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

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2022

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 November 2, 2022, 62,966,320 ordinary shares of the registrant, nominal value $0.0001 per share, were outstanding.

JAZZ PHARMACEUTICALS PLC
QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED SEPTEMBER 30, 2022

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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, Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, Epidiolex® (cannabidiol) oral solution, Epidyolex® (the trade name in Europe for Epidiolex), Defitelio® (defibrotide sodium), Defitelio® (defibrotide), CombiPlex®, Vyxeos® (daunorubicin and cytarabine) liposome for injection, Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion, Zepzelca® (lurbinectedin), Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) and Sativex® (nabiximols) oral solution. This Quarterly Report on Form 10-Q also includes trademarks, service marks and trade names of other companies. Trademarks, service marks and trade names appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

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

	September 30, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 839,358	$ 591,448
Investments	60,000	—
Accounts receivable, net of allowances	601,179	563,360
Inventories	728,074	1,072,721
Prepaid expenses	92,877	131,413
Other current assets	250,016	252,392
Total current assets	2,571,504	2,611,334
Property, plant and equipment, net	216,339	256,837
Operating lease assets	73,728	86,586
Intangible assets, net	5,570,394	7,152,328
Goodwill	1,592,635	1,827,609
Deferred tax assets, net	314,965	311,103
Deferred financing costs	9,949	12,029
Other non-current assets	35,153	40,813
Total assets	$ 10,384,667	$ 12,298,639
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 102,249	$ 100,298
Accrued liabilities	668,390	666,304
Current portion of long-term debt	31,000	31,000
Income taxes payable	10,444	9,608
Deferred revenue	871	2,093
Total current liabilities	812,954	809,303
Deferred revenue, non-current	116	463
Long-term debt, less current portion	5,695,814	6,018,943
Operating lease liabilities, less current portion	72,984	87,200
Deferred tax liabilities, net	933,670	1,300,541
Other non-current liabilities	123,935	116,998
Commitments and contingencies (Note 10)		
Shareholders' equity:		
Ordinary shares	6	6
Non-voting euro deferred shares	55	55
Capital redemption reserve	472	472
Additional paid-in capital	3,387,997	3,534,792
Accumulated other comprehensive loss	(1,617,646)	(400,360)
Retained earnings	974,310	830,226
Total shareholders' equity	2,745,194	3,965,191
Total liabilities and shareholders' equity	$ 10,384,667	$ 12,298,639

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenues:				
Product sales, net	$ 935,766	$ 834,247	$ 2,673,903	$ 2,186,118
Royalties and contract revenues	4,886	3,868	13,348	11,389
Total revenues	940,652	838,115	2,687,251	2,197,507
Operating expenses:				
Cost of product sales (excluding amortization of acquired developed technologies)	133,661	145,224	373,153	304,607
Selling, general and administrative	358,478	363,682	1,033,764	1,053,221
Research and development	148,870	141,036	417,898	350,305
Intangible asset amortization	141,232	159,804	461,782	368,476
Acquired in-process research and development	—	—	69,148	—
Impairment charge	133,648	—	133,648	—
Total operating expenses	915,889	809,746	2,489,393	2,076,609
Income from operations	24,763	28,369	197,858	120,898
Interest expense, net	(80,244)	(93,372)	(214,117)	(190,168)
Foreign exchange gain (loss)	(4,649)	(2,631)	(16,532)	1,262
Loss before income tax expense (benefit) and equity in loss (gain) of investees	(60,130)	(67,634)	(32,791)	(68,008)
Income tax expense (benefit)	(43,027)	(18,057)	(58,603)	228,583
Equity in loss (gain) of investees	2,545	3,256	9,148	(2,274)
Net income (loss)	$ (19,648)	$ (52,833)	$ 16,664	$ (294,317)
Net income (loss) per ordinary share:				
Basic	$ (0.31)	$ (0.86)	$ 0.27	$ (4.98)
Diluted	$ (0.31)	$ (0.86)	$ 0.26	$ (4.98)
Weighted-average ordinary shares used in per share calculations - basic	62,785	61,284	62,365	59,084
Weighted-average ordinary shares used in per share calculations - diluted	62,785	61,284	63,388	59,084

