT
Vyxeos	AML or high-risk myelodysplastic syndrome, or MDS (AML19) (cooperative group study)
Vyxeos	AML or high-risk MDS (AML18) (cooperative group study)
Vyxeos	Newly diagnosed adults with standard and high-risk AML (cooperative group study)
Vyxeos	Newly diagnosed pediatric patients (planned cooperative group study)
Phase 2/3	
JZP-458 (recombinant crisantaspase)	ALL/LBL (planned study)
Phase 2	
Defitelio	Prevention of acute Graft versus Host Disease following allogeneic HSCT
Defitelio	Treatment of transplant-associated thrombotic microangiopathy (planned study)
Defitelio	Prevention of chimeric antigen receptor T-cell therapy-associated neurotoxicity (planned study)
Vyxeos + venetoclax	De novo or relapsed/refractory, or R/R, AML (MD Anderson Cancer Center, or MD Anderson, collaboration study)
Vyxeos	High-risk MDS (cooperative group study)
Vyxeos	R/R AML (Children's Oncology Group cooperative group study)

Product Candidates	Description
Vyxeos	Newly diagnosed older adults with high-risk AML (planned cooperative group study)
Vyxeos + venetoclax	High-risk AML (planned cooperative group study)
Phase 1	
Vyxeos + gemtuzumab	R/R AML or hypomethylating agent failure MDS (MD Anderson collaboration study)
Vyxeos + venetoclax	Low intensity therapy for first-line, unfit AML (planned Phase 1b study)
Vyxeos	Low intensity dosing for higher risk MDS (MD Anderson collaboration study)
IMGN632	CD123+ hematological malignancies including AML and blastic plasmacytoid dendritic cell neoplasm (Jazz opt-in opportunity with ImmunoGen)
Preclinical	
CombiPlex	Solid tumors candidate
CombiPlex	Hematology/oncology exploratory activities
Recombinant crisantaspase-HLE	ALL and other hematological malignancies (collaboration with Pfenex, Inc., or Pfenex)
Recombinant pegaspargase	Hematological malignancies (Jazz opt-in opportunity with Pfenex)
Defitelio	Exploratory activities
Exosome NRAS candidate	Hematological malignancies (collaboration with Codiak Biosciences, Inc., or Codiak)
Exosome STAT3 candidate	Hematological malignancies (collaboration with Codiak)
Exosome-based candidates	Solid tumors/hematological malignancies (collaboration with Codiak)
Pan-RAF inhibitor program	RAF and RAS mutant tumors (acquired from Redx, which is continuing development)

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

Xyrem. Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which were 79% and 76% of our net product sales for the three and six months ended June 30, 2019, respectively, and 75% of our net product sales for the year ended December 31, 2018. Our future plans assume that sales of Xyrem will increase, but there is no guarantee that we can maintain sales of Xyrem at or near current levels, or that Xyrem sales will continue to grow. We have periodically increased the price of Xyrem, most recently in July 2019, and there is no guarantee that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes and revenues from Xyrem.

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 abbreviated new drug applications, or ANDAs, seeking approval to market a generic version of Xyrem, and we have filed and settled patent lawsuits with all nine companies. To date, the FDA has approved or tentatively approved three of these ANDAs, and we believe that it is likely that the FDA will approve or tentatively approve additional ANDAs. In connection with the ANDA settlement agreements, we granted four of the filers the right to sell an authorized generic version of Xyrem, or an AG Product, and we granted each of the nine filers a license to launch its own generic sodium oxybate product. The actual timing of the launch of an AG Product or generic sodium oxybate product is uncertain because the launch dates of the AG Products and generic sodium oxybate products under our settlement agreements are subject to acceleration under certain circumstances. In the absence of any circumstances triggering acceleration, the earliest launch of an AG Product would be January 1, 2023. For a further description of the settlement agreements, including a more complete description of potential dates of market entry for an AG Product(s) and generic sodium oxybate product(s) and circumstances that might trigger acceleration of such dates, see the risk factor under the heading “*The*

introduction of a new product in the U.S. market that competes with, or otherwise disrupts the market for, Xyrem would adversely affect sales of Xyrem" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

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

Non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy, even if not directly competitive with Xyrem, could have the effect of changing treatment regimens and payor coverage of Xyrem, and indirectly materially and adversely affect sales of Xyrem. Prescribers often prescribe stimulants or wake-promoting agents for treatment of EDS, and anti-depressants for cataplexy, before prescribing or instead of prescribing Xyrem, and payors often require patients to try such medications before they will cover Xyrem. It is possible that additional branded or generic products that treat symptoms of narcolepsy will also be prescribed before or instead of Xyrem, or that payors will require patients to try such products before they will cover Xyrem, or that payors will exclude Xyrem from formulary coverage in favor of a newly-launched product. Our product Sunosi is an example of a new market entrant recently approved by the FDA to improve wakefulness in adult patients with EDS associated with narcolepsy or OSA and that we launched in July 2019. Another example is pitolisant, a drug that has already been approved in Europe to treat adult patients with narcolepsy with or without cataplexy. Harmony Biosciences LLC, which has exclusive U.S. rights to seek approval of and commercialize pitolisant, announced in February 2019 that the FDA had accepted its pitolisant NDA for filing with priority review.

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

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

Erwinaze/Erwinase. Sales of our second largest product, Erwinaze/Erwinase (which we refer to in this report as Erwinaze unless otherwise indicated or the context otherwise requires), were 5% and 9% of our net product sales for the three and six months ended June 30, 2019, respectively, and 9% for the year ended December 31, 2018. Erwinaze is licensed from and manufactured by a single source, Porton Biopharma Limited, or PBL, a company that is wholly owned by the UK Department of Health and Social Care. Our license and supply agreement with PBL, which includes our license for Erwinaze, expires on December 31, 2020. We and PBL had been engaged in discussions related to entry into a replacement agreement to extend the term of our commercial relationship past 2020, but we did not reach agreement. Unless we and PBL enter into a new agreement, we will lose our rights to Erwinaze effective December 31, 2020, other than our right to sell certain Erwinaze inventory for a post-termination sales period of 12 months. In such event, we may not be able to replace the product sales we would lose from Erwinaze, which in 2018 totaled $174.7 million, and our business, financial condition, results of operations and growth prospects would be materially adversely affected. In addition, we cannot predict whether and to what extent uncertainty related to our rights to, and availability of, Erwinaze after 2020 will negatively impact sales of and revenues from this product.

A continuing and significant challenge to maintaining sales of Erwinaze and a barrier to increasing sales is PBL's inability to consistently supply product adequate to meet market demand. All Erwinaze that PBL has been able to supply is currently completely absorbed by demand for the product. In addition, PBL is subject to a January 2017 warning letter issued by the FDA citing significant violations of the FDA's current Good Manufacturing Practices, or cGMP, as well as an inspection report from the UK Medicines and Healthcare Products Regulatory Agency listing several major findings, including major deficiencies and failures by PBL to comply with cGMP. PBL's product quality and manufacturing issues have resulted, and continue to result, in disruptions in our ability to supply markets from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions during 2019 and 2020. These supply disruptions will continue to adversely impact our ability to generate sales of and revenues from Erwinaze and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Defitelio/defibrotide. Sales of Defitelio/defibrotide were 9% of our net product sales for the three and six months ended June 30, 2019 and for the year ended December 31, 2018. Our ability to maintain and grow sales and to realize the anticipated benefits from our investment in Defitelio is subject to a number of risks and uncertainties, including continued acceptance by hospital pharmacy and therapeutics committees in the U.S., the continued availability of favorable pricing and adequate coverage and reimbursement, the limited experience of, and need to educate, physicians in recognizing, diagnosing and treating VOD, and the limited size of the population of VOD patients who are indicated for treatment with Defitelio. If sales of Defitelio do not reach the levels we expect, our anticipated revenue from the product will be negatively affected and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Vyxeos. Sales of Vyxeos were 6% of our net product sales for the three and six months ended June 30, 2019 and 5% of our net product sales for the year ended December 31, 2018. We began selling Vyxeos in the U.S. in August 2017 following NDA approval. In August 2018, the European Commission, or EC, granted marketing authorization for Vyxeos. We are continuing our rolling launch of Vyxeos in the EU and are continuing to make pricing and reimbursement submissions in EU member states.

Our ability to realize the anticipated benefits from our investment in Vyxeos is subject to a number of risks and uncertainties, including acceptance by hospital pharmacy and therapeutics committees in the U.S., the EU and other countries, the availability of adequate coverage, pricing and reimbursement approvals, competition from new and existing products and potential competition from products in development, and delays or problems in the supply or manufacture of Vyxeos. If sales of Vyxeos do not reach the levels we expect, our anticipated revenue from the product will be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Sunosi/solriamfetol. The FDA approved Sunosi in March 2019, and we launched Sunosi in July 2019. In the fourth quarter of 2018, we submitted an MAA to the EMA for solriamfetol. We cannot predict whether our solriamfetol MAA will be approved in a timely manner, or at all. Our ability to realize the anticipated benefits from our investment in Sunosi is subject to a number of risks and uncertainties, including, among other things, market acceptance of Sunosi, including our ability, in a competitive retail pharmacy market, to differentiate Sunosi from other branded and generic products that treat EDS in patients with narcolepsy with which physicians are more familiar; the availability of adequate formulary positions and pricing and adequate coverage and reimbursement by government programs and other third party payors, including the impact of any delays in coverage decisions by payors; restrictions on permitted promotional activities based on any additional limitations on the labeling for the product that may be required by the FDA in the future and any such limitations that may be required by the EC or other regulatory authority on any approved labeling; market acceptance of Sunosi; delays or problems in the supply or manufacture of Sunosi; and our ability to satisfy the FDA's post-marketing requirements and other post-marketing requirements or commitments, if any, imposed by the EC in connection with its potential marketing authorization. If we are unable to successfully launch and commercialize Sunosi in the U.S., if we are unable to obtain approval of our solriamfetol MAA in a timely manner, or at all, if the EC requires product labeling that negatively impacts patient, physician or payor acceptance of the product, or if sales of Sunosi in the U.S. and in the EU (if approved) 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.

JZP-258. In March 2019, we announced positive top-line results from our Phase 3 study evaluating the efficacy and safety of JZP-258 for the treatment of cataplexy and EDS in adult patients with narcolepsy, and we expect to submit an NDA for this product by as early as the end of 2019. We cannot predict whether we will be able to submit our planned NDA in a timely manner or at all. Any failure or delay in successfully completing necessary clinical trials and conducting other activities, including chemistry, manufacturing and controls activities, that are required to complete our planned NDA submission and obtain regulatory approval, could materially and adversely affect our growth prospects. If we submit an NDA to the FDA for approval and the FDA determines that our safety or efficacy data do not warrant marketing approval, we may be required to conduct additional clinical trials, which could be costly and time-consuming, or we may not be able to commercialize JZP-258, in which event we would not receive any return on our investment.

Other Challenges and Risks. We anticipate that we will continue to face a number of other challenges and risks to our business and our ability to execute our strategy in 2019 and beyond. Some of these challenges and risks are specific to our business, and others are common to companies in the pharmaceutical industry with development and commercial operations. In this regard, a key aspect of our growth strategy is our continued and growing investment in research and development activities. Our ability to successfully develop product candidates for one or more indications as well as our ability to identify new indications for existing products are subject to a number of risks and uncertainties, such as the difficulty and uncertainty of pharmaceutical product development, including the timing thereof, and the uncertainty of clinical success, such as the risk that results from preclinical studies and/or early clinical trials may not be predictive of results obtained in later and larger clinical trials. In addition, obtaining regulatory approval for product candidates is subject to the inherent uncertainty associated with the regulatory approval process, especially as we continue to increase investment in our product pipeline development projects and undertake planned regulatory submissions for our product candidates.

We also seek to expand our business through corporate development activities. Our ability to identify and acquire, in-license or develop additional products or product candidates to grow our business are subject to a number of risks and uncertainties, including the risks associated with business combination or product or product candidate acquisition transactions, such as the challenges inherent in the integration of acquired businesses with our historical business, the increase in geographic dispersion among our centers of operation and the risks that we may acquire unanticipated liabilities along with acquired businesses or otherwise fail to realize the anticipated benefits (commercial or otherwise) from such transactions. In addition, we may not realize the anticipated benefits of our collaborations with third parties for the acquisition and development of product candidates, including as a result of the inability of a collaboration partner to obtain and maintain adequate funding to pursue development activities or our inability to agree with our collaboration partners on our respective contractual rights.

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

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 June 30,		Increase/	Six Months Ended June 30,		Increase/
	2019	2018	(Decrease)	2019	2018	(Decrease)
Product sales, net	$ 523,423	$ 496,095	6 %	$ 1,026,754	$ 936,942	10 %
Royalties and contract revenues	10,710	4,384	144 %	15,565	8,150	91 %
Cost of product sales (excluding amortization of intangible assets)	27,676	34,714	(20)%	61,182	68,633	(11)%
Selling, general and administrative	176,014	158,579	11 %	343,961	365,792	(6)%
Research and development	62,384	56,132	11 %	122,489	118,799	3 %
Intangible asset amortization	61,576	54,959	12 %	118,461	107,966	10 %
Impairment charges	—	42,896	N/A(1)	—	42,896	N/A(1)
Acquired in-process research and development	2,200	—	N/A(1)	58,200	—	N/A(1)
Interest expense, net	18,234	19,646	(7)%	36,156	40,251	(10)%
Foreign exchange loss	1,933	2,697	(28)%	2,544	4,425	(43)%
Loss on extinguishment and modification of debt	—	1,425	N/A(1)	—	1,425	N/A(1)
Income tax provision (benefit)	(78,650)	36,524	N/A(1)	(49,534)	55,670	N/A(1)
Equity in loss of investees	868	586	48 %	1,761	923	91 %

(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 June 30,		Increase/	Six Months Ended June 30,		Increase/
	2019	2018	(Decrease)	2019	2018	(Decrease)
Xyrem	$ 413,212	$ 356,008	16 %	$ 781,529	$ 672,785	16 %
Erwinaze/Erwinase	27,622	58,713	(53)%	88,521	109,340	(19)%
Defitelio/defibrotide	46,055	40,498	14 %	87,555	75,559	16 %
Vyxeos	31,362	27,951	12 %	60,305	54,179	11 %
Other	5,172	12,925	(60)%	8,844	25,079	(65)%
Product sales, net	523,423	496,095	6 %	1,026,754	936,942	10 %
Royalties and contract revenues	10,710	4,384	144 %	15,565	8,150	91 %
Total revenues	$ 534,133	$ 500,479	7 %	$ 1,042,319	$ 945,092	10 %

Product Sales, Net

Xyrem product sales increased in the three and six months ended June 30, 2019 compared to the same periods in 2018 due to a higher average net selling price and, to a lesser extent, an increase in sales volume. Price increases were instituted in January 2019 and January 2018. Xyrem product sales volume increased by 5% in the three and six months ended June 30, 2019 compared to the same periods in 2018 primarily driven by an increase in the average number of patients on Xyrem. Erwinaze/Erwinase product sales decreased in the three and six months ended June 30, 2019 compared to the same periods in 2018 primarily due to a decrease in product availability. Ongoing supply challenges at PBL continue to negatively impact our ability to supply the market. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions during 2019 and 2020. Defitelio/defibrotide product sales increased in the three and six months ended June 30, 2019 compared to the same periods in 2018 primarily due to higher volumes as a result of increased use by transplant centers that treat adult and pediatric patients. Vyxeos product sales increased in the three and six months ended June 30, 2019 compared to the same periods in 2018 following the commercial launch in the EU in September 2018. Other product

sales decreased in the three and six months ended June 30, 2019 compared to the same periods in 2018 primarily due to the sale of our rights to Prialt to TerSera Therapeutics LLC, or TerSera, in September 2018. We expect total product sales will increase in 2019 over 2018, primarily due to expected growth in sales of Xyrem, Defitelio and Vyxeos.

Royalties and Contract Revenues

Royalties and contract revenues increased in the three and six months ended June 30, 2019 compared to the same periods in 2018 due to higher contract revenues from out-licensing agreements resulting from a regulatory approval milestone. We expect royalties and contract revenues to increase in 2019 compared to 2018, due to higher contract revenues from out-licensing arrangements.

Cost of Product Sales

Cost of product sales decreased in the three and six months ended June 30, 2019 compared to the same periods in 2018 primarily due to product mix. Gross margin as a percentage of net product sales was 94.7% and 94.0% in the three and six months ended June 30, 2019, respectively, compared to 93.0% and 92.7% for the same periods in 2018. The increase in the gross margin percentage in the three and six months ended June 30, 2019 was primarily due to a change in product mix. We do not expect our gross margin as a percentage of net product sales to change materially in 2019 compared to 2018.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased in the three months ended June 30, 2019 compared to the same period in 2018 primarily due to higher expenses related to the launch of Sunosi in the U.S., an increase in compensation-related expenses driven by higher headcount, and an increase in other expenses related to the expansion and support of our business. Selling, general and administrative expenses decreased in the six months ended June 30, 2019 compared to the same period in 2018 primarily due to the loss contingency of $57.0 million recorded in the 2018 period. In April 2019, we finalized a settlement agreement with the DOJ and the OIG. For a further description of this matter, see Note 11, Commitments and Contingencies—Other Contingencies of the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q. We expect selling, general and administrative expenses in 2019 to increase compared to 2018, primarily due to an increase in compensation-related expenses driven by higher headcount, other expenses related to the expansion and support of our business and an increase in expenses related to the commercial launch of Sunosi in the U.S., the continuation of the commercial launch of Vyxeos in the EU and the preparation for the planned commercial launch of Sunosi in the EU.

Research and Development Expenses

Research and development expenses consist primarily of costs related to clinical studies and outside services, personnel expenses, milestone payments and other research and development costs. Clinical studies 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 June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Clinical studies and outside services	$ 33,034	$ 32,199	$ 63,265	$ 60,388
Personnel expenses	20,855	18,044	42,165	35,248
Milestone expense	—	—	—	11,000
Other	8,495	5,889	17,059	12,163
Total	$ 62,384	$ 56,132	$ 122,489	$ 118,799

Research and development expenses increased by $6.3 million and $3.7 million in the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018. Clinical studies and outside services costs increased by $0.8 million and $2.9 million for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018 primarily due to an increase in expenses related to our ongoing pre-clinical and clinical development programs and regulatory activities. Personnel expenses increased by $2.8 million and $6.9 million in the three and six months ended June 30, 2019 compared to the same periods in 2018, primarily due to increased headcount in support of our development programs. Milestone expense of $11.0 million in the six months ended June 30, 2018 related to milestone payments following FDA acceptance of our NDA for solriamfetol in March 2018.

For 2019 and beyond, we expect that our research and development expenses will continue to increase from historical levels, particularly as we prepare for anticipated regulatory submissions and data read-outs from clinical trials, initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates. A discussion of the risks and uncertainties with respect to our research and development activities, including completing the development of and regulatory submissions for our product candidates, and the consequences to our business, financial position and growth prospects can be found in "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Intangible Asset Amortization

Intangible asset amortization increased by $6.6 million and $10.5 million in the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018, primarily due to the reduction in the estimated remaining useful life of the Erwinaze intangible asset resulting from the contract termination notice we received from PBL in February 2019, partially offset by the cessation of amortization of the Prialt intangible asset following our entry into an Asset Purchase Agreement, or APA, with TerSera in 2018. Intangible asset amortization is expected to increase in 2019 compared to 2018 as a result of the reduction in the estimated remaining useful life of the Erwinaze intangible asset.

Impairment Charges

In June 2018, we entered into an APA with TerSera, pursuant to which TerSera purchased substantially all of the assets held by us related to Prialt. In connection with the entry into the APA, 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 three and six months ended June 30, 2018.

Acquired In-Process Research and Development

Acquired IPR&D expense in the six months ended June 30, 2019 primarily related to an upfront payment of $56.0 million to Codiak in connection with our strategic collaboration agreement.

Interest Expense, Net

Interest expense, net decreased by $1.4 million and $4.1 million in the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018, primarily due to higher interest income. We expect interest expense, net will be lower in 2019 compared to 2018, primarily due to 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 three and six months ended June 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 (Benefit)

Our income tax benefit was $78.7 million and $49.5 million in the three and six months ended June 30, 2019, respectively, compared to an income tax provision of $36.5 million and $55.7 million for the same periods in 2018. The effective tax rates were (42.7)% and (16.5)% in the three and six months ended June 30, 2019, respectively, compared to 28.2%

and 28.6% for the same periods in 2018. The income tax benefit for the three and six months ended June 30, 2019 includes a discrete tax benefit of $112.3 million resulting from an intra-entity intellectual property asset transfer. The tax benefit, which represents a deferred future benefit, was recorded as a deferred tax asset. The decrease in the effective tax rates for the three and six months ended June 30, 2019 compared to the same periods in 2018 was primarily due to the impact of the intra-entity intellectual property asset transfer Excluding this effect, the decrease in the effective tax rate for the three months ended June 30, 2019 compared to the same period in 2018 was primarily due to the impairment charge recognized on the Prialt assets held for sale in 2018 and the decrease in the effective tax rate for the six months ended June 30, 2019 compared to the same period in 2018 was primarily due to the impairment charge recognized on the Prialt assets held for sale and the impact of the loss contingency expense in 2018. The effective tax rates for the three and six months ended June 30, 2019 were lower than the Irish statutory rate of 12.5%, primarily due to the impact of the intra-entity intellectual property asset transfer.

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 June 30, 2019, we had cash, cash equivalents and investments of $0.9 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 $634.3 million aggregate principal amount term loan, $575.0 million principal amount of our 1.875% exchangeable senior notes due 2021 and $575.0 million principal amount of our 1.50% exchangeable senior notes due 2024. We generated cash flows from operations of $351.1 million during the six months ended June 30, 2019, and we expect to continue to generate positive cash flows from operations during 2019.

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

To continue to grow our business over the longer term, we plan to commit substantial resources to product acquisition and in-licensing, product development, clinical trials of product candidates and expansion of our commercial, development, manufacturing and other operations. In this regard, we have evaluated and expect to continue to evaluate a wide array of 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 new share repurchase program pursuant to which we were authorized to repurchase a number of ordinary shares having an aggregate purchase price of up to $300 million, exclusive of any brokerage commissions. In November and December 2018, our board of directors increased the existing share repurchase program authorization by $320.0 million and $400.0 million, respectively, thereby increasing the total amount authorized to $1.02 billion. Under this program, which has no expiration date, we may repurchase ordinary shares from time to time on the open market. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under our amended credit agreement, corporate and regulatory requirements and market conditions. The repurchase program may be modified, suspended or discontinued at any time without prior notice. In the six months ended June 30, 2019, we spent a total of $171.1 million to purchase 1.3 million of our ordinary shares under the share repurchase program at an average total purchase price, including commissions, of $131.17 per share. All

ordinary shares repurchased were canceled. As of June 30, 2019, the remaining amount authorized under the share repurchase program was $208.0 million.

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

	Six Months Ended June 30,	
	2019	2018
Net cash provided by operating activities	$ 351,100	$ 359,333
Net cash provided by (used in) investing activities	163,414	(242,733)
Net cash used in financing activities	(186,502)	(18,702)
Effect of exchange rates on cash and cash equivalents	105	1,148
Net increase in cash and cash equivalents	$ 328,117	$ 99,046

Net cash provided by operating activities of $351.1 million for the six months ended June 30, 2019 related to net income of $347.1 million, adjusted for acquired IPR&D expense of $58.2 million and non-cash items of $52.3 million primarily related to intangible asset amortization, share-based compensation expense and deferred income taxes, offset by a net cash outflow of $106.5 million related to changes in operating assets and liabilities. Net cash provided by operating activities of $359.3 million for the six months ended June 30, 2018 related to net income of $138.3 million, adjusted for non-cash items of $213.4 million primarily related to intangible asset amortization, share-based compensation expense, impairment charges and a net cash inflow of $7.6 million related to changes in operating assets and liabilities.

Net cash provided by investing activities for the six months ended June 30, 2019 primarily related to the net proceeds on maturity of investments of $269.0 million, partially offset by upfront payments for acquired IPR&D of $58.2 million primarily related to our strategic collaboration agreement with Codiak, milestone payments of $25.5 million triggered by FDA approval of Sunosi in March 2019 and subsequent U.S. DEA scheduling in June 2019 and purchases of property and equipment of $21.9 million. Net cash used in investing activities for the six months ended June 30, 2018 primarily related to the net acquisition of investments of $120.4 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 $11.3 million.

Net cash used in financing activities for the six months ended June 30, 2019 primarily related to repurchase of ordinary shares under our share repurchase program of $171.1 million, repayment of our term loan principal of $16.7 million and payment of employee withholding taxes of $14.8 million related to share-based awards, partially offset by proceeds from employee equity incentive and purchase plans of $16.1 million. Net cash used in financing activities for the six months ended June 30, 2018 primarily related to repurchase of ordinary shares under our share repurchase program of $55.6 million, payment of employee withholding taxes of $16.0 million related to share-based awards, repayment of our term loan principal of $9.0 million and payment of debt modification costs of $6.4 million, partially offset by proceeds from employee equity incentive and purchase plans of $67.1 million and proceeds from tenant improvement allowance on a build-to-suit lease of $1.3 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 June 30, 2019, no amounts were outstanding under our revolving credit facility. During the six months ended June 30, 2019, there were no material changes to our credit agreement and the 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, 2018.

Contractual Obligations

During the three and six months ended June 30, 2019, there were no material changes to our contractual obligations as set forth in Part II, Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2018.

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 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, 2018. Except for the operating leases and financing obligations policy that was updated as a result of adopting Accounting Standards Update No. 2016-02, "Leases", 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, 2018.

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 six months ended June 30, 2019, 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, 2018.

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 June 30, 2019.

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 June 30, 2019, 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 11, Commitments and Contingencies—Other Contingencies 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 Our Other Marketed Products

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

Xyrem® (sodium oxybate) oral solution is the only product approved by the U.S. Food and Drug Administration, or FDA, and marketed in the U.S. for the treatment of both cataplexy and excessive daytime sleepiness, or EDS, in both adult and pediatric patients with narcolepsy. Xyrem is our largest selling product, and our financial results are significantly influenced by sales of Xyrem, which accounted for 79% and 76% of our net product sales for the three and six months ended June 30, 2019, respectively, and 75% of our net product sales for the year ended December 31, 2018. Our future plans assume that sales of Xyrem will increase, but there is no guarantee that we can maintain sales of Xyrem at or near current levels, or that Xyrem sales will continue to grow. We have periodically increased the price of Xyrem, most recently in July 2019, and there is no guarantee that price adjustments we have taken or may take in the future will not negatively affect Xyrem sales volumes and revenues from Xyrem.

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

- the introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, Xyrem in the treatment of cataplexy and/or EDS in narcolepsy, including our recently-launched product, Sunosi™ (solriamfetol);
- the introduction of a generic version of Xyrem in the U.S. market before the entry dates specified in our settlements with the abbreviated new drug application, or ANDA, filers or on terms that are different from those contemplated by the settlement agreements;
- increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including pressure to agree to discounts, rebates or other restrictive pricing terms for Xyrem;
- changes in healthcare laws and policy, including changes in requirements for patient assistance programs, rebates, reimbursement and coverage by federal healthcare programs, and changes resulting from increased scrutiny on pharmaceutical pricing and risk evaluation and mitigation strategy, or REMS, programs by government entities;
- changes to or uncertainties around our Xyrem REMS, or any failure to comply with our REMS obligations to the satisfaction of the FDA;
- challenges to our intellectual property around Xyrem, including the possibility of new ANDA or new drug application, or NDA, filers or new post-grant patent review proceedings;
- operational disruptions at the Xyrem central pharmacy;
- any supply or manufacturing problems, including any problems with our sole source Xyrem active pharmaceutical ingredient, or API, provider;
- continued acceptance of Xyrem by physicians and patients, including as a result of negative publicity that surfaces from time to time; and
- changes to our label, including new safety warnings or changes to our boxed warning, that further restrict how we market and sell Xyrem.

If sales of Xyrem were to decline significantly, we might need to reduce our operating expenses or seek to raise additional funds, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including on our ability to acquire, in-license or develop new products to grow our business.

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

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

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

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

Any ANDA holder launching an AG Product or another generic sodium oxybate product will establish the price of the AG Product and/or its own generic sodium oxybate product. Generic competition often results in decreases in the prices at which branded products can be sold. After any introduction of a generic product, whether or not it is an AG Product, a significant percentage of the prescriptions written for Xyrem may be filled with the generic product. Certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. This would result in reduction in sales of, and revenue from, Xyrem, although we would continue to receive royalty and other revenue based on sales of an AG Product in accordance with the terms of our settlement agreements. For more information on the impact of generic competition, see the risk factors under the heading "*Adequate coverage and reimbursement from third party payors may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably*" and "*The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition"* in this Part II, Item 1A.

It is possible that additional companies may file ANDAs seeking to market a generic version of Xyrem which could lead to additional patent litigation or challenges with respect to Xyrem. Such patent litigation or challenges could potentially trigger acceleration of the launch dates in our settlement agreements. For example, the launch dates in our settlement agreements

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

Another circumstance that could trigger acceleration of West-Ward's launch date for an AG Product, which would also accelerate Amneal, Lupin and Par's launch dates for their AG Products and ultimately could lead to acceleration of the other settling ANDA filers' launch dates for their generic sodium oxybate products, is a substantial reduction in Xyrem net sales. Such a reduction could occur under various circumstances, including if we introduce, or a third party introduces, a product to treat EDS or cataplexy in narcolepsy that leads to a substantial decline in Xyrem net sales prior to January 1, 2023. For example, we are developing JZP-258, an oxybate product candidate that contains 92% less sodium than Xyrem, for the treatment of cataplexy and EDS in adult patients with narcolepsy. In March 2019, we announced positive top-line results from a Phase 3 study of JZP-258, and we expect to submit an NDA for this product by as early as the end of 2019. Given the well-accepted relationship between dietary sodium and blood pressure as well as published hypertension guidelines underscoring that excessive consumption of sodium is independently associated with an increased risk of stroke, cardiovascular disease and other adverse outcomes, we believe that significantly lowering sodium intake would be beneficial for patients. Other companies may similarly develop a sodium oxybate product for treatment of narcolepsy, using an alternative formulation or a different delivery technology, and seek approval in the U.S. using an NDA approval pathway under Section 505(b)(2) and referencing the safety and efficacy data for Xyrem, which could lead to additional patent litigation or challenges. We are aware that a company called Avadel Pharmaceuticals plc, or Avadel, is conducting a Phase 3 clinical trial of a once-nightly formula of sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy, and has indicated that it intends to seek approval using the Section 505(b)(2) approval pathway. Approval and successful commercialization of JZP-258, or Avadel's sodium oxybate formulation, or any other new non-generic sodium oxybate or other product for treatment of narcolepsy patients could negatively impact our ability to maintain and grow sales of Xyrem.

Although, as noted above, Xyrem is currently the only product approved by the FDA and marketed in the U.S. for the treatment of cataplexy associated with narcolepsy, we are aware that prescribers often prescribe branded or generic medications for cataplexy before prescribing or instead of prescribing Xyrem, and that payors often require patients to try such medications before they will cover Xyrem, even if they are not labeled for this use. For example, prescribers often treat mild cataplexy with drugs that have not been approved by the FDA for this indication, including tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors. We are also aware that branded or generic stimulants may be prescribed off label for treatment of EDS in narcolepsy. Wake-promoting agents Provigil® (modafinil) and Nuvigil® (armodafinil), and their generic equivalents are labeled for treatment of EDS in narcolepsy and other conditions, and may be used in conjunction with or instead of Xyrem. Prescribers often prescribe these medications before prescribing or instead of prescribing Xyrem, and payors often require patients to try such medications before they will cover Xyrem.

It is possible that additional branded or generic products may be introduced to treat symptoms of narcolepsy that will also be prescribed before or instead of Xyrem, or that payors will require patients to try before they will cover Xyrem, or that payors will exclude Xyrem from formulary coverage in favor of a newly-launched product. For more information, see the risk factor under the heading "*Adequate coverage and reimbursement from third party payors may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably*" in this Part II, Item 1A. Our product, Sunosi, is an example of a new market entrant recently approved by the FDA to improve wakefulness in adult patients with EDS associated with narcolepsy or obstructive sleep apnea, or OSA. Another example is pitolisant, a drug that has already been approved in Europe to treat adult patients with narcolepsy with or without cataplexy. Published data and prescribing patterns in the European Union, or EU, suggest that pitolisant would likely be appropriately used in patients with less severe cataplexy than those treated with Xyrem. While pitolisant is not currently approved in the U.S., Harmony Biosciences LLC, which has exclusive U.S. rights to seek approval of and commercialize pitolisant, has established an expanded access program for pitolisant, received Breakthrough Therapy and Fast Track designations from the FDA and, in February 2019, announced that the FDA had accepted its pitolisant NDA for filing with priority review.

Non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy, even if not directly competitive with Xyrem, could have the effect of changing treatment regimens and payor coverage of Xyrem, which could materially and adversely affect sales of Xyrem.

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

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

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

In October 2018, the FDA approved a modification to the Xyrem REMS in connection with our submission of our pediatric supplemental NDA to include information for pediatric patients and their caregivers and, in March 2019, we completed the implementation of the approved REMS modification. We have also submitted and expect to continue to submit ongoing assessments as required by the FDA. However, we cannot guarantee that the ongoing assessments will be completed on our expected timing or be satisfactory to the FDA, or that the operation of the Xyrem REMS will satisfy the FDA's expectations in its evaluation of the Xyrem REMS on an ongoing basis.

We depend on outside vendors, including the central certified pharmacy, to implement the requirements of the Xyrem REMS. We have an exclusive agreement with Express Scripts Specialty Distribution Services, Inc., the central pharmacy for Xyrem, which expires on July 1, 2020. The agreement may be terminated by either party at any time without cause on 180 days' prior written notice to the other party. If the central pharmacy fails to meet the requirements of the Xyrem REMS applicable to the central pharmacy or otherwise does not fulfill its contractual obligations to us, provides timely notice that it wants to terminate our agreement, refuses or fails to adequately serve patients, or fails to promptly and adequately address operational challenges or challenges in implementing REMS modifications, the fulfillment of Xyrem prescriptions and our sales would be adversely affected. If we change to a new central pharmacy, new contracts might be required with government payors and other insurers who pay for Xyrem, and the terms of any new contracts could be less favorable to us than current agreements. In addition, any new central pharmacy would need to be registered with the U.S. Drug Enforcement Administration, or DEA, and certified and would also need to implement the particular processes, procedures and activities necessary to distribute Xyrem under the Xyrem REMS. Transitioning to a new pharmacy could result in product shortages, which would negatively affect sales of Xyrem, result in additional costs and expenses for us and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

A generic version of a drug subject to a REMS with ETASU is required to have the same REMS as the brand drug, and generics and brands are mandated to use a single shared system REMS. However, the FDA may waive this requirement for a

single shared system and approve an ANDA with a separate REMS with differing but comparable aspects of ETASU under certain circumstances. In its approval of West-Ward's ANDA, the FDA waived the shared REMS requirement, approving West-Ward's ANDA with a generic sodium oxybate REMS, on the condition that the generic sodium oxybate REMS be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. In connection with the waiver, FDA issued a statement that it considers the generic sodium oxybate REMS to have the same ETASU as the Xyrem REMS and operationalizes those elements in a comparable manner to achieve the same level of safety as the Xyrem REMS. However, the generic sodium oxybate REMS, unlike the Xyrem REMS, permits multiple certified pharmacies and multiple databases that are connected via an electronic "switch" system. The generic sodium oxybate REMS also requires the certified pharmacies in its system to contact the Xyrem REMS program to verify that the patient has no other active prescriptions for Xyrem that overlap with the generic prescription to be filled and to identify any patient and prescriber disenrollments from the Xyrem system for suspected abuse, misuse and diversion.