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Net income (loss)	$ (19,648)	$ (52,833)	$ 16,664	$ (294,317)
Other comprehensive loss:				
Foreign currency translation adjustments	(511,617)	(206,819)	(1,217,414)	(265,342)
Loss on fair value hedging activities reclassified from accumulated other comprehensive income (loss) to foreign exchange gain (loss), net of income tax benefit of $—, $—, $43 and $—, respectively	—	—	128	—
Loss on cash flow hedging activities reclassified from accumulated other comprehensive income (loss) to interest expense, net of income tax benefit of $—, $22, $— and $355, respectively	—	153	—	2,482
Unrealized loss on cash flow hedging activities, net of income tax benefit of $—, $—, $— and $2, respectively	—	—	—	(14)
Unrealized gain (loss) on fair value hedging activities, net of income tax provision (benefit) of $—, $28, $— and ($97), respectively	—	84	—	(291)
Other comprehensive loss	(511,617)	(206,582)	(1,217,286)	(263,165)
Total comprehensive loss	$ (531,265)	$ (259,415)	$ (1,200,622)	$ (557,482)

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 Loss	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2021	61,633	$ 6	4,000	$ 55	$ 472	$ 3,534,792	$ (400,360)	$ 830,226	$ 3,965,191
Cumulative effect adjustment from adoption of ASU 2020-06	—	—	—	—	—	(333,524)	—	127,474	(206,050)
Issuance of ordinary shares in conjunction with exercise of share options	207	—	—	—	—	21,729	—	—	21,729
Issuance of ordinary shares in conjunction with vesting of restricted stock units	404	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(33,776)	—	—	(33,776)
Share-based compensation	—	—	—	—	—	50,106	—	—	50,106
Other comprehensive loss	—	—	—	—	—	—	(190,360)	—	(190,360)
Net income	—	—	—	—	—	—	—	1,647	1,647
Balance at March 31, 2022	62,244	$ 6	4,000	$ 55	$ 472	$ 3,239,327	$ (590,720)	$ 959,347	$ 3,608,487
Issuance of ordinary shares in conjunction with exercise of share options	194	—	—	—	—	16,640	—	—	16,640
Issuance of ordinary shares under employee stock purchase plan	81	—	—	—	—	8,234	—	—	8,234
Issuance of ordinary shares in conjunction with vesting of restricted stock units	104	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(6,289)	—	—	(6,289)
Share-based compensation	—	—	—	—	—	54,407	—	—	54,407
Shares repurchased	—	—	—	—	—	—	—	(54)	(54)
Other comprehensive loss	—	—	—	—	—	—	(515,309)	—	(515,309)
Net income	—	—	—	—	—	—	—	34,665	34,665
Balance at June 30, 2022	62,623	$ 6	4,000	$ 55	$ 472	$ 3,312,319	$ (1,106,029)	$ 993,958	$ 3,200,781
Issuance of ordinary shares in conjunction with exercise of share options	207	—	—	—	—	21,260	—	—	21,260
Issuance of ordinary shares in conjunction with vesting of restricted stock units	60	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(2,567)	—	—	(2,567)
Share-based compensation	—	—	—	—	—	56,985	—	—	56,985
Other comprehensive loss	—	—	—	—	—	—	(511,617)	—	(511,617)
Net loss	—	—	—	—	—	—	—	(19,648)	(19,648)
Balance at September 30, 2022	62,890	$ 6	4,000	$ 55	$ 472	$ 3,387,997	$ (1,617,646)	$ 974,310	$ 2,745,194