We were not involved in development of the generic sodium oxybate REMS and were not consulted regarding any features of this REMS. A sodium oxybate distribution system that is less restrictive than the Xyrem REMS, such as the generic sodium oxybate REMS, which provides that generic sodium oxybate products and potentially sodium oxybate products approved under a Section 505(b)(2) NDA approval pathway could be distributed through multiple pharmacies, could increase the risks associated with sodium oxybate distribution. Because patients, consumers and others may not differentiate generic sodium oxybate from Xyrem or differentiate between the different REMS programs, any negative outcomes, including risks to the public, caused by or otherwise related to a separate sodium oxybate REMS, could have a significant negative impact in terms of product liability, our reputation and good will, public acceptance of Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xyrem, any of which could have a material adverse effect on our Xyrem business.

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

REMS programs have increasingly drawn public scrutiny from the U.S. Congress, the Federal Trade Commission, or FTC, and the FDA, with allegations that such programs are used as a means of improperly blocking or delaying competition. The U.S. Congress, for example, has introduced proposed legislation aimed at preventing companies from using REMS and other restricted distribution programs as a means to deny potential competitors access to product samples needed for bioequivalence testing. The FDA has stated that it will seek to coordinate with the FTC in identifying and publicizing practices the FTC finds to be anticompetitive and has further stated that the FDA has concerns related to the role of REMS programs in delaying approval of generic products. For example, in May 2018, FDA published a list of companies that it said had potentially been blocking access to the samples of their branded products, including one of our subsidiaries that sells FazaClo® (clozapine, USP) through a REMS program. It is possible that the FTC, the FDA, other governmental authorities or other third parties could claim that, or launch an investigation into whether, we are using our REMS programs in an anticompetitive manner or have engaged in other anticompetitive practices. The Federal Food, Drug and Cosmetic Act further states that a REMS ETASU shall not be used by an NDA holder to block or delay generic drugs or drugs covered by an application under Section 505(b)(2) from entering the market. In its 2015 letter approving the Xyrem REMS, the FDA expressed concern that we were aware that the Xyrem REMS could have the effect of blocking or delaying generic competition. We cannot predict whether we would face a government investigation or a complaint by a third party premised on a claim that the Xyrem REMS is blocking competition, or the outcome or impact of any such claim.

Pharmaceutical companies, including their agents and employees, are required to monitor adverse events occurring during the use of their products and report them to the FDA. The patient counseling and monitoring requirements of the Xyrem REMS provide more extensive information about adverse events, including deaths, than is generally available for other products that are not subject to similar REMS requirements. As required by the FDA and other regulatory agencies, the adverse event information that we collect for Xyrem is regularly reported to the FDA and could result in the FDA requiring changes to Xyrem labeling, including additional warnings or additional boxed warnings, or requiring us to take other actions that could have an adverse effect on patient and prescriber acceptance of Xyrem. As required by the FDA, Xyrem's current labeling includes a boxed warning regarding the risk of central nervous system depression and misuse and abuse.

Any failure to demonstrate our substantial compliance with the REMS or any other applicable regulatory requirements to the satisfaction of the FDA or another regulatory authority could result in such regulatory authorities taking actions in the future

which could have a material adverse effect on Xyrem sales and therefore on our business, financial condition, results of operations and growth prospects. For more information, see the risk factor under the heading "*In addition to those specifically described in other risk factors, we are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products*" in this Part II, Item 1A.

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

In addition to Xyrem, we are commercializing a portfolio of products, including our other lead marketed products, Erwinaze, Defitelio and Vyxeos. We also are in the early stages of launching and commercializing Sunosi, which received FDA approval in March 2019 and was launched in the U.S. in July 2019. We are making significant investments in maximizing the value and therapeutic reach of Defitelio, Vyxeos and Sunosi by conducting additional research and development activities, which include generating additional supportive clinical data and seeking regulatory approval for new indications, as appropriate. Our inability to effectively commercialize Defitelio, Vyxeos and Sunosi and to maximize their potential where possible through successful research and development activities, and our inability to retain rights to Erwinaze after the current contract terminates, could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Erwinaze

Erwinaze® (asparaginase *Erwinia chrysanthemi*) is a treatment approved in the U.S. and in certain markets in Europe (where it is marketed as Erwinase®) for patients with acute lymphoblastic leukemia, or ALL, who have developed hypersensitivity to *E. coli*-derived asparaginase. Erwinaze is licensed from, and manufactured by, a single source, Porton Biopharma Limited, or PBL, a company that is wholly owned by the UK Department of Health and Social Care. In February 2019, we received a contract termination notice from PBL. As a result of our receipt of the contract termination notice, our license and supply agreement with PBL, which includes our license for Erwinaze, will expire on December 31, 2020. We and PBL had been engaged in discussions related to entry into a replacement agreement to extend the term of our commercial relationship past 2020, but we did not reach agreement. Unless we and PBL enter into a new agreement, we will lose our rights to Erwinaze effective December 31, 2020, other than our right to sell certain Erwinaze inventory for a post-termination sales period of 12 months. In such event, we may not be able to replace the product sales we would lose from Erwinaze, which in 2018 totaled $174.7 million, and our business, financial condition, results of operations and growth prospects would be materially adversely affected. In addition, we cannot predict whether and to what extent uncertainty related to our rights to, and availability of, Erwinaze after 2020 will negatively impact sales of and revenues from this product.

A continuing and significant challenge to our ability to maintain sales of Erwinaze and a barrier to increasing sales is PBL's inability to consistently supply product adequate to meet market demand. PBL's product quality and manufacturing issues have resulted, and continue to result, in supply disruptions, and our need for PBL to minimize or avoid additional supply disruptions due to capacity constraints, production delays, quality or regulatory challenges and other manufacturing difficulties. In addition, we have incurred and continue to incur significant internal and external costs and expenses as a result of these issues, including due to managing the increased need for regulatory and customer interaction. See the discussion regarding Erwinaze supply issues in the risk factor under the heading "*Delays or problems in the supply of our products for sale or our for use in clinical trials, loss of our single source suppliers or failure to comply with manufacturing regulations could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A.

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

- the limited population of patients with ALL, and the incidence of hypersensitivity reactions to *E. coli*-derived asparaginase within that population;
- the development and/or approval of new asparaginase treatments or treatment protocols for ALL that may not include asparaginase-containing regimens and prescribers' use of alternate methods to address hypersensitivity reactions;
- the failure to obtain regulatory approval from the FDA or UK Medicines and Healthcare Products Regulatory Agency, or MHRA, to release batches of Erwinaze requiring batch-specific approval due to quality and manufacturing issues;
- difficulties with obtaining and maintaining favorable pricing and reimbursement arrangements;
- potential competition from future biosimilar products;
- PBL's ability to meet the manufacturing post-marketing commitments imposed by the FDA in connection with its approval of our biologics license application, or BLA;
- our failure to comply with obligations under our agreement with PBL resulting in PBL claiming an uncured material breach; and

- our need to apply for and receive marketing authorizations, through the EU's, mutual recognition procedure or otherwise, in certain additional countries if we decide to launch promotional efforts in those countries.

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

To expand our asparaginase franchise beyond Erwinaze, we are pursuing activities related to the development of improved asparaginase products for patients with ALL or other hematological malignancies. Several of our external research and development collaborations are focused on these efforts, including our agreement with Pfenex, Inc., or Pfenex, which includes worldwide rights to develop and commercialize multiple early-stage hematology product candidates and an option to negotiate a license for a recombinant pegaspargase product candidate, and our agreement with XL-protein GmbH, or XLp, for rights to use XLp's PASylation® technology to extend the plasma half-life of selected asparaginase product candidates. Among the product candidates in collaboration with Pfenex is JZP-458, a recombinant crisantaspase product candidate, for the potential treatment of ALL and lymphoblastic lymphoma for which we plan to commence a single-arm, pivotal Phase 2/3 clinical trial by the end of 2019. If these activities are unsuccessful, our growth prospects could be materially adversely affected.

Defitelio

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

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

- the continued acceptance of Defitelio in the U.S., the EU and other countries by hospital pharmacy and therapeutics committees and the continued availability of favorable pricing and adequate coverage and reimbursement by government programs and third party payors;
- the limited experience of, and need to educate, physicians in recognizing, diagnosing and treating VOD, particularly in adults;
- the possibility that physicians recognizing VOD symptoms may not initiate or may delay initiation of treatment while waiting for those symptoms to improve, or may terminate treatment before the end of the recommended dosing schedule;
- our ability to successfully maintain or grow sales of Defitelio in Europe and other non-U.S. countries, including our ability to obtain marketing approval in new countries;
- delays or problems in the supply or manufacture of the product;
- the limited size of the population of VOD patients who are indicated for treatment with Defitelio (particularly if changes in HSCT treatment protocols reduce the incidence of VOD diagnosis);
- our ability to meet the post-marketing commitments and requirements imposed by the FDA in connection with its approval of our NDA and by the European Commission, or EC, in connection with its marketing authorization granted "under exceptional circumstances"; and
- our ability to maintain favorable pricing and reimbursement approvals across Europe, particularly in countries that represent significant markets.

To expand the potential of Defitelio, our clinical development strategy generally focuses on the prevention and treatment of serious diseases associated with endothelial cell damage, including an ongoing Phase 3 clinical trial in prevention of VOD in high-risk patients following HSCT, ongoing Phase 2 trials in prevention of acute Graft versus Host Disease following allogeneic HSCT, and planned Phase 2 trials in the treatment of transplant-associated thrombotic microangiopathy and the prevention of chimeric antigen receptor T-cell therapy-, or CAR-T-, associated neurotoxicity. In addition to clinical trials we are sponsoring, there are more than 20 investigator-sponsored trials ongoing in the U.S. and EU to evaluate defibrotide in multiple conditions. If these development activities are unsuccessful, our growth prospects could be materially adversely affected.

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

Vyxeos

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

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

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

To expand the potential of Vyxeos, our clinical development strategy is designed to target potential new patient segments across the AML landscape, to pursue indications related to myelodysplastic syndrome and to generate clinical data on Vyxeos when used in combination with other therapeutic agents. We are pursuing this strategy by sponsoring clinical trials, working with cooperative groups who are conducting clinical trials and partnering with The University of Texas MD Anderson Cancer Center to evaluate potential treatment options for hematologic malignancies, with a near-term focus on Vyxeos. In addition, there are multiple investigator-sponsored trials ongoing. Because combination regimens and the continual generation of new data have become particularly important in AML, if we are unable to initiate multiple combination studies, safely combine Vyxeos with novel agents, or if efficacy results do not meet clinicians' expectations, our growth prospects could be materially adversely affected.

If sales of Vyxeos do not reach the levels we expect, our anticipated revenue from the product will be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Sunosi

Sunosi™ (solriamfetol) is a product approved in the U.S. to improve wakefulness in adult patients with EDS associated with narcolepsy or OSA. Sunosi was launched in the U.S. in July 2019, and our launch of this product is at an early stage. Sunosi faces competition from existing branded and generic products that treat EDS or improve wakefulness in adult patients with narcolepsy or OSA in a competitive retail pharmacy market. For further discussion of the competition that Sunosi faces, see the risk factor under the heading "*We face substantial competition from other companies, including companies with larger sales organizations and more experience working with large and diverse product portfolios*" in this Part II, Item 1A.

We submitted a marketing authorization application, or MAA, for solriamfetol for the potential treatment of EDS in adult patients with narcolepsy or OSA to the European Medicines Agency, or EMA, in the fourth quarter of 2018. We cannot predict whether our solriamfetol MAA will be approved in a timely manner, or at all. If we fail to obtain approval for solriamfetol in the EU, or if the EC requires product labeling that negatively impacts patient, physician or payor acceptance of the product, our growth prospects could be materially adversely affected.

In addition to challenges and uncertainties related to Sunosi competition and obtaining regulatory approval of solriamfetol in the EU, our ability to realize the anticipated benefits from our investment in Sunosi is subject to a number of

risks and uncertainties, including the following as well as other risks and uncertainties described elsewhere in this Part II, Item 1A:

- our ability to successfully launch and grow sales of Sunosi in the U.S. and, if approved, in the EU;
- our ability to obtain marketing approval, successfully launch and grow sales of Sunosi in other non-U.S. countries;
- the availability of adequate formulary positions and pricing and adequate coverage and reimbursement by third party payors, including government programs, including the impact of any delays in coverage decisions by payors;
- restrictions on permitted promotional activities based on any additional limitations on the labeling for the product that may be required by the FDA in the future and any such limitations that may be required by the EC or other regulatory authority on any approved labeling;
- market acceptance of Sunosi;
- delays or problems in the supply or manufacture of Sunosi; and
- our ability to satisfy the FDA's post-marketing requirements and other post-marketing requirements or commitments, if any, imposed by the EC in connection with its potential marketing authorization.

To expand the potential of Sunosi, our clinical development strategy is designed to target potential new indications for solriamfetol for the potential treatment of EDS in other sleep or central nervous system disorders, including pursuing development activities for solriamfetol for the potential treatment of EDS in patients with major depressive disorder, or MDD. If these development activities are unsuccessful, our growth prospects could be materially adversely affected.

If we are unable to successfully launch and commercialize Sunosi in the U.S., if we are unable to obtain approval of our solriamfetol MAA in a timely manner, or at all, if the EC requires product labeling that negatively impacts patient, physician or payor acceptance of the product, or if sales of Sunosi in the U.S. and EU (if approved) do not reach the levels we expect, our anticipated revenue from Sunosi will be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

For a discussion of the risks inherent in implementing our research and clinical development strategy with respect to Defitelio, Vyxeos, and Sunosi, see the discussion in the risk factor under the heading "*Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A.

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

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

We also face competition, and may in the future face additional competition, from manufacturers of generic drugs. Certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. Generic competition often results in decreases in the net revenue for branded products.

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, are more convenient or are less expensive than our products.

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

While there is currently no direct competition to Erwinaze to treat ALL patients with hypersensitivity to *E. coli*-derived asparaginase, other companies have developed or are developing new treatments for ALL. Some new asparaginase treatments could reduce the rate of hypersensitivity in patients with ALL, and new treatment protocols are being developed and approved for ALL that may not include asparaginase-containing regimens, including some for the treatment of relapsed or refractory ALL patients. We have experienced frequent intermittent shortages of the product that have impacted prescribing habits for

Erwinaze, including prescribers' use of alternate methods to address hypersensitivity reactions. The development of these new treatments could negatively impact our ability to maintain, and potentially in the future grow, sales of Erwinaze in patient populations where the benefit of an asparaginase-containing regimen is not well established. As a biologic product, Erwinaze also faces potential competition from biosimilar products.

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

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

Sunosi faces competition from existing branded and generic products that treat EDS or improve wakefulness in adult patients with narcolepsy or OSA in a competitive retail pharmacy market. To successfully launch and commercialize Sunosi, we need to differentiate Sunosi from other branded and generic products that treat EDS in patients with narcolepsy with which physicians are more familiar, including stimulants, wake-promoting agents, such as Provigil and Nuvigil, and generic versions of stimulants and wake-promoting agents. We are also aware that stimulants are prescribed for patients to treat excessive sleepiness in OSA. Sunosi will likely face competition from this genericized market. In addition, we are aware of several other products in development as potential treatments for EDS 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, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources than we do. They can spend more on, and have more expertise in, research and development, regulatory, manufacturing, distribution and sales and marketing activities. As a result, our competitors may obtain FDA or other regulatory approvals for their product candidates more rapidly than we can and may market their products more effectively than we do. Smaller or earlier stage companies may also prove to be significant competitors, particularly through focused development programs and collaborative arrangements with large, established companies.

We have a relatively small number of sales representatives compared with most other pharmaceutical companies with marketed products. Each of our sales representatives is responsible for a territory of significant size. Many of our competitors deploy more personnel to market and sell their products than we do. In particular, we compete with companies with extensive sales, marketing and promotional experience in hematology/oncology markets, and our failure to compete effectively in this area could negatively affect sales of our hematology/oncology products. If our sales force and sales support organization are not appropriately resourced and sized to adequately promote our products, the commercial potential of our current and any future products may be diminished.

The growth of our current products and the launch of any future products may require expansion of our sales force and sales support organization, and we may need to commit significant additional funds, management and other resources to such growth. We may not be able to expand in a timely or cost-effective manner, or we may not have the financial resources to achieve the necessary growth. We also compete with other companies to recruit, hire, train and retain pharmaceutical sales and marketing personnel, and excessive turnover in such personnel could negatively affect sales of our products.

Adequate coverage and reimbursement from third party payors may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably.

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

Third party payors' reimbursement practices are complex, vary widely from payor to payor and can impose time-consuming burdens for patients and prescribing physicians. As part of the overall trend toward cost containment, third party

payors often require prior authorization for, and require reauthorization for continuation of, prescription products or impose step edits, which require prior use of another medication, usually a generic or preferred brand, prior to approving coverage for a new or more expensive product. Such restrictive conditions for reimbursement and an increase in reimbursement-related activities can extend the time required to fill prescriptions and may discourage patients from seeking treatment. For example, we are experiencing increasingly restrictive conditions for reimbursement required by some third party payors for Xyrem, which have extended the time required to fill some prescriptions and could continue to do so in the future and which may have a material effect on the overall level of reimbursement coverage for Xyrem. Moreover, other companies with products that compete with ours may seek to disadvantage our products' reimbursement coverage or formulary position with third party payors, leading to reduced access for our patients. We cannot predict actions that third party payors may take, or whether they will limit the access and level of reimbursement for our products or refuse to provide any approvals or coverage. From time to time, third party payors have refused to provide reimbursement for our products, and others may do so in the future.

Reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a significant impact on the prescribing physicians' willingness to prescribe our products. For example, the U.S. federal government follows a Medicare severity diagnosis-related group, or MS-DRG, payment system for certain inpatient hospital services provided under Medicare, which some states also use for Medicaid. The MS-DRG system entitles a hospital to a fixed reimbursement based on discharge diagnoses rather than actual costs incurred in providing inpatient treatment, thereby increasing the incentive for the facility to limit or control expenditures for many healthcare products. For our hematology/oncology products, all of which are used primarily or exclusively in the inpatient hospital setting, there may not be sufficient reimbursement under the relevant MS-DRG to fully cover the cost of our products. This risk is in part mitigated by a New Technology Add-on Payment, or NTAP, which is in addition to the MS-DRG-based reimbursement that hospitals receive. In 2017, Centers for Medicare and Medicaid Services, or CMS, approved an NTAP for Defitelio, which was renewed by CMS for 2018 and 2019. NTAP designations are reviewed by CMS on a yearly basis and may only be renewed for two years. Because Defitelio has already been renewed twice, the product will not be eligible for renewal after 2019. For 2019, CMS approved an NTAP for Vyxeos, but we cannot guarantee that CMS will renew our NTAP for Vyxeos for 2020.

In addition, a significant portion of our revenue from our hematology/oncology products, particularly Erwinaze and Vyxeos, is obtained through government payors, including Medicare, Medicaid and similar types of payors in other countries, and any failure to qualify for or receive adequate reimbursement under those programs, including as a result of legislative changes to these programs, would have a material adverse effect on revenues from such products. Significant attention has been paid to legislation proposing federal rebates on Medicare Part D and Medicare Advantage utilization for drugs issued to certain groups of lower income beneficiaries and the desire to change the provisions that treat these dual-eligible patients differently from traditional Medicare patients. Any such changes could have a negative impact on revenues from sales of our affected products. Any failure to cover our products appropriately, in addition to legislative and regulatory changes and others that may occur in the future, could impact our ability to maximize revenues in the federal marketplace.

Medicaid and other governmental programs are described under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2018. For a discussion of specific risks relating to our reporting and payment obligations to government payors, see the risk factor under the heading "*If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects*" in this Part II, Item 1A. Third party payors outside the federal government are also increasingly considering new metrics as the basis for reimbursement rates, including those used by federal government payors such as average net sales price, average manufacturer price and actual acquisition cost. It is not possible to predict the impact of these evolving reimbursement mechanics on the willingness of payors to cover our products.

Third party payors increasingly examine the cost effectiveness of pharmaceutical products, in addition to their safety and efficacy, when making coverage and reimbursement decisions. We may need to conduct expensive pharmacoeconomic and/or clinical studies in order to demonstrate the cost-effectiveness of our products. Even with such studies, our products may be considered less safe, less effective or less cost-effective than other products, and third party payors may not provide and maintain coverage and reimbursement for our products. If our competitors offer their products at prices that provide lower treatment costs than our products, or otherwise suggest that their products are safer, more effective or more cost-effective than our products, this may result in a greater level of access for their products relative to our products, which would reduce our sales and harm our results of operations. In some cases, for example, third party payors try to encourage the use of less expensive generic products through their prescription benefits coverage and reimbursement and co-pay policies. Because some of our products compete in a market with both branded and generic products, obtaining and maintaining access and reimbursement coverage for our products may be more challenging than for products that are new chemical entities for which no therapeutic alternatives exist.

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

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

Sunosi, which was approved by the FDA in March 2019 to improve wakefulness in adults with EDS associated with narcolepsy or OSA and was launched in the U.S. in July 2019, is being commercialized in a competitive retail pharmacy market of branded and generic products. Any delays or unforeseen difficulties in obtaining access or reimbursement approvals could adversely impact our commercial launch and the growth prospects for Sunosi. Third party payors could impose step edits that require patients to try alternative, including generic, treatments before authorizing payment for Sunosi, exclude Sunosi from formulary coverage lists, limit the types of diagnoses for which coverage will be provided or demand rebates, discounts, exclusivity or other concessions for Sunosi and potentially our other products. Additionally, at launch, many payors impose a moratorium on coverage for products while the payor makes a coverage decision. These potential utilization management strategies could limit patient access to Sunosi and depress therapy adherence rates. We expect to enter into rebate agreements with third party payors in an effort to obtain adequate formulary positions for Sunosi. We cannot predict market acceptance of, and our ability to obtain or maintain adequate formulary positions, access to and reimbursement coverage for Sunosi. An inability to obtain or maintain adequate formulary positions could increase patient cost-sharing for Sunosi and cause some patients to determine not to use Sunosi. If we are unsuccessful in obtaining broad coverage for Sunosi, our anticipated revenue from and growth prospects for Sunosi could be negatively affected. For more information on Sunosi, see the risk factor under the heading "*While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products.*" in this Part II, Item 1A.

In addition, new products indicated for the treatment of symptoms of narcolepsy, like pitolisant (if approved by the FDA) and Sunosi, could impact access to Xyrem, particularly for newly diagnosed narcolepsy patients, if, for example, payors impose a step edit requiring a narcolepsy patient to try another medicine before authorizing payment for Xyrem, or exclude Xyrem from formulary coverage in favor of a newly-launched product.

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

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

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U.S. We expect there will continue to be legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably.

Policies to address healthcare costs and drug pricing have been identified as high priorities by both major political parties. We anticipate that the U.S. Congress, state legislatures, regulators and the private sector will continue to consider and may adopt healthcare policies and reforms intended to curb healthcare costs. These cost containment measures may include federal and state controls on government-funded reimbursement for drugs (including Medicare and Medicaid), new or increased requirements to pay prescription drug rebates and penalties to government health care programs, and additional pharmaceutical cost transparency bills that aim to require drug companies to justify their prices through required disclosures.

There is increasing bipartisan support and activity within the U.S. Congress, and continuing support by the Trump Administration, for drug pricing reform-related policies. Specific reforms that may be enacted or implemented remain uncertain, both as to their final substance and timing, and may affect a broad range of public policy considerations, the Medicare and Medicaid programs and the FDA regulatory regime, including the potential authorization of prescription drug

importation from other countries, the approval of generic drugs and changes to REMS provisions related to generic products, legislative proposals to limit the terms of patent litigation settlements with generic sponsors, redefine certain conduct around patenting and new product development as unfair competition, create a private right of action related to access to samples of innovator products and ease the approval of REMS for generic applicants. In addition, heightened scrutiny of drug pricing-related issues by the U.S. Congress, the Trump Administration, the media and other stakeholders is expected to continue. All such considerations may adversely affect our business in ways that we cannot accurately predict.

There is also ongoing activity related to the Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act of 2010, together, the Healthcare Reform Act. The Healthcare Reform Act has substantially changed the way healthcare is financed by both governmental and private insurers. These changes have impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment-for-performance initiatives. Some of the provisions of the Healthcare Reform Act have yet to be fully implemented, and certain provisions have been subject to judicial and Congressional challenges, including pending litigation in which several states and the Trump Administration have taken the position that the Healthcare Reform Act in its entirety is invalid. In addition, there have been efforts by the Trump Administration to repeal or replace certain aspects of the Healthcare Reform Act and to alter the implementation of the Healthcare Reform Act and related laws. Additional legislative and regulatory changes and judicial challenges related to the Healthcare Reform Act remain possible. For example, while "repeal and replace" efforts by the Trump Administration and the U.S. Congress have failed, aspects of the Healthcare Reform Act have been changed legislatively, such as the repeal of the requirement that certain individuals who fail to maintain qualifying health coverage for all or part of a year make a tax-based shared responsibility payment commonly referred to as the "individual mandate." In addition, there have been delays in the implementation of key provisions of the Healthcare Reform Act, including the excise tax on generous employer-based health plans. We expect that the Healthcare Reform Act and its implementation, efforts to repeal or replace, or invalidate, the Healthcare Reform Act or portions thereof and other healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of our products.

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 July 2019, and may do so again in the future. We also have made and may in the future make similar price increases on our other products. There is no guarantee that such price adjustments will not negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our products, which could limit the prices that we charge for our products, including Xyrem, limit the commercial opportunities for our products and/or negatively impact revenues from sales of our products.

If we become the subject of any future government investigation or U.S. Congressional hearing with respect to drug pricing or other business practices, we could incur significant expense and could be distracted from operation of our business and execution of our strategy. Any such investigation or hearing could also result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. For more information, see the risk factor under the heading "*In addition to those specifically described in other risk factors, we are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products*" in this Part 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, which could have an adverse impact on reimbursement status. We cannot predict the outcome of any periodic reviews required to maintain pricing and reimbursement approvals across Europe. In addition, orphan products that have a significant impact on patient survival, such as Defitelio, may be budgeted on a local rather than national level. The balance of all of these factors will determine our ability to maintain favorable pricing and reimbursement approvals across Europe. Furthermore, after initial pricing and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or external reference pricing, which consists of arbitrage between low-priced and high-priced countries. Changes in the pricing of our medicinal products in one of the EU member states could, therefore, affect the price of our medicinal products in other EU member states. If we are unable to maintain favorable pricing and reimbursement approvals in EU member states that represent significant markets, especially where an EU member state's reimbursed price influences other EU member states, our anticipated revenue from and growth prospects for our products in the EU could be negatively affected.

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

In various EU member states we expect to be subject to continuous cost-cutting measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including those representing the larger markets. The HTA process, which is currently governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU member states, although a recently proposed EU regulation governing HTA procedures may lead to harmonization.

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

We expect that legislators, policymakers and healthcare insurance funds in the EU member states will continue to propose and implement cost-containing measures to keep healthcare costs down. Such measures could include limitations on the prices we will be able to charge for our products or the amounts of reimbursement available for these products from governmental authorities or third party payors, may increase the tax obligations on pharmaceutical companies, or may facilitate the introduction of generic competition with respect to our products. Further, an increasing number of EU member states and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere. Moreover, in order to obtain reimbursement for our products in some European 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 Europe. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted, could negatively affect our growth prospects in Europe.

In addition to access, coverage and reimbursement, the commercial success of our products depends upon their market acceptance by physicians, patients, third party payors and the medical community.

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

- the clinical indications for which a product is approved and any restrictions placed upon the product in connection with its approval, such as a REMS, patient registry requirements or labeling restrictions;
- the prevalence of the disease or condition for which the product is approved and its diagnosis;
- the severity of side effects;
- acceptance by physicians and patients of each product as a safe and effective treatment;
- availability of sufficient product inventory to meet demand, particularly with respect to Erwinaze;
- physicians' decisions relating to treatment practices based on availability of product, particularly with respect to Erwinaze;
- perceived advantages over alternative treatments;
- relative convenience and ease of administration;
- with respect to Xyrem, physician and patient assessment of the burdens associated with obtaining or maintaining the certifications required under the Xyrem REMS;
- the cost of treatment in relation to alternative treatments, including generic products; and
- the availability of financial or other assistance for patients who are uninsured or underinsured.

Because of our dependence upon market acceptance of our products, any adverse publicity associated with harm to patients or other adverse events resulting from the use or misuse of our products or any similar products distributed by other companies, including generic versions of our products, could materially and adversely affect our business, financial condition,

results of operations and growth prospects. For example, from time to time, there is negative publicity about illicit GHB and its effects, including with respect to illegal use, overdoses, serious injury and death. Because sodium oxybate, the API in Xyrem, is a derivative of GHB, Xyrem sometimes also receives negative mention in publicity relating to GHB. Patients, physicians and regulators may therefore view Xyrem as the same as or similar to illicit GHB. In addition, there are regulators and some law enforcement agencies that oppose the prescription and use of Xyrem generally because of its connection to GHB. Xyrem's label includes information about adverse events from GHB.

For additional discussion about payor acceptance, see the risk factor under the heading "*Adequate coverage and reimbursement from third party payors may not be available for our products, which could diminish our sales or affect our ability to sell our products profitably*" in this Part II, Item 1A.

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

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of process controls required to consistently produce the API and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. We and our suppliers may encounter difficulties in production, including difficulties with production costs and yields, process controls, quality control and quality assurance, including testing of stability, impurities and impurity levels and other product specifications by validated test methods, and compliance with strictly enforced U.S., state and non-U.S. regulations. In addition, we and our suppliers are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and equivalent rules and regulations prescribed by non-U.S. regulatory authorities. We have cGMP responsibilities for the products we manufacture in our facilities and also have oversight responsibilities for the manufacturing conducted by our third party suppliers operating under contract. If we or any of our suppliers encounter manufacturing, quality or compliance difficulties with respect to any of our products, we may be unable to obtain or maintain regulatory approval or meet commercial demand for such products, which could adversely affect our business, financial condition, results of operations and growth prospects. In addition, the failure of any of our suppliers to comply with cGMP or other rules and regulations while manufacturing products on our behalf could result in regulatory action directed at the adequacy of our oversight of our contract suppliers, which could result in enforcement actions against us by the FDA and other regulatory entities.

We have a manufacturing and development facility in Ireland where we manufacture Xyrem and development-stage oxybate products, including JZP-258, and a manufacturing plant in Italy where we produce the defibrotide drug substance. We currently do not have our own commercial manufacturing or packaging capability for our other products, product candidates or their APIs. As a result, our ability to develop and supply products in a timely and competitive manner depends primarily on third party suppliers being able to meet our ongoing commercial and clinical trial needs for API, other raw materials, packaging materials and finished products. For details of our arrangements with our suppliers, see "Business—Manufacturing" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2018.

In part due to the limited market size for our products and product candidates, we have a single source of supply for most of our marketed products, product candidates and their APIs. We are the sole supplier of the defibrotide compound. We have single source suppliers for sodium oxybate, the API for Xyrem, for Erwinaze, for the finished vial form of Defitelio and for Vyxeos. Single sourcing puts us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties. There is no guarantee that our suppliers can or will continue to supply on a timely basis, or at all, the quantities of API or finished product that we need. If one of our suppliers fails or refuses to supply us for any reason, it would take a significant amount of time and expense to implement and execute the necessary technology transfer to, and to qualify, a new supplier. The FDA and similar international regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and certain packaging materials used in our products. The loss of one of our suppliers could require us to obtain regulatory clearance in the form of a "prior approval supplement" and to incur validation and other costs associated with the transfer of the API or product manufacturing process. We believe that it could take up to two years, or longer in certain cases, to qualify a new supplier, and we may not be able to obtain APIs or finished products from new suppliers on acceptable terms and at reasonable prices, or at all. If there are delays in qualifying new suppliers or facilities or a new supplier is unable to meet FDA's or similar international regulatory body's requirements for approval, there could be a shortage of the affected products for the marketplace or for use in clinical studies, or both, which could negatively impact our anticipated revenues and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

Erwinaze is licensed from, and manufactured for us by, a single source, PBL. The Erwinaze BLA includes a number of post-marketing commitments related to the manufacture of Erwinaze by PBL.

In January 2017, the FDA issued a warning letter to PBL indicating that it was not satisfied with PBL's response to the FDA Form 483 issued to PBL in March 2016 and citing significant violations of cGMP for finished pharmaceuticals and

significant deviations from cGMP for APIs. In March 2017, PBL filed a response to the warning letter with the FDA. In August 2018, the FDA conducted an inspection of the PBL manufacturing facility and issued an FDA Form 483 to PBL citing observations related to items referenced in the warning letter as well as other manufacturing practices, including data and records management. PBL continues to address the issues identified by the FDA in the warning letter and has submitted its response to the August 2018 Form 483.

In the United Kingdom, or UK, where PBL's manufacturing facilities are located, PBL is subject to similar inspections conducted by the MHRA. Following a site inspection of PBL by MHRA in December 2017, MHRA issued an inspection report listing several major findings, including major deficiencies and failures by PBL to comply with cGMP. In January 2018, PBL filed a response to the report with the MHRA.

Inability to comply with regulatory requirements of the FDA, the MHRA or other competent authorities in the EU member states in which Erwinaze is subject to marketing authorization, including any failure by PBL to correct the violations and deviations referenced above to the satisfaction of the FDA and MHRA, could further adversely affect Erwinaze supply, particularly in light of the ongoing limited supply of Erwinaze, and could result in enforcement actions by the FDA, MHRA or other EU member states' competent authorities (including the issuance of the local equivalents of FDA Form 483s or warning letters), the approval of the FDA or other competent authorities being suspended, varied, or revoked, product release being delayed or suspended, including potentially the FDA refusing admission of Erwinaze in the U.S., or product being seized or recalled. Any of these actions could have a material adverse effect on our sales of, and revenues from, Erwinaze and further limit our future maintenance and potential growth of the market for this product. We have incurred and continue to incur significant internal and external costs and expenses as a result of these issues, including due to managing the increased need for regulatory and customer interaction. In addition, if the FDA or any non-U.S. regulatory authority mandates any changes to the specifications for Erwinaze, we may face challenges having product produced to meet such specifications, and PBL may increase its price to supply Erwinaze meeting such specifications, which may result in additional costs to us or a delay in supply and may decrease any profit we would otherwise achieve with Erwinaze.