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 Loss	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2020	56,171	$ 6	4,000	$ 55	$ 472	$ 2,633,670	$ (134,352)	$ 1,159,894	$ 3,659,745
Issuance of ordinary shares in conjunction with exercise of share options	408	—	—	—	—	50,407	—	—	50,407
Issuance of ordinary shares in conjunction with vesting of restricted stock units	294	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(23,784)	—	—	(23,784)
Share-based compensation	—	—	—	—	—	34,565	—	—	34,565
Other comprehensive loss	—	—	—	—	—	—	(45,076)	—	(45,076)
Net income	—	—	—	—	—	—	—	121,832	121,832
Balance at March 31, 2021	56,873	$ 6	4,000	$ 55	$ 472	$ 2,694,858	$ (179,428)	$ 1,281,726	$ 3,797,689
Issuance of ordinary shares in connection with the acquisition of GW Pharmaceuticals plc	3,798	—	—	—	—	608,456	—	—	608,456
Share-based payment - precombination service in connection with the acquisition of GW Pharmaceuticals plc	—	—	—	—	—	3,555	—	—	3,555
Issuance of ordinary shares in conjunction with exercise of share options	328	—	—	—	—	43,600	—	—	43,600
Issuance of ordinary shares under employee stock purchase plan	79	—	—	—	—	8,282	—	—	8,282
Issuance of ordinary shares in conjunction with vesting of restricted stock units	37	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(3,388)	—	—	(3,388)
Share-based compensation	—	—	—	—	—	48,119	—	—	48,119
Other comprehensive loss	—	—	—	—	—	—	(11,507)	—	(11,507)
Net loss	—	—	—	—	—	—	—	(363,316)	(363,316)
Balance at June 30, 2021	61,115	$ 6	4,000	$ 55	$ 472	$ 3,403,482	$ (190,935)	$ 918,410	$ 4,131,490
Issuance of ordinary shares in conjunction with exercise of share options	202	—	—	—	—	14,822	—	—	14,822
Issuance of ordinary shares in conjunction with vesting of restricted stock units	63	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(2,431)	—	—	(2,431)
Share-based compensation	—	—	—	—	—	54,011	—	—	54,011
Other comprehensive loss	—	—	—	—	—	—	(206,582)	—	(206,582)
Net loss	—	—	—	—	—	—	—	(52,833)	(52,833)
Balance at September 30, 2021	61,380	$ 6	4,000	$ 55	$ 472	$ 3,469,884	$ (397,517)	$ 865,577	$ 3,938,477

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

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

	Nine Months Ended September 30,	
	2022	**2021**
Operating activities		
Net income (loss)	$ 16,664	$ (294,317)
Adjustments to reconcile net income (loss) to net cash provided by operating activities:		
Intangible asset amortization	461,782	368,476
Acquisition accounting inventory fair value step-up adjustment	203,189	148,637
Share-based compensation	160,438	135,887
Deferred tax expense (benefit)	(146,874)	96,593
Impairment charge	133,648	—
Acquired in-process research and development	69,148	—
Loss on disposal of a business	39,258	—
Non-cash interest expense	32,002	66,055
Depreciation	22,958	19,387
Provision for losses on accounts receivable and inventory	13,066	13,444
Other non-cash transactions	(26,352)	9,622
Changes in assets and liabilities:		
Accounts receivable	(43,868)	(27,956)
Inventories	(50,458)	(33,891)
Prepaid expenses and other current assets	23,801	(34,722)
Operating lease assets	10,672	12,054
Other non-current assets	(4,006)	(1,837)
Accounts payable	4,188	19,167
Accrued liabilities	17,864	93,534
Income taxes payable	(172)	9,171
Deferred revenue	(1,570)	(1,608)
Operating lease liabilities, less current portion	(12,139)	(13,423)
Other non-current liabilities	6,767	16,479
Net cash provided by operating activities	930,006	600,752
Investing activities		
Proceeds from sale of a business	53,000	—
Purchases of property, plant and equipment	(19,668)	(17,674)
Acquisition of intangible assets	(25,000)	(17,891)
Acquisition of investments	(61,036)	(26,694)
Acquired in-process research and development	(69,148)	—
Proceeds from maturity of investments	—	1,095,000
Acquisition of a business, net of cash acquired	—	(6,234,792)
Net cash used in investing activities	(121,852)	(5,202,051)
Financing activities		
Proceeds from employee equity incentive and purchase plans	67,863	117,111
Share repurchases	(54)	—
Payment of employee withholding taxes related to share-based awards	(42,632)	(29,603)
Repayments of long-term debt	(574,264)	(843,028)
Net proceeds from issuance of borrowings under credit agreement	—	3,719,930
Net proceeds from issuance of Senior Secured Notes, due 2029	—	1,471,533
Payments for repurchase of Exchangeable Senior Notes, due 2021	—	(218,812)
Net cash (used in) provided by financing activities	(549,087)	4,217,131
Effect of exchange rates on cash and cash equivalents	(11,157)	(1,821)
Net increase (decrease) in cash and cash equivalents	247,910	(385,989)
Cash and cash equivalents, at beginning of period	591,448	1,057,769
Cash and cash equivalents, at end of period	$ 839,358	$ 671,780