All Erwinaze that PBL has been able to supply is currently completely absorbed by demand for the product. As a consequence, there is no product inventory that can be used to absorb supply disruptions resulting from quality, manufacturing, regulatory or other issues. PBL has experienced and continues to experience product quality and manufacturing issues that have resulted, and continue to result, in disruptions in our ability to supply markets from time to time and have caused, and may in the future cause, us to implement batch-specific, modified product use instructions. We have been experiencing, and continue to experience, supply disruptions globally and expect further supply disruptions in 2019 and 2020. We cannot predict whether the required remediation activities by PBL in connection with its January 2017 FDA warning letter, the December 2017 MHRA report or the August 2018 FDA Form 483 will further strain PBL's manufacturing capacity or otherwise further adversely affect Erwinaze supply. As capacity constraints and supply disruptions continue, whether as a result of continued quality or manufacturing challenges at PBL, regulatory issues or otherwise, we will be unable to build product inventory, our ability to supply the market will continue to be compromised and physicians' decisions to use Erwinaze will continue to be negatively impacted.

If PBL's quality, manufacturing or regulatory issues persist and supply disruptions continue, our agreement with PBL, which will expire on December 31, 2020, only gives us the right to engage a backup supplier for Erwinaze in very limited circumstances, such as following termination of the agreement by us due to uncured material breach or the cessation of manufacturing by our supplier. If we are required to engage a backup or alternative supplier, the transfer of technical expertise and manufacturing process to the backup or alternative supplier would be difficult, costly and time-consuming, might not be successful and would increase the likelihood of a delay or disruption in manufacturing or exacerbate the supply shortage. In addition, if our contract is not extended, there would not be sufficient time for us to engage a backup or alternative supplier before the contract expires at the end of 2020. 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.

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

Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. Given that our Vyxeos launch is still at a relatively early stage, there is limited experience with the complex manufacturing process relating to Vyxeos. Baxter manufactured batches that were used in the Phase 3 clinical trial for Vyxeos; there have since been batch failures due to mechanical, component and other issues, and batches have been produced that have otherwise not been in compliance with applicable specifications. We are continuing to work with Baxter to address manufacturing complexities. Moreover, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. Consequently, engaging an alternate manufacturer may be difficult, costly and time-consuming. If we fail to obtain a sufficient

supply of Vyxeos in accordance with applicable specifications on a timely basis for any reason or due to manufacturing or regulatory challenges, our sales of and revenues from Vyxeos, our future maintenance and potential growth of the market for this product, our ability to conduct ongoing and future clinical trials of Vyxeos, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

In addition, while the APIs in Vyxeos, daunorubicin and cytarabine are available from a number of suppliers, certain suppliers have received warning letters from the FDA. As a result, we have qualified other suppliers for each API, and we provided the qualification data to the FDA. If the FDA restricts importation of API from either supplier, and we are unable to qualify API from additional suppliers in a timely manner, or at all, our ability to successfully commercialize Vyxeos and generate sales of this product at the level we expect and to conduct ongoing and future clinical trials of Vyxeos could be materially and adversely affected.

To conduct our ongoing and any future clinical trials of, complete marketing authorization submissions for, and potentially launch our other product candidates, we need to have sufficient quantities of product manufactured. For example, Siegfried USA, LLC, or Siegfried, is our sole supplier of both the API and finished product for Sunosi for both commercial sale as well as development activities. If Siegfried does not or is not able to supply us with Sunosi 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 Sunosi.

We or our suppliers may not be able to produce sufficient supplies of our product candidates in a timely manner or in accordance with applicable specifications. If any of our suppliers fail or refuse to comply with their obligations to us under our supply and manufacturing arrangements, we may not have adequate remedies for any breach. In addition, to obtain FDA approval of any product candidate, we or our supplier or suppliers for that product must obtain approval by the FDA to manufacture and supply product, in some cases based on qualification data provided to the FDA as part of our NDA submission. Any delay in generating, or failure to generate, data required in connection with submission of the chemistry, manufacturing and controls, or CMC, portions of any NDA could negatively impact our ability to meet our anticipated submission dates, and therefore our anticipated timing for obtaining FDA approval, or our ability to obtain FDA approval at all. In addition, any failure of us or a supplier to obtain approval by the FDA to manufacture and supply product or any delay in receiving, or failure to receive, adequate supplies of a product on a timely basis or in accordance with applicable specifications could negatively impact our ability to successfully launch and commercialize products and generate sales of products at the levels we expect.

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

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

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

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

Solriamfetol

We submitted an MAA for solriamfetol to the EMA in the fourth quarter of 2018. In addition, we are targeting potential new indications for solriamfetol for the potential treatment of EDS in other sleep or central nervous system disorders, including pursuing development activities for solriamfetol for the potential treatment of EDS in patients with MDD. For more information, see the risk factor under the heading "*While Xyrem remains our largest product, our success also depends on our ability to effectively commercialize our other products*" in this Part II, Item 1A.

JZP-258

JZP-258 is an oxybate product candidate that contains 92% less sodium than Xyrem. Given the well-accepted relationship between dietary sodium and blood pressure as well as published hypertension guidelines, we believe that significantly lowering sodium intake would be beneficial for patients. On March 26, 2019, we announced positive top-line results from our Phase 3 study evaluating the efficacy and safety of JZP-258 for the treatment of cataplexy and EDS in adult patients with narcolepsy, and we expect to submit an NDA for this product by as early as the end of 2019. Although we received positive results from that Phase 3 study, we cannot guarantee the timing or acceptance of our planned NDA by the FDA. We are also conducting a Phase 3 clinical trial for use of JZP 258 for the treatment of idiopathic hypersomnia, a chronic neurological disorder that is primarily characterized by EDS. Any failure or delay in successfully completing necessary clinical trials and conducting other activities, including CMC activities, that are required to complete our planned NDA submission and obtain regulatory approval could materially and adversely affect our growth prospects. If we submit an NDA to the FDA for approval and the FDA determines that our safety or efficacy data do not warrant marketing approval, we may be required to conduct additional clinical trials, which could be costly and time-consuming, or we may not be able to commercialize JZP-258, in which event we would not receive any return on our investment.

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

For a discussion of the risks inherent in product development and regulatory approval, see the discussions in the risk factors under the headings "*Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects*" and "*The regulatory approval process is expensive, time-consuming and uncertain and may prevent us or our partners from obtaining and maintaining approvals for the commercialization of some or all of our product candidates"* in this Part II, Item 1A. If we are not successful in the clinical development of our product candidates, if we are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, or if sales of an approved product do not reach the levels we expect, our anticipated revenue from our product candidates would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

In addition to continued investment in our research and development pipeline, we intend to grow our business by acquiring or in-licensing, and developing, including with collaboration partners, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. Future growth through acquisition or in-licensing will depend upon the availability of suitable products and product candidates for acquisition or in-licensing on acceptable prices, terms and conditions.

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

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

- we or a collaboration partner are unable to obtain and maintain adequate funding to complete the development of, obtain regulatory approval for and commercialize an acquired product candidate;
- we and our collaboration partners are unable to agree on our respective contractual rights or other disputes arise between us and our collaboration partners;
- our collaborations with third parties are terminated or allowed to expire;
- a product candidate proves not to be safe or effective in later clinical trials or its development is otherwise discontinued by us or a collaboration partner;

- 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.

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

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

Any adverse events or other data generated during the course of clinical trials of our product candidates and/or clinical trials related to additional indications for our commercialized products could result in action by the FDA or a non-U.S.

regulatory agency, which may restrict our ability to sell, or adversely affect sales of, currently marketed products, or such events or other data could otherwise have a material adverse effect on a related commercial product, including with respect to its safety profile. Any failure or delay in completing such clinical trials could materially and adversely affect the maintenance and growth of the markets for the related marketed products, which could adversely affect our business, financial condition, results of operations and overall growth prospects.

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

- difficulty identifying or enrolling eligible patients, often based on the number of clinical trials, particularly in hematology and oncology, with enrollment criteria targeting the same patient population;
- difficulty identifying a clinical development pathway, including viable indications and appropriate clinical trial protocol design, particularly where there is no applicable regulatory precedent;
- 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;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites;
- failure of our third party clinical trial managers to satisfactorily perform their contractual duties, comply with regulations or meet expected deadlines; or
- insufficient funds to complete the trials.

We rely on contract research organizations and other third parties, such as cooperative groups, to assist us in designing, coordinating, managing, monitoring and otherwise conducting clinical trials with our product candidates. If we, contract research organizations assisting us with clinical trials, other third parties conducting clinical trials with our product candidates, or our trial sites fail to comply with applicable good clinical practices, the clinical data generated in these clinical trials may be deemed unreliable, and the FDA and/or other global regulatory agencies may require us to perform additional clinical trials before approving our marketing applications. In addition, clinical trials must be conducted with product candidates produced under the FDA's cGMP regulations and similar regulations outside of the U.S. Our failure, or the failure of our product suppliers, to comply with these regulations may require us to repeat or redesign clinical trials, which would delay the completion of clinical trials and the regulatory approval process.

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

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

We are not permitted to market a pharmaceutical product in the U.S. or in the EU member states until we receive approval from the FDA or a marketing authorization from the EC or the competent authorities of the EU member states, as applicable. Submission of an application for marketing authorization does not assure approval for marketing in any jurisdiction, and we may encounter significant difficulties or costs in our efforts to obtain approval to market products.

Although the Prescription Drug User Fee Act, or PDUFA, provides a ten-month deadline for the FDA to review an NDA, or a six-month deadline for priority review, there is no guarantee that the FDA will meet that deadline, and the FDA can extend a PDUFA action date under certain circumstances. If the FDA fails to meet PDUFA targeted action dates established for any of our product candidates, the commercialization of the affected product candidate could be delayed or impaired.

We submitted an MAA to the EMA in November 2018 for solriamfetol as a treatment to improve wakefulness and reduce EDS in adult patients with narcolepsy (with or without cataplexy) or OSA. We cannot predict whether we will be able to obtain marketing authorization in the EU in a timely manner and on what terms, or at all.

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

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

Even if we receive approval, an approved product may be subject to significant labeling restrictions, including limitations on the dosing of the product, indicated uses for which we may market the product, the imposition of a boxed warning or other warnings and precautions, and/or the requirement for a REMS to ensure that the benefits of the drug outweigh the risks. A boxed warning is the strongest type of warning that the FDA can require for a drug product and warns prescribers that the drug carries a significant risk of serious or even life-threatening adverse effects. The FDA requires a REMS and a boxed warning for Xyrem, and similar restrictions could be imposed on other products in the future. For example, we expect that the FDA would require a REMS for an approved JZP-258 product.

Regulatory authorities may also impose post-marketing obligations as part of their approval. Post-marketing obligations may lead to additional costs and burdens associated with commercialization of the drug, and may pose a risk to maintaining approval of the drug. We are subject to certain post-marketing requirements and commitments in connection with the approval of certain of our products, including Erwinaze, Defitelio, Vyxeos and Sunosi. For example, for Defitelio, in the U.S. the FDA imposed several post-marketing commitments and requirements in connection with its approval, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients, and in the EU marketing authorization was granted under exceptional circumstances and requires us to comply with a number of post-marketing obligations, including the conduct of a Phase 3, randomized adaptive study of Defitelio as compared to the best supportive care in the prevention of VOD in adult and pediatric patients undergoing HSCT. Similarly, the FDA imposed post-marketing requirements in connection with its approval of our NDA for Vyxeos, including the requirement that we conduct a safety study to characterize infusion-related reactions in patients treated with Vyxeos and a clinical trial to determine dosing to minimize toxicity in patients with moderate and severe renal impairment, and the marketing authorization in the EU also requires us to comply with certain manufacturing-related post-approval commitments. The FDA also required us to conduct additional post-marketing safety studies related to pregnancy and lactation for Sunosi. In the event that we are unable to comply with our post-marketing obligations imposed as part of the marketing approvals in the U.S. or EU, our approval may be varied, suspended or revoked, product supply may be delayed and our sales of and revenues from our products could be materially adversely affected.

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

Risks Related to Our Intellectual Property

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

Our commercial success depends in part on obtaining, maintaining and defending intellectual property protection for our products and product candidates, including protection of their use and methods of manufacturing and distribution. Our ability to protect our products and product candidates from unauthorized making, using, selling, offering to sell or importation by third parties depends on the extent to which we have rights under valid and enforceable patents or have adequately protected trade secrets that cover these activities.

The patent position of pharmaceutical companies can be highly uncertain and involve complex and often changing legal, regulatory and factual questions. The degree of protection to be afforded by our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- our patent applications, or those of our licensors or partners, may not result in issued patents;
- others may independently develop similar or therapeutically equivalent products without infringing our patents, or those of our licensors, such as products that are not covered by the claims of our patents, or for which we do not have adequate exclusive rights under our license agreements;
- our issued patents, or those of our licensors or partners, may be held invalid or unenforceable as a result of legal challenges by third parties or may be vulnerable to legal challenges as a result of changes in applicable law;
- we or our licensors or partners might not have been the first to invent or file, as appropriate, subject matters covered by our issued patents or pending patent applications or those of our licensors or partners;
- competitors may manufacture products in countries where we have not applied for patent protection or that have a different scope of patent protection or that do not respect our patents; or
- others may be issued patents that prevent the sale of our products or require licensing and the payment of significant fees or royalties.

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

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 Sunosi. Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Even if we are able to obtain patents covering our products and product candidates, any patent may be challenged, and potentially invalidated or held unenforceable, including through patent litigation or through patent office procedures that permit challenges to patent validity. Patents can also be circumvented, potentially including by FDA approval of an ANDA or Section 505(b)(2) application that avoids infringement of our intellectual property.

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

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

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

For a discussion regarding the risks associated with our ANDA litigation settlement agreements, the potential launch of AG Products or other generic versions of Xyrem, or the approval and launch of other sodium oxybate or other products that

compete with Xyrem, as well as other risks and challenges we face with respect to Xyrem, see the risk factors under the headings "Risks Related to Xyrem and the Our Other Marketed Products" and "*We have incurred and may in the future incur substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products"* in this Part II, Item 1A.

We also rely on trade secrets and other unpatented proprietary information to protect our products and their commercial position, particularly with respect to our products with limited or no patent protection, such as Erwinaze, which has no patent protection. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality and invention agreements with our employees, consultants, advisors and partners. Nevertheless, our employees, consultants, advisors and partners may unintentionally or willfully disclose our proprietary information to competitors, and we may not have adequate remedies for such disclosures. Enforcing a claim that a third party illegally obtained or is using any of our inventions or trade secrets would be expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside of the U.S. are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

In some instances, we also rely on regulatory exclusivity to protect our commercial position. In addition to relying on trade secret protection, Erwinaze was granted orphan drug exclusivity by the FDA for the treatment of ALL in the U.S. for a seven-year period from its FDA approval, which had precluded approval of another product with the same principal molecular structure for the same indication until November 2018. As a biologic product approved under a BLA, Erwinaze is also subject to the U.S. Biologics Price Competition and Innovation Act, or BPCIA. We believe that Erwinaze is protected by exclusivity that prevents approval of a biosimilar in the U.S. through late 2023 under the BPCIA. However, interpretation of regulatory exclusivity under the BPCIA may evolve over time based on FDA issuance of guidance documents, proposed regulations or decisions made by the FDA in the course of considering specific applications. In addition, the BPCIA exclusivity period does not prevent another company from independently developing a product that is highly similar to Erwinaze, generating all the data necessary for a full BLA and seeking approval. BPCIA exclusivity only assures that another company cannot rely on the FDA's prior approvals of Erwinaze to support the biosimilar product's approval. As a result, it is possible that a potential competing drug product might obtain FDA approval before the expected BPCIA exclusivity period has expired, which would adversely affect sales of Erwinaze. In the EU, the regulatory data protection that provides an exclusivity period for Erwinase has lapsed. Any new marketing authorizations for Erwinase in other EU member states will not receive any regulatory data protection. If a biosimilar product to Erwinaze is approved as interchangeable to Erwinaze in the U.S. or in other countries where Erwinaze is sold, a significant percentage of the prescriptions that would have been written for Erwinaze may be filled with the biosimilar version, resulting in a loss in sales of Erwinaze, and there may be a decrease in the price at which Erwinaze can be sold. Competition from a biosimilar product to Erwinaze could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

Our ability, and that of our partners, to commercialize any approved products will depend, in part, on our ability to obtain patents, enforce those patents and operate without infringing the proprietary rights of third parties. If we choose to go to court to stop a third party from infringing our patents, our licensed patents or our partners' patents, that third party has the right to ask the court or an administrative agency to rule that these patents are invalid and/or should not be enforced. These lawsuits and administrative proceedings are expensive and consume time and other resources, and we may not be successful in these proceedings or in stopping infringement. In addition, the inter partes review, or IPR, process under the Leahy-Smith America Invents Act permits any person, whether they are accused of infringing the patent at issue or not, to challenge the validity of certain patents. As a result, many types of entities, including ANDA filers, have challenged valuable pharmaceutical patents through the IPR process, and six of our Orange Book-listed patents for Xyrem were invalidated through this process.

There is a risk that a court or the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office could decide that our patents or certain claims in our patents are not valid or infringed, and that we do not have the right to stop a

third party from using the inventions covered by those claims, as happened with the decision of the PTAB that certain of our patent claims covering the Xyrem REMS are invalid. In addition, even if we prevail in establishing that another product infringes a valid claim of one of our patents, a court may determine that we can be compensated for the infringement in damages, and refuse to issue an injunction. As a result, we may not be entitled to stop another party from infringing our patents for their full term. For more information, see the risk factors under the headings "Risks Related to Xyrem and Our Other Marketed Products" and "*It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection"* in this Part II, Item 1A. Lawsuits or proceedings we may file in the future, or our defense against any lawsuits or other proceedings that may be brought against us, may not costly and time-consuming and may not be successful in stopping the infringement of our patents.

Litigation involving patent matters is frequently settled between the parties, rather than continuing to a court ruling, and we have settled patent litigation with all nine Xyrem ANDA filers. The FTC has publicly stated that, in its view, certain types of agreements between branded and generic pharmaceutical companies related to the settlement of patent litigation or the manufacture, marketing and sale of generic versions of branded drugs violate the antitrust laws and has commenced investigations and brought actions against some companies that have entered into such agreements. In particular, the FTC has expressed its intention to take aggressive action to challenge settlements that include an alleged transfer of value from the brand company to the generic company (so-called "pay for delay" patent litigation settlements) and to call on legislators to pass stronger laws prohibiting such settlements. The U.S. Congress and state legislatures have also identified pharmaceutical patent settlements as potential impediments to generic competition and have suggested that they may introduce legislation to regulate them. Because there is currently no precise legal standard with respect to the lawfulness of such settlements, there could be extensive litigation over whether any settlement that we have entered into or might enter into in the future constitutes a reasonable and lawful patent settlement. Parties to such settlement agreements in the U.S. are required by law to file the agreements with the FTC and the U.S Department of Justice, or DOJ, for review. Accordingly, we have submitted our ANDA litigation settlement agreements to the FTC and the DOJ for review. We may receive formal or informal requests from the FTC regarding our ANDA litigation settlements, and there is a risk that the FTC may commence a formal investigation or action against us, or a third party may initiate civil litigation regarding such settlements, which could divert the attention of management and cause us to incur significant costs, regardless of the outcome. Any claim or finding that we or our business partners have failed to comply with applicable laws and regulations could be costly to us and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

Because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, because patent applications in the U.S. and many non-U.S. jurisdictions are typically not published until 18 months after their priority date, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for inventions covered by our or our licensors' issued patents or pending applications, or that we or our licensors were the first inventors.

Some of our competitors may be able to sustain the costs of complex patent and other intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations. For further discussion of our Xyrem-related patent matters, see the risk factors under the headings "Risks Related to Xyrem and Our Other Marketed Products" and "Risks Related to Our Intellectual Property."

Other Risks Related to Our Business and Industry

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

We are headquartered in Dublin, Ireland and have multiple offices in the U.S., Canada, the UK, Italy and other countries in Europe. Our headcount has grown to approximately 1,500 as of August 2019. This includes employees in 18 countries in North America and Europe, a European commercial presence, a complex distribution network for products in Europe and additional territories, and manufacturing facilities in Italy and Ireland. We may further expand our international operations into other countries in the future, either organically or by acquisition. While we have management and other personnel with substantial international experience, conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects. These risks and complexities include:

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

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

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

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

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

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

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

affected by Brexit. Should this foreign exchange volatility continue or be exacerbated by UK's withdrawal from the EU, it could cause volatility in our quarterly financial results.

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

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

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

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

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

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

We are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store, process and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such information. We have also outsourced some of our operations (including parts of our information technology infrastructure) to a number of third party vendors who may have, or could gain, access to our confidential information. In addition, many of those third parties, in turn, subcontract or outsource some of their responsibilities to third parties.

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

Significant disruptions of our, our third party vendors' and/or business partners' information technology systems or security breaches could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), and could result in financial, legal, business and reputational harm to us. Any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect the privacy and

security of personal information, which could disrupt our business, result in increased costs or loss of revenue, and/or result in significant legal and financial exposure. In addition, security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may further harm us. Moreover, the prevalent use of mobile devices to access confidential information increases the risk of security breaches. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business. In addition, failure to maintain effective internal accounting controls related to security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and subject us to regulatory scrutiny.

In addition to those specifically described in other risk factors, we are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and limit our ability to commercialize our products.

FDA and Equivalent Non-U.S. Regulatory Authorities

Our activities are subject to extensive regulation encompassing the entire life cycle of our products, from research and development activities to marketing approval (including specific post-marketing obligations), manufacturing, labeling, packaging, adverse event and safety reporting, storage, advertising, promotion, sale, pricing and reimbursement, recordkeeping, distribution, importing and exporting. These requirements apply both to us and to third parties we contract with to perform services and supply us with products. The failure by us or any of our third party partners, including our corporate development and collaboration partners, clinical trial sites, suppliers, distributors and our central pharmacy for Xyrem, to comply with applicable requirements could subject us to administrative or judicial sanctions or other negative consequences, such as delays in approval or refusal to approve a product candidate, restrictions on our products, our suppliers, our other partners or us, the withdrawal, suspension or variation of product approval or manufacturing authorizations, untitled letters, warning letters, fines and other monetary penalties, unanticipated expenditures, product recall, withdrawal or seizure, total or partial suspension of production or distribution, interruption of manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, civil penalties and/or criminal prosecution, any of which could result in a significant drop in our revenues from the affected products and harm to our reputation and could have a significant impact on our sales, business and financial condition.

We monitor adverse events resulting from the use of our products, as do the regulatory authorities, and we file periodic reports with the authorities concerning adverse events. The authorities review these events and reports, and if they determine 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 variation, withdrawal or suspension of the marketing authorization, any of which could result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. The FDA and the competent authorities of the EU member states on behalf of the EMA also periodically inspect our records related to safety reporting. Following such inspections, the FDA may issue notices on FDA Form 483 and warning letters that could cause us to modify certain activities. The EMA's Pharmacovigilance Risk Assessment Committee may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps or advise that the existing marketing authorization be varied, suspended or revoked. Failure to adequately and promptly correct the observation(s) can result in further regulatory enforcement action, which could include the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures. The failure to adequately address and promptly correct any matters identified by the FDA or other foreign regulatory authorities could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Erwinaze, defibrotide and Vyxeos are available on a named patient basis in many countries where they are not commercially available. If any such country's regulatory authorities determine that we are promoting such products without proper authorization, we could be found to be in violation of pharmaceutical advertising laws or the regulations permitting sales under named patient programs. In that case, we may be subject to financial or other penalties. Moreover, any failure to maintain revenues from sales of Erwinaze, defibrotide and/or Vyxeos on a named patient basis and/or to generate revenues from commercial sales of these products exceeding historical sales on a named patient basis could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The FDA, the competent authorities of the EU member states and other governmental authorities require advertising and promotional materials to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. Regulatory authorities actively investigate allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. If we are found to have promoted an approved product for off-label uses, we may be subject to significant liability, including civil and administrative financial penalties and other remedies as well as criminal financial penalties, other sanctions and imprisonment. Even if we are not determined to have engaged in off-label promotion, an allegation that we have engaged in such activities could have a significant impact on our sales, business and financial condition. The U.S. government has also required companies to enter into complex corporate integrity agreements and/or non-prosecution agreements that impose significant reporting and other burdens on the affected

companies. Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could subject us to a range of regulatory actions that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

In the EU, the advertising and promotion of our products are also subject to EU member states' laws and industry codes of practice governing promotion of medicinal products, including limitations on our promotional activities with health care professionals, prohibition of the advertising and promotion of our products to the general public, misleading and comparative advertising and unfair commercial practices. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, limitations on promotional activities, fines and imprisonment. These laws may also impose limitations on our promotional activities with health care professionals.

Other Regulatory Authorities

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

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

The U.S. federal False Claims Act, or False Claims Act, prohibits, among other things, making a fraudulent claim for payment of federal funds, causing such a fraudulent claim to be made, or making a false statement to get a false claim paid. The government may assert that a claim resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim under the False Claims Act. Many companies have faced government investigations or lawsuits by whistleblowers who bring a *qui tam* action under the False Claims Act on behalf of themselves and the government for a variety of alleged improper marketing activities, including providing free product to customers expecting that the customers would bill federal programs for the product, providing consulting fees, grants, free travel and other benefits to physicians to induce them to prescribe the company's products, and inflating prices reported to private price publication services, which are used to set drug reimbursement rates under government healthcare programs. In addition, the government and private whistleblowers have pursued False Claims Act cases against pharmaceutical companies for causing false claims to be submitted as a result of the marketing of their products for unapproved uses. Pharmaceutical and other healthcare companies also are subject to other federal false claim laws, including federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs. If we become the subject of a government False Claims Act or other investigation or whistleblower suit, we could incur substantial legal costs (including settlement costs) and business disruption responding to such investigation or suit, regardless of the outcome. Violations of the False Claims Act may result in significant financial penalties (on a per claim or statement basis), treble damages and exclusion from participation in federal health care programs.

The majority of individual states also have statutes or regulations similar to the federal anti-kickback law and the False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Certain states and cities require identification or licensing of our sales representatives. Other states restrict our ability to offer co-pay support to patients for certain prescription drugs. We must comply with these state laws to avoid being subject to civil or criminal penalties.

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 to certain additional covered recipients beginning in 2022) and ownership interests held by physicians and their families, and provides for public disclosures of these data. Public reporting under the Sunshine provisions has resulted in increased scrutiny of the financial relationships between industry, teaching hospitals and physicians. Such scrutiny may negatively impact our ability to engage with physicians on matters of importance to us. In addition, government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports. Moreover, certain states require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and gifts and

payments to individual physicians, and/or restrict when and to what extent pharmaceutical companies may provide meals to prescribers or engage in other marketing related activities. If the data reflected in our reports are found to be in violation of any of the Sunshine provisions or any other U.S. federal, state or local laws or regulations that may apply, or if we otherwise fail to comply with the Sunshine provisions or similar requirements of state or local regulators, we may be subject to significant civil, criminal and administrative penalties, damages or fines.

Outside the U.S., interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products, which is prohibited in the EU, is governed by the national anti-bribery laws of the EU member states, as described below and by industry codes of practice. Violation of these laws could result in substantial fines and imprisonment. The national laws of certain EU member states and industry codes of practice require that payments made to physicians be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her competent professional organization, and/or the competent authorities of the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Xyrem and Sunosi are controlled substances under the Controlled Substances Act. Our suppliers, distributors, clinical sites and prescribers, as well as retail pharmacies for Sunosi and the central pharmacy for Xyrem, are subject to DEA and state regulations relating to manufacturing, storage, distribution and physician prescription procedures, including limitations on prescription refills, and are required to maintain DEA registration and state licenses, when handling these drugs and their APIs. The DEA periodically inspects facilities for compliance with its rules and regulations. Failure to comply with current and future regulations of the DEA, relevant state authorities or any comparable international requirements could lead to a variety of sanctions, including revocation or denial of renewal of DEA registrations, fines, injunctions, or civil or criminal penalties, could result in, among other things, additional operating costs to us or delays in shipments outside or into the U.S. and could have an adverse effect on our business and financial condition. DEA quotas are required for any U.S. supplier to manufacture sodium oxybate or Xyrem. New oxybate market entrants, including generic products, may impact the amount of quota available in the U.S., and if, our suppliers cannot obtain the quotas that are needed on a timely basis, or at all, our business, financial condition, results of operations and growth prospects could be materially and adversely affected.

We have various programs to help patients access our products, including patient assistance programs, which include co-pay coupons for certain of our products, services that help patients determine their insurance coverage for our products, and a free product program. Co-pay coupon programs for commercially insured patients, including our program for Xyrem, have received negative publicity related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. In the past, payors brought class action lawsuits challenging the legality of manufacturer co-pay programs under a variety of federal and state laws and insurers have taken actions through their network pharmacies and PBMs to restrict manufacturer co-pay programs. In September 2014, the OIG issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and other laws if they do not take appropriate steps to exclude Medicare Part D beneficiaries from using co-pay coupons. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, including Xyrem, and therefore could have a material adverse effect on our sales, business and financial condition.

We have established programs to consider grant applications submitted by independent charitable organizations, including organizations that provide co-pay support to patients who suffer from the diseases treated by our drugs. The OIG has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. If we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, such facts could be used as the basis for an enforcement action against us by the federal government or other enforcement agencies or private litigants.

In 2016 and 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of charitable organizations that provide financial assistance to Medicare patients. On April 4, 2019, we finalized our civil settlement agreement with the DOJ and OIG in the amount of $57.0 million plus interest. In connection with the settlement agreement, we entered into a corporate integrity agreement requiring us to maintain our ongoing corporate compliance program and obligating us to implement or continue, as applicable, a set of defined corporate integrity activities for a period of five years from the effective date of the corporate integrity agreement. In the event of a breach of the corporate integrity agreement, we could become liable for payment of certain stipulated penalties or could be excluded from

participation in federal health care programs, which would have a material adverse effect on our sales, business and financial condition.

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

Our business activities outside of the U.S. are subject to the U.S. Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the UK Bribery Act of 2010, or the UK Bribery Act. Our heavily regulated business involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in certain countries, the health care providers who prescribe pharmaceuticals are employed by their government and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers may be subject to regulation under the FCPA and the UK Bribery Act. Recently the U.S. Securities and Exchange Commission, or SEC, and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, private individuals who report original information to the SEC that leads to successful enforcement actions may be eligible for a monetary award. There is no certainty that all employees and third party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of suppliers and other third party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

We are also subject to data protection and privacy laws and regulations governing the processing of personal data. The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Failure to comply with current and future laws and regulations, such as the EU General Data Protection Regulation that became effective in May 2018 and the California Consumer Privacy Act of 2018 that will become effective beginning January 2020, could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors, private litigation and/or adverse publicity that negatively affects our business. If we or our vendors fail to comply with applicable data privacy laws, or if the legal mechanisms we or our vendors rely upon for the transfer of personal data are ever deemed inadequate, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted if our ability to transfer personal data outside of the European Economic Area or Switzerland is restricted, which could adversely impact our operating results. In addition, although we are not directly subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, other than with respect to providing certain employee benefits, we potentially could be subject to criminal penalties if we, our affiliates or our agents knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, agreements between branded pharmaceutical companies and potential generic competitors settling patent litigation must be submitted to the FTC and the DOJ for review. The FTC has publicly stated that, in its view, certain brand-generic settlement agreements violate the antitrust laws and has brought actions against some companies that have entered into such agreements. In particular, the FTC has expressed its intention to take aggressive action to challenge settlements that include an alleged transfer of value from the brand company to the generic company (so-called “pay for delay” patent litigation settlements) and to call on legislators to pass stronger laws prohibiting such settlements. Because there is currently no precise legal standard with respect to the lawfulness of such settlements, there could be extensive litigation over whether any settlement that we have entered into or might enter into in the future constitutes a reasonable and lawful patent settlement. We may receive formal or informal requests from the FTC regarding our Xyrem patent settlements, and there is a risk that the FTC may commence a formal investigation or action against us, or a third party may initiate civil litigation regarding such settlements, which could divert the attention of management and cause us to incur significant costs, regardless of the outcome. We cannot predict the outcome of any potential government investigation of any antitrust claims, including those described above, or the impact of any such claims.

In addition to those described in this and other risk factors, numerous federal, state and non-U.S. statutes and regulations govern the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including preclinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information, promotion, marketing, and pricing to government purchasers and government

healthcare programs. Such laws and regulations are subject to change as activities relating to prescription pharmaceutical products have become the subject of active legislative activity. Any claim or finding that we or our business partners have failed to comply with applicable laws and regulations could be costly to us and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

Our reporting and payment obligations under the Medicaid Drug Rebate program and other governmental programs are described under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2018. Our failure to comply with these obligations could negatively impact our financial results.

CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the Healthcare Reform Act. The issuance of the final regulation, as well as any other regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate program, has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final regulation.

We also participate in the 340B program, which is described in more detail under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2018. The Health Resources and Services Administration, or HRSA, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. It is currently unclear how HRSA will apply its enforcement authority under the new regulation. Implementation of this regulation could affect our obligations and potential liability under the 340B program in ways we cannot anticipate. Any charge by HRSA that we have violated the requirements of the program or the regulation could negatively impact our financial results. HRSA also began to implement a ceiling price reporting requirement related to the 340B program during the first quarter of 2019, under which we are required to report the 340B ceiling prices for our covered outpatient drugs to HRSA, which then publishes them to 340B covered entities. There is no guarantee that our submissions will not be found by HRSA to be incomplete or incorrect. Further, 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. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

We have obligations to report the average sales price for certain of our drugs to the Medicare program. 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 or product information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, or if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. There is no guarantee that our submissions will not be found by CMS to be incomplete or incorrect.

We participate in the U.S. Department of Veterans Affairs, Federal Supply Schedule, or FSS, pricing program and the Tricare Retail Pharmacy program, as described in more detail under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2018. Pursuant to applicable law, knowing provision of false information in connection with

price reporting under these programs can subject a manufacturer to civil monetary penalties. These program obligations also contain extensive disclosure and certification requirements.

If we overcharge the government in connection with our arrangements with FSS or Tricare, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

Product liability and product recalls could harm our business.

The development, manufacture, testing, marketing and sale of pharmaceutical products are associated with significant risks of product liability claims or recalls. Side effects or adverse events known or reported to be associated with, or manufacturing defects in, the products sold by us could exacerbate a patient's condition, or could result in serious injury or impairment or even death. This could result in product liability claims against us and/or recalls of one or more of our products. In many countries, including in EU member states, national laws provide for strict (no-fault) liability which applies even where damages are caused both by a defect in a product and by the act or omission of a third party.