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 whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases - often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we strive to identify new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science.

Our lead marketed products are:

Neuroscience

- **Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution**, a product approved by the U.S. Food and Drug Administration, or FDA, in July 2020 and launched in the U.S. in November 2020 for the treatment of cataplexy or excessive daytime sleepiness, or EDS, in patients with narcolepsy aged seven years of age and older, and also approved by FDA in August 2021 for the treatment of idiopathic hypersomnia, or IH, in adults and launched in the U.S. in November 2021. Xywav contains 92% less sodium than Xyrem®;
- **Xyrem® (sodium oxybate) oral solution**, a product approved by FDA and distributed in the U.S. for the treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy; Jazz also markets Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. Xyrem is also approved and distributed in the EU, Great Britain and other markets through a licensing agreement;
- **Epidiolex® (cannabidiol) oral solution**, a product approved by FDA and launched in the U.S. in 2018 by GW Pharmaceuticals plc, or GW, and currently indicated for the treatment of seizures associated with Lennox-Gastaut syndrome, or LGS, Dravet syndrome, or DS, or tuberous sclerosis complex, or TSC, in patients one year of age or older; in the EU (where it is marketed as Epidyolex®) and other markets, it is approved for adjunctive treatment of seizures associated with LGS or DS, in conjunction with clobazam (EU and Great Britain only), in patients 2 years of age and older and for adjunctive treatment of seizures associated with TSC in patients 2 years of age and older; and
- **Sativex® (nabiximols) oral solution**, a product approved and commercialized in 29 countries outside the U.S. as treatment for symptom improvement in adult patients with moderate to severe spasticity due to multiple sclerosis, or MS, who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity-related symptoms during an initial trial of therapy.

Oncology

- **Zepzelca® (lurbinectedin)**, a product approved by FDA in June 2020 under FDA's accelerated approval pathway and launched in the U.S. in July 2020 for the treatment of adult patients with metastatic small cell lung cancer, or SCLC, with disease progression on or after platinum-based chemotherapy; in Canada, Zepzelca received conditional approval in September 2021 for the treatment of adults with Stage III or metastatic SCLC, who have progressed on or after platinum-containing therapy;
- **Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)**, a product approved by FDA in June 2021 and launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia, or ALL, or lymphoblastic lymphoma, or LBL, in adults and pediatric patients one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase;
- **Vyxeos® (daunorubicin and cytarabine) liposome for injection**, a product approved in the U.S., Canada, EU, Great Britain, Switzerland, Israel and Australia (marketed as Vyxeos® liposomal in the EU, Great Britain, Switzerland and Israel) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia, or t-AML, or AML with myelodysplasia-related changes, or AML-MRC. An expanded indication was granted in the U.S. for the treatment of newly diagnosed t-AML or AML-MRC in pediatric patients aged 1 year and older; and
- **Defitelio® (defibrotide sodium)**, a product approved in the U.S. and Brazil for the treatment of hepatic veno-occlusive disease, or VOD, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT, and in Japan for the treatment of hepatic sinusoidal obstruction syndrome (hepatic veno-occlusive disease). It is currently approved in the EU, Great Britain and other markets for the treatment of severe hepatic VOD, also known as sinusoidal obstructive syndrome, or SOS, in HSCT therapy. It is indicated in adults and pediatric patients over 1 month of age.