Product liability insurance coverage is expensive, can be difficult to obtain and may not be available in the future on acceptable terms, or at all. Our product liability insurance may not cover all of the future liabilities we might incur in connection with the development, manufacture or sale of our products. In addition, we may not continue to be able to obtain insurance on satisfactory terms or in adequate amounts. A successful claim or claims brought against us in excess of available insurance coverage could subject us to significant liabilities and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Such claims could also harm our reputation and the reputation of our products, adversely affecting our ability to market our products successfully. In addition, defending a product liability lawsuit is expensive and can divert the attention of key employees from operating our business.

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

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

Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Italy and Ireland where we have manufacturing facilities. Environmental and health and safety authorities in Italy and Ireland administer laws governing, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. Our manufacturing facilities are involved in the controlled storage, use and disposal of chemicals and solvents. Even if our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by EU laws, we cannot completely eliminate the risk of contamination or injury from hazardous materials. If an accident occurs, an injured party could seek to hold us liable for any damages that result and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance on acceptable terms, or at all. In certain cases, laws may impose strict liability for pollution of the environment and contamination resulting from spills, disposals or other releases of hazardous substances or waste or any migration of such hazardous substances or waste.

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

We may incur significant costs to comply with current or future EU environmental laws.

Risks Related to Our Financial Condition and Results

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

As of June 30, 2019, we had total indebtedness of approximately $1.8 billion, which included $634.3 million in outstanding term loan indebtedness under a secured credit agreement that we entered into in June 2015 and subsequently amended in July 2016 and in June 2018, which we refer to as the amended credit agreement, $575.0 million of outstanding indebtedness under our 1.875% exchangeable senior notes due 2021, or the 2021 Notes, which were issued in August 2014, and $575.0 million of outstanding indebtedness under our 1.50% exchangeable senior notes due 2024, or the 2024 Notes, which were issued in August 2017 and which we refer to, together with the 2021 Notes, as the Exchangeable Senior Notes.

Our debt may:

- limit our ability to borrow additional funds for working capital, capital expenditures, acquisitions or other general business purposes;
- limit our ability to use our cash flow or obtain additional financing for working capital, capital expenditures, acquisitions or other general business purposes;
- require us to use a substantial portion of our cash flow from operations to make debt service payments;
- limit our flexibility to plan for, or react to, changes in our business and industry;
- result in dilution to our existing shareholders in the event exchanges of the Exchangeable Senior Notes are settled in our ordinary shares;
- place us at a competitive disadvantage compared to our less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

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

Covenants in our amended credit agreement restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected.

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

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

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

agreement could also lead to a default under other debt agreements or obligations, including the indentures governing the Exchangeable Senior Notes.

In addition, the holders of the Exchangeable Senior Notes have the ability to require us to repurchase their notes for cash if we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution, or the delisting of our ordinary shares from The Nasdaq Global Select Market. Moreover, upon exchange of the Exchangeable Senior Notes, unless we elect to deliver only our ordinary shares to settle such exchange, we will be required to make cash payments in respect of the Exchangeable Senior Notes. It is our intent and policy to settle the principal amount of the Exchangeable Senior Notes in cash upon exchange. However, we may not have enough available cash or be able to obtain financing at the time we are required to make any required repurchases of surrendered Exchangeable Senior Notes or to pay cash upon exchanges of the Exchangeable Senior Notes. Our failure to repurchase the Exchangeable Senior Notes at a time when the repurchase is required by the indentures governing the Exchangeable Senior Notes or to pay any cash payable on future exchanges of the Exchangeable Senior Notes as required by the indentures governing the Exchangeable Senior Notes would constitute a default under that indenture. A default under those indentures could also lead to a default under other debt agreements or obligations, including the amended credit agreement. If the repayment of the related indebtedness were to be accelerated, we may not have sufficient funds to repay the related indebtedness, which could have a material adverse effect on our financial condition and our business. In this regard, if we are unable to repay amounts under the amended credit agreement, the lenders under the amended credit agreement could proceed against the collateral granted to them to secure that debt, which would seriously harm our business.

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

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

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

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

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

The scope of our business and operations has grown substantially since 2012 through a series of transactions, including the business combination between Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company, which we refer to as the Azur Merger, and our acquisitions of EUSA Pharma Inc., Gentium S.r.l. and Celator Pharmaceuticals, Inc. To continue to grow our business over the longer term, we will need to commit substantial additional resources to our business and execution of our strategy. Our ongoing capital requirements will depend on many factors, including:

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

Our strategy includes the expansion of our business through acquiring or in-licensing, and developing, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. See the

risk factor under the heading "*We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these acquisitions*" in this Part II, Item 1A. We may be unable to expand our business if we do not have sufficient capital or cannot borrow or raise additional capital on attractive terms. Our substantial indebtedness may limit our ability to borrow additional funds for acquisitions or to use our cash flow or obtain additional financing for future acquisitions. In addition, if we use a substantial amount of our funds to acquire or in-license products or product candidates, we may not have sufficient additional funds to conduct all of our operations in the manner we would otherwise choose.

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

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

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

Our intangible assets and goodwill are significant. As of June 30, 2019, we had recorded $3.6 billion of intangible assets and goodwill related to our past acquisitions. Intangible assets and goodwill are subject to an impairment analysis whenever events or changes in circumstances indicate the carrying amount of the asset may not be recoverable. For example, in connection with entry into an asset purchase agreement in June 2018 to sell substantially all of the assets held by us related to Prialt® (ziconotide) intrathecal infusion, we recognized an impairment charge of $42.9 million in our consolidated statements of income in 2018, primarily related to the carrying balances of intangible assets. Additionally, goodwill and indefinite-lived assets are subject to an impairment test at least annually.

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, Erwinase and Vyxeos product sales outside of the U.S. are primarily denominated in the euro, our sales of those products have been and may continue to be adversely affected by fluctuations in foreign currency exchange rates. In this regard, when the U.S. dollar strengthens against a foreign currency, the relative value of sales made in the foreign currency decreases. Conversely, when the U.S. dollar weakens against a foreign currency, the relative value of such sales increases. Accordingly, increases in the value of the U.S. dollar relative to foreign currencies, primarily the euro, could adversely affect our foreign revenues, perhaps significantly. In addition, as we continue to expand our international operations, we will conduct more transactions in currencies other than the U.S. dollar, which could increase our foreign currency exchange risk. Given the volatility of exchange rates, as well as our expanding operations, there is no guarantee that we will be able to effectively manage currency transaction and/or translation risks. We use foreign exchange forward contracts to manage currency risk primarily related to certain intercompany balances denominated in non-functional currencies. These foreign exchange forward contracts are not designated as hedges. Gains and losses on these derivative instruments are designed to offset gains and losses on the underlying balance sheet exposures. Fluctuations in foreign currency exchange rates could have a material adverse effect on our results of operations and financial condition.

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

We are incorporated in Ireland and maintain subsidiaries in North America and a number of other foreign jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various jurisdictions where we operate. Our effective tax rate may fluctuate depending on a number of factors, including, but not limited to, the distribution of our profits or losses between the jurisdictions where we operate and differences in interpretation of tax laws. In addition, the tax laws of any jurisdiction in which we operate may change in the future, which could impact our effective tax rate. We are subject to reviews and audits by the U.S. Internal Revenue Services, or IRS, and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure, transfer pricing arrangements and tax positions through an audit or lawsuit. Responding to or defending against challenges from taxing authorities could be expensive and consume time and other resources. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our products or seek to raise additional funds. Any of these actions could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In December 2015, we received proposed tax assessment notices, and, in October 2018, we received revised tax assessment notices from the French tax authorities for 2012 and 2013 and in December 2018, we received a proposed tax assessment notice for 2015, relating to certain transfer pricing adjustments. The notices propose additional French tax of approximately $43 million for 2012 and 2013 and approximately $4 million for 2015, including interest and penalties through the respective dates of the proposed assessments, translated at the foreign exchange rate at June 30, 2019.

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

The IRS may not agree with the conclusion that we should be treated as a foreign corporation for U.S. federal tax purposes.

Although we are incorporated in Ireland, the IRS may assert that we should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal tax purposes pursuant to Section 7874 of the U.S. Internal Revenue Code, or the Code. For U.S. federal tax purposes, a corporation generally is considered a tax resident in the jurisdiction of its organization or incorporation. Because we are an Irish incorporated entity, we would be classified as a foreign corporation (and, therefore, a non-U.S. tax resident) under these rules. Section 7874 of the Code provides an exception under which a foreign incorporated entity may, in certain circumstances, be treated as a U.S. corporation for U.S. federal tax purposes. Because we indirectly acquired all of Jazz Pharmaceuticals, Inc.'s assets through the acquisition of the shares of Jazz Pharmaceuticals, Inc. common stock in the Azur Merger, the IRS could assert that we should be treated as a U.S. corporation for U.S. federal tax purposes under Section 7874. The IRS continues to scrutinize transactions that are potentially subject to Section 7874, and has issued several sets of final and temporary regulations under Section 7874 since 2012. We do not expect these regulations to affect the U.S. tax consequences of the Azur Merger. Nevertheless, new statutory and/or regulatory provisions under Section 7874 of the Code or otherwise could be enacted that adversely affect our status as a foreign corporation for U.S. federal tax purposes, and any such provisions could have prospective or retroactive application to us, our shareholders, Jazz Pharmaceuticals, Inc. and/or the Azur Merger.

Our U.S. affiliates' ability to use their net operating losses to offset potential taxable income and related income taxes that would otherwise be due is limited under Section 7874 of the Code and could be subject to further limitations if we do not generate taxable income in a timely manner or if the "ownership change" provisions of Sections 382 and 383 of the Code result in further annual limitations.

Following certain acquisitions of a U.S. corporation by a foreign corporation, Section 7874 of the Code can limit the ability of the acquired U.S. corporation and its U.S. affiliates to utilize U.S. tax attributes such as net operating losses, or NOLs, to offset U.S. taxable income resulting from certain transactions. Based on the limited guidance available, this limitation applies to us. Our U.S. affiliates have a significant amount of NOLs. As a result of Section 7874 of the Code, after the Azur Merger, our U.S. affiliates have not been able and will continue to be unable, for a period of time, to utilize their U.S. tax attributes to offset their U.S. taxable income, if any, resulting from certain taxable transactions. While we expect to be able to fully utilize our U.S. affiliates' U.S. NOLs prior to their expiration, as a result of this limitation, it may take our U.S. affiliates longer to use their NOLs.

Our ability to use these NOLs to offset potential future taxable income and related income taxes that would otherwise be due is also dependent upon our generation of future taxable income before the expiration dates of the NOLs, and we cannot predict with certainty when, or whether, our U.S. affiliates will generate sufficient taxable income to use all of the NOLs. In addition, the use of NOLs to offset potential future taxable income and related income taxes that would otherwise be due is subject to annual limitations under the "ownership change" provisions of Sections 382 and 383 of the Code and similar state provisions, which may result in the expiration of additional NOLs before future utilization.

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

The U.S. Congress, the EU, the Organization for Economic Co-operation and Development, or OECD, and other government agencies in jurisdictions where we and our affiliates do business have had an extended focus on issues related to the taxation of multinational corporations. One example is the OECD's initiative in the area of "base erosion and profit shifting," where payments are made between affiliates from a jurisdiction with high tax rates to a jurisdiction with lower tax rates. Some countries are beginning to implement legislation and other guidance to align their international tax rules with the OECD's recommendation. As a result of the focus on the taxation of multinational corporations, the tax laws in Ireland, the U.S. and other countries in which we and our affiliates do business could change on a prospective or retroactive basis, and any such changes could adversely affect us.

A substantial portion of our indebtedness bears interest at variable interest rates based on USD LIBOR and certain of our financial contracts are also indexed to USD LIBOR. Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate, may adversely affect interest rates on our current or future indebtedness and may otherwise adversely affect our financial condition and results of operations.

In July 2017, the Financial Conduct Authority, the authority that regulates the London Inter-bank Offered Rate, or LIBOR, announced that it intended to stop compelling banks to submit rates for the calculation of LIBOR after 2021. The Alternative Reference Rates Committee, or ARRC, in the U.S. has proposed that the Secured Overnight Financing Rate, or SOFR, is the rate that represents best practice as the alternative to the U.S. dollar, or USD, LIBOR for use in derivatives and other financial contracts that are currently indexed to USD LIBOR. ARRC has proposed a paced market transition plan to SOFR from USD LIBOR and organizations are currently working on industry-wide and company-specific transition plans as relating to derivatives and cash markets exposed to USD LIBOR. We have certain financial contracts, including the amended credit agreement and our interest rate swaps, that are indexed to USD LIBOR. Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate, may adversely affect interest rates on our current or future indebtedness. Any transition process may involve, among other things, increased volatility or illiquidity in markets for instruments that rely on LIBOR, reductions in the value of certain instruments or the effectiveness of related transactions such as hedges, increased borrowing costs, uncertainty under applicable documentation, or difficult and costly consent processes. We are monitoring this activity and evaluating the related risks, and any such effects of the transition away from LIBOR may result in increased expenses, may impair our ability to refinance our indebtedness or hedge our exposure to floating rate instruments, or may result in difficulties, complications or delays in connection with future financing efforts, any of which could adversely affect our financial condition and results of operations.

Risks Related to Our Ordinary Shares

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

The market price for our ordinary shares has fluctuated significantly from time to time, for example, varying between a high of $181.46 on August 7, 2018 and a low of $113.52 on December 24, 2018 during the period from June 30, 2018 through June 30, 2019. The market price of our ordinary shares is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market, industry and other factors, including the risk factors described above. The stock market in general, including the market for life sciences companies, has experienced extreme price and trading volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. In particular, negative publicity regarding pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact, the market for life sciences companies. These broad market and industry factors have harmed, and in the future may seriously harm, the market price of our ordinary shares, regardless of our operating performance.

Our share price may be dependent upon the valuations and recommendations of the analysts who cover our business. If our results do not meet these analysts' forecasts, the expectations of our investors or the financial guidance we provide to investors in any period, the market price of our ordinary shares could decline. Our ability to meet analysts' forecasts, investors' expectations and our financial guidance is substantially dependent on our ability to maintain or increase sales of our marketed products. The risks and uncertainties associated with our ability to maintain or increase sales of our products include those

discussed elsewhere in these risk factors. In the past, following periods of volatility in the market or significant price decline, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

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

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

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

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

Our articles of association, Irish law and the indentures governing the Exchangeable Senior Notes contain provisions that could delay or prevent a takeover of us by a third party.

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

- impose advance notice requirements for shareholder proposals and nominations of directors to be considered at shareholder meetings;
- stagger the terms of our board of directors into three classes;
- require the approval of a supermajority of the voting power of the shares of our share capital entitled to vote generally at a meeting of shareholders to amend our articles of association; and
- permit our board of directors to issue one or more series of preferred shares with rights and preferences, as our shareholders may determine by ordinary resolution.

In addition to our articles of association, several mandatory provisions of Irish law could prevent or delay an acquisition of us. For example, Irish law does not permit shareholders of an Irish public limited company to take action by written consent with less than unanimous consent, and the shareholder approval requirements for certain types of transactions differ from those in the U.S., and in some cases are greater, under Irish law. We are also subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in our shares in certain circumstances. Furthermore, the indentures governing the Exchangeable Senior Notes require us to repurchase the Exchangeable Senior Notes for cash if we undergo certain fundamental changes and, in certain circumstances, to increase the exchange rate for a holder of 2021 Notes or 2024 Notes. A takeover of us may trigger the requirement that we purchase the Exchangeable Senior Notes and/or increase the exchange rate, which could make it more costly for a potential acquiror to engage in a business combination transaction with us.

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

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

Other than funds we have allocated for the purposes of supporting our share repurchase program, we anticipate that we will retain all earnings, if any, to support our operations and our proprietary drug development programs, acquire or in-license additional products and product candidates, and pursue other opportunities. If we propose to pay dividends in the future, we must do so in accordance with Irish law, which provides that distributions including dividend payments, share repurchases and redemptions be funded from "distributable reserves." In addition, our ability to pay cash dividends on or repurchase our ordinary shares is restricted under the terms of the amended credit agreement. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, compliance with the terms of the amended credit agreement and other factors our board of directors deems relevant. Accordingly, holders of our ordinary shares must rely on increases in the trading price of their shares for returns on their investment in the foreseeable future. In addition, in the event that we pay a dividend on our ordinary shares, in certain circumstances, as an Irish tax resident company, some shareholders may be subject to withholding tax, which could adversely affect the price of our ordinary shares.

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

In certain circumstances, the transfer of shares in an Irish incorporated company will be subject to Irish stamp duty, which is a legal obligation of the buyer. This duty is currently charged at the rate of 1.0% of the price paid or the market value of the shares acquired, if higher. Because our ordinary shares are traded on a recognized stock exchange in the U.S., an exemption from this stamp duty is available in respect of transfers by shareholders who hold our ordinary shares beneficially through brokers which in turn hold those shares through the Depository Trust Company, or DTC, to holders who also hold through DTC. However, a transfer by or to a record holder who holds our ordinary shares directly in his, her or its own name could be subject to this stamp duty. We, in our absolute discretion and insofar as the Irish Companies Act 2014 or any other applicable law permits, may, or may provide that a subsidiary of ours will, pay Irish stamp duty arising on a transfer of our ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of our ordinary shares which would otherwise be payable by the transferee is paid by us or any of our subsidiaries on behalf of the transferee, then in those circumstances, we will, on our behalf or on behalf of our subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) claim a first and permanent lien on the ordinary shares on which stamp duty has been paid by us or our subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares.

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 June 30, 2019:

	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)
April 1 - April 30, 2019	261,560	$ 135.49	261,560	$ 232,471,113
May 1 - May 31, 2019	137,503	$ 132.47	137,503	$ 214,258,570
June 1 - June 30, 2019	47,500	$ 130.81	47,500	$ 208,045,973
Total	446,563	$ 134.07	446,563	

(1) This column includes ordinary shares that we reacquired in satisfaction of the exercise price of employee stock options upon exercise, but does not include ordinary shares that we withheld in order to satisfy minimum tax withholding requirements in connection with the vesting of restricted stock units.

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

(3) The ordinary shares reported in this column above were purchased pursuant to our publicly announced share repurchase program. In November 2016, we announced that our board of directors authorized the use of up to $300 million to repurchase our ordinary shares. In November and December 2018, our board of directors increased the existing share repurchase program authorization by $320.0 million and $400.0 million, respectively, thereby increasing the total amount authorized for repurchase to $1.02 billion. This authorization has no expiration date.

(4) The dollar amount shown represents, as of the end of each fiscal month, the approximate dollar value of ordinary shares that may yet be purchased under our publicly announced share repurchase program, exclusive of any brokerage commissions. 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 5. Other Information

Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

(b) On August 1, 2019, Karen J. Wilson notified us of her decision to resign from her position as our Principal Accounting Officer, effective as of August 7, 2019. Ms. Wilson will continue in her current role as Senior Vice President, Finance.

(c) On August 1, 2019, Patricia Carr, currently our Vice President, Finance, was appointed as our Principal Accounting Officer effective as of August 7, 2019. Ms. Carr, age 48, has served as our Vice President, Finance since July 2012. Prior to that, from September 2011 to July 2012, she served as Vice President, Finance of Alkermes plc, a global biopharmaceutical company. From June 2002 to September 2011, she served in a number of roles at Elan Corporation, plc, a neuroscience-based biotechnology company, culminating in her role as Vice President, Finance. Ms. Carr is a Fellow of the Institute of Chartered Accountants (Ireland) and received a Bachelor of Commerce from the National University of Ireland, Galway. There are no family relationships among Ms. Carr and any of our other executive officers or directors.

In connection with her appointment as our Principal Accounting Officer, Ms. Carr received an increase in her annual base salary to 275,000 Euros and an increase in her annual cash bonus target percentage under the Company's cash bonus plan to 40% of her annual base salary, which bonus plan is described under the heading "Executive Compensation" in our definitive proxy statement on Schedule 14A, filed with the Securities and Exchange Commission on June 14, 2019, or our 2019 proxy statement. In connection with her appointment, Ms. Carr received an RSU award covering 1,200 of our ordinary shares under our 2011 Equity Incentive Plan, or 2011 EIP, which 2011 EIP is described under the heading "Executive Compensation" in our 2019 proxy statement, and the standard form of award agreement thereunder. The RSU award granted to Ms. Carr will vest in four equal annual installments from the vesting commencement date of August 5, 2019. On February 28, 2019, similar to our other employees, she received her 2019 annual equity awards under our 2011 EIP and the standard forms of award agreement thereunder. Her 2019 equity awards consisted of a stock option award to purchase 4,250 of our ordinary shares and an RSU award covering 1,700 of our ordinary shares, in each case under the 2011 EIP and the standard forms of award agreements thereunder. The stock option award carries an exercise price of $140.03, equal to the fair market value of our ordinary shares on the grant date, with the ordinary shares subject to the option vesting over four years, with 25% vesting one year after the grant date and the remainder vesting in equal monthly installments thereafter. The RSU award granted to Ms. Carr will vest in four equal annual installments from the vesting commencement date of March 5, 2019. Similar to certain other officers who are not employed by our U.S. affiliates, Ms. Carr receives change in control and severance benefits comparable to those of our U.S. executive officers under our Amended and Restated Executive Change in Control and Severance Benefit Plan as described under the heading "Executive Compensation" in our 2019 proxy statement.

In connection with her appointment, we expect that Ms. Carr will enter into our standard indemnification agreement which requires us, under the circumstances and to the extent provided for therein, to indemnify Ms. Carr to the fullest extent permitted by applicable law against certain expenses and other amounts incurred by Ms. Carr as a result of Ms. Carr being made a party to certain actions, suits, proceedings and other actions by reason of the fact that Ms. Carr is or was a director, officer, employee, consultant, agent or fiduciary of Jazz Pharmaceuticals plc or any of its subsidiaries or other affiliated enterprises.

Results of Matters Presented at the 2019 Annual General Meeting of Shareholders

On August 1, 2019, we held our 2019 annual general meeting of shareholders, or the annual meeting, at our corporate headquarters in Dublin, Ireland. At the annual meeting, our shareholders voted on three proposals, each of which is described in more detail in our definitive proxy statement on Schedule 14A as filed with the SEC on June 14, 2019, or the Proxy Statement. The results of the matters presented at the annual meeting, based on the presence in person or by proxy of holders of 48,502,372 of the 56,635,552 ordinary shares entitled to vote, are described below.

Proposal 1

Proposal 1 was to elect by separate resolutions each of the four nominees for director named below to hold office until our 2022 annual general meeting of shareholders. Each of the four nominees for director was elected as follows:

Director Nominees	For	Against	Abstain	Broker Non-Votes
Paul L. Berns	43,681,364	1,778,547	10,352	3,032,109
Patrick G. Enright	43,407,466	2,052,285	10,512	3,032,109
Seamus Mulligan	43,662,917	1,772,520	34,826	3,032,109
Norbert G. Riedel	35,176,745	10,283,093	10,425	3,032,109

Proposal 2

Proposal 2 was to ratify, on a non-binding advisory basis, the appointment of KPMG, Dublin as the independent auditors of the company for the fiscal year ending December 31, 2019 and to authorize, in a binding vote, the board of directors, acting through the audit committee, to determine the auditors' remuneration. This proposal was approved as follows:

For	Against	Abstain	Broker Non-Votes
47,922,470	567,853	12,049	—

Proposal 3

Proposal 3 was to approve, on an advisory basis, the compensation of our named executive officers as disclosed in the Proxy Statement. This proposal was approved as follows:

For	Against	Abstain	Broker Non-Votes
41,000,402	4,403,926	65,935	3,032,109

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	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).
4.2B	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).
4.3A	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).
4.3B	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	Corporate Integrity Agreement, dated as of April 3, 2019, by and between Jazz Pharmaceuticals plc and the Office of Inspector General of the United States Department of Health and Human Services (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.2	Settlement Agreement, dated as of April 4, 2019, by and among United States of America, acting through the United States Department of Justice and on behalf of the Office of Inspector General of the Department of Health and Human Services, Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., and Jazz Pharmaceuticals Ireland Ltd. (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.3	Amendment No. 1 to Pharmacy Master Services Agreement, effective as of June 30, 2019, by and between Jazz Pharmaceuticals, Inc. and Express Scripts Specialty Distribution Services, Inc. (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.4+	Offer Letter from Jazz Pharmaceuticals, Inc. to Robert Iannone dated as of April 11, 2019.
10.5+	Letter Agreement, dated as of June 10, 2019, by and between Jazz Pharmaceuticals, Inc. and Suzanne Sawochka Hooper.
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 - The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	Inline 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: August 6, 2019

JAZZ PHARMACEUTICALS PUBLIC LIMITED COMPANY
(Registrant)

/s/ Bruce C. Cozadd

Bruce C. Cozadd

Chairman and Chief Executive Officer and Director
(Principal Executive Officer)

/s/ Matthew P. Young

Matthew P. Young

Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

/s/ Karen J. Wilson

Karen J. Wilson

Senior Vice President, Finance
(Principal Accounting Officer)

Exhibit 10.4

[Jazz Pharmaceuticals Letterhead]

11 April 2019

Robert Iannone

Re: Offer of employment with Jazz Pharmaceuticals

Dear Robert,

I am very pleased to invite you to join Jazz Pharmaceuticals. This letter sets out the basic terms of your employment with Jazz Pharmaceuticals.

1. ***Duties and Responsibilities***. Your initial assignment will be as Head of R&D, reporting to me. This offer is for a full time position, located at Jazz Pharmaceuticals' offices in Philadelphia, PA. The position may require you to travel from time to time to other locations as may be necessary to fulfill your responsibilities. As part of your employment relationship, you agree to comply with Jazz Pharmaceuticals' policies and procedures in effect from time to time during your employment. As an exempt employee, you are expected to work the number of hours required to do your job well.

2. ***Salary; Annual Bonus; Signing Bonus***. Your initial annual base salary will be $550,000 payable in accordance with Jazz Pharmaceuticals' customary payroll practices, for all hours worked. Salary is subject to periodic review and adjustment by Jazz Pharmaceuticals, in accordance with its normal practices; we have a company-wide performance review process that takes place early in each calendar year. The Company has a cash bonus plan under which annual bonuses may be given based on the Company meeting its annual objectives, and each employee's meeting of his or her objectives, subject to the terms and conditions of the cash bonus plan. Bonuses are not guaranteed, and whether there will be a bonus in any year, and the size of any bonus if there is one, is within the discretion of the Board of Directors. In this role, you will be eligible for an annual incentive bonus with a target currently set at 55% of your annual base salary, prorated for 2019 in accordance with your start date. In addition, Jazz Pharmaceuticals will pay you a signing bonus of $205,000, less all required withholdings, paid to you in two equal installments. The first payment of $102,500 is payable on the first regular pay date occurring 90 days after your employment start date, and the second payment of $102,500 on the first regular pay date occurring 180 days after your employment start date, subject to your continued employment in good standing with Jazz Pharmaceuticals through each date. Should you voluntarily resign within one year of your employment start date, you will be expected to repay to Jazz Pharmaceuticals $205,000 of the sign on bonus. If your resignation or termination date is between 12 and 24 months of your start date, you will be expected to repay $125,000 of the sign on bonus paid to you. Such payment would be due within 30 days of the later of your resignation or termination date.

3. **Benefits**. You generally will be eligible to receive all benefits which are extended to other similarly-situated employees at Jazz Pharmaceuticals, including medical and dental benefits, life insurance and other benefits offered to regular employees. You will be eligible for paid time off and holidays in accordance with Jazz Pharmaceuticals' policies, and you will be a participant in the Company's Amended and Restated Executive Change in Control and Severance Benefit Plan.

4. ***Equity***. Your offer includes a grant of options to purchase 30,500 Jazz Pharmaceuticals plc ordinary shares and a grant of 12,200 restricted stock units (RSUs) giving you a right to receive Jazz Pharmaceuticals plc ordinary shares at a future date, subject to approval by the Compensation Committee, the terms and conditions of the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan, and the terms and conditions of the applicable award agreements, which will be provided to you as soon as practicable after the grant date. Subject to your continued employment on each vesting date, the options will vest 1/4th on the first annual anniversary of your start date and 1/48th of the total granted per month thereafter, and the RSUs will vest 1/4th annually over four years. The options will have an exercise price that equals the fair market value of Jazz Pharmaceuticals plc ordinary shares on the date of grant. The RSUs will have no exercise price. The options and RSUs will be granted on the second trading day following the filing date of the Company's next quarterly or annual report filed with the Securities and Exchange Commission following your start date in accordance with the Company's Equity Incentive Grant Policy.

5. ***Confidential Information; Employee Confidential Information and Inventions Agreement***. To enable Jazz Pharmaceuticals to safeguard its proprietary and confidential information, it is a condition of employment that you sign Jazz Pharmaceuticals' standard form of "Employee Confidential Information and Inventions Agreement." We understand that you are likely to have signed similar agreements with prior employers, and wish to impress upon you that Jazz Pharmaceuticals does not want to receive the confidential or proprietary information of others, and will support you in respecting your lawful obligations to prior employers. By accepting this offer, you are representing to Jazz Pharmaceuticals that your performance of your duties will not violate any agreements you may have with, or trade secrets of, any third parties. You agree that, during your employment with Jazz Pharmaceuticals, you will not engage in any business activity that competes with Jazz Pharmaceuticals, and you will notify your supervisor if you are considering accepting outside work.

6. ***Code of Conduct***. Jazz Pharmaceuticals is committed to integrity and the pursuit of excellence in all we do. We fulfill these commitments while upholding a high level of ethical conduct. The Code of Conduct is one element of Jazz Pharmaceuticals' efforts to ensure lawful and ethical conduct by the company and its subsidiaries and their employees, officers and directors. It is a condition of employment that you read, agree to and sign Jazz Pharmaceuticals' Code of Conduct in the first week of employment. If you have questions about the Code of Conduct, please let Human Resources know and we will ensure that you receive answers to your inquiries as quickly as possible.

7. ***At-Will Employment***. Should you decide to accept our offer, you will be an "at-will" employee of Jazz Pharmaceuticals. This means that either you or Jazz Pharmaceuticals may terminate

the employment relationship with or without cause at any time. Participation in any benefit, compensation or bonus program does not change the nature of the employment relationship, which remains “at-will”.

8. ***Authorization to Work***. Federal government regulations require that all prospective employees present documentation verifying their identity and demonstrating that they are authorized to work in the United States. If you have any questions about this requirement, which applies to U.S. citizens and non-U.S. citizens alike, please contact Heidi Manna, our Senior Vice President and Chief Human Resources Officer. Your employment is contingent on your ability to prove your identity and authorization to work in the United States, and your complying with the government’s employment verification requirements.

9. ***Complete Offer and Agreement***. This letter contains our complete understanding and agreement regarding the terms of your employment by Jazz Pharmaceuticals. There are no other, different or prior agreements or understandings on this or related subjects. Changes to the terms of your employment can be made only in a writing signed by you and President of Jazz Pharmaceuticals, although it is understood that as part of the policy of employment at will, Jazz Pharmaceuticals may, from time to time, in its sole discretion, adjust your salary, incentive compensation and benefits, as well as your job title, location, duties, responsibilities, assignments and reporting relationships.

10. ***Start Date; Acceptance of Offer***. We hope that you will accept this offer promptly, and begin your full-time employment at Jazz Pharmaceuticals no later than Monday, 29 July but as soon as Monday, 27 May 2019. If our offer is acceptable to you, please sign the enclosed copy of this letter in the space indicated and return it to me by 15 April 2019.

11. ***Severability.*** If any provision of this offer is held to be invalid, void or unenforceable, the remainder of the agreement set forth herein will remain unaffected, and you and Jazz Pharmaceuticals will work together to achieve the intent of the affected provisions.

Robert, we are impressed by your accomplishments and potential, and we are enthusiastic at the prospect of you joining us. I look forward to your early acceptance of this offer, and to your contributions to the growth and success of Jazz Pharmaceuticals.

Sincerely,

/s/ Dan Swisher

Dan Swisher
President & Chief Operating Officer

ACCEPTANCE OF EMPLOYMENT OFFER:

I accept the offer of employment by Jazz Pharmaceuticals on the terms described in this letter.

Signature:	/s/ Robert Iannone
Date:	12 April 2019

My start date will be On or before July 29, 2019

Exhibit 10.5

[JAZZ PHARMACEUTICALS LETTERHEAD]

June 10, 2019

Dear Suzanne:

As discussed, this letter confirms the changes to your employment terms with Jazz Pharmaceuticals, Inc. (the "**Company**"), effective as of June 3, 2019 (the "**Effective Date**") and ending on September 30, 2019 unless extended by further agreement.

As you know, you previously moved from a full-time work schedule to a half-time work schedule, although you remained a salaried exempt employee. Effective as of the Effective Date, your status was converted from an exempt salaried employee to a non-exempt hourly part-time employee. Your work hours will be variable and on an as-needed basis, as determined between you and Jana Gold, although you are expected to work materially less than half-time. Your work will continue to be performed off-site.

As a non-exempt employee, your regular hourly rate will be $450, and you will be paid based on the amount of time actually worked. We do not anticipate that you will be working overtime, but as a non-exempt employee you will be eligible for overtime pay if you work more than eight hours in a day or over forty hours in a week; any overtime must be approved in advance by Jana. Additionally, as a non-exempt employee, you must timely report your time worked on our timekeeping system for non-exempt employees.

Because your regular work schedule will be less than 20 hours per week, you will no longer be eligible for continued health insurance or other insurance benefits (unless required by law, including worker's compensation coverage). Under the terms of the health insurance plans, your health insurance coverage will continue through the end of June 2019; thereafter, you will be able to elect continued coverage at your own expense (if you wish) under COBRA laws. You will separately receive more information about COBRA continuation coverage within the timing required by law. As of the Effective Date, you also ceased to accrue vacation time, and you will not be eligible for Company holidays.

We anticipate that your employment relationship with the Company will be reevaluated around the end of September 2019, in order to determine whether to continue your employment or if your employment will end due to your resignation (which was originally planned to be effective as of the day before the Effective Date). Except as otherwise specifically provided below, your other terms and conditions of employment will remain in effect, including your at-will employment status and your continued compliance with any agreements that you have signed with the Company (such as your Employee Confidential Information and Inventions Agreement) and applicable policies.

This letter amends and supersedes in its entirety any and all prior agreements (whether oral or written) between you and the Company concerning your continuing employment arrangements on and after the Effective Date; *provided, however*, that for clarity, your Employee Confidential Information and Inventions Agreement and applicable policies will remain in full force and effect.

Please let me know if you have any questions. If this arrangement is agreeable to you, then please sign and date this letter in the space provided below and return it at your earliest convenience.

Sincerely,

JAZZ PHARMACEUTICALS, INC.

By: /s/ Eric Fink
Eric Fink
Vice President, Human Resources

Reviewed and agreed:

/s/ Suzanne Hooper
Suzanne Sawochka Hooper

June 10, 2019
Date

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: August 6, 2019

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: August 6, 2019

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 June 30, 2019, 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: August 6, 2019

/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.