Throughout this Quarterly Report on Form 10-Q, unless otherwise indicated or the context otherwise requires, all references to “Jazz Pharmaceuticals,” “the registrant,” "the Company", “we,” “us,” and “our” refer to Jazz Pharmaceuticals plc and its consolidated subsidiaries. Throughout this Quarterly Report on Form 10-Q, 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, 2021.

In the opinion of management, these condensed consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and include all adjustments, consisting only of normal recurring adjustments, considered necessary for the fair presentation of our financial position and operating results. The results for the three and nine months ended September 30, 2022 are not necessarily indicative of the results to be expected for the year ending December 31, 2022, 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, 2021, other than as described below.

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

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

Use of Estimates

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

Adoption of New Accounting Standards

In August 2020, the Financial Accounting Standards Board, or FASB, issued ASU No. 2020-06, “Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging— Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity”, or ASU 2020-06. ASU 2020-06 simplifies the accounting for convertible instruments by eliminating the requirement to separate embedded conversion features from the host contract when the conversion features are not required to be accounted for as derivatives under Topic 815, Derivatives and Hedging, or that do not result in substantial premiums accounted for as paid-in capital. The Company adopted ASU 2020-06 on January 1, 2022, on a modified retrospective basis. This impacted the accounting for our 1.50% exchangeable senior notes due 2024, or the 2024 Notes, and our 2.00% exchangeable senior notes due 2026, or the 2026 Notes, collectively known as the Exchangeable Senior Notes. As a result of the adoption of ASU 2020-06, the Exchangeable Senior Notes are now accounted for entirely as liabilities measured at amortized cost. ASU 2020-06 also removes certain settlement conditions that are required for contracts to qualify for equity classification and eliminates the treasury stock method to calculate diluted earnings per share for convertible instruments and requires the use of the if-converted method.

The adoption of ASU 2020-06 resulted in the following adjustments to the condensed consolidated balance sheet (in thousands):

Balance Sheet Item:	December 31, 2021	Adoption of ASU 2020-06	January 1, 2022
Deferred tax assets, net	$ 311,103	$ 109	$ 311,212
Long-term debt, less current portion	6,018,943	206,159	6,225,102
Retained earnings	830,226	127,474	957,700
Additional paid-in capital	3,534,792	(333,524)	3,201,268

Interest expense on the Exchangeable Senior Notes is lower as a result of adoption of this guidance. During the three and nine months ended September 30, 2022 the effect of adoption reduced interest expense, net and increased net income by approximately $12 million and $36 million, respectively, and increased basic and diluted EPS by approximately $0.20 per share and $0.57 per share, respectively. The Exchangeable Senior Notes were determined to be anti-dilutive for the three and nine months ended September 30, 2022. The adoption of ASU 2020-06 did not impact our cash flows or compliance with debt covenants.

Significant Risks and Uncertainties

We have implemented a comprehensive response strategy designed to manage the ongoing impact of the COVID-19 pandemic on our employees, patients and our business. The prolonged nature of the pandemic is negatively impacting our business in a varied manner due to the emergence of variants with increased transmissibility, even in vaccinated people, including with respect to limited access to health care provider offices and institutions and the willingness of patients or parents of patients to seek treatment. We believe these dynamics have negatively impacted new patient starts in the U.S. and Europe. We expect that our business, financial condition, results of operations and growth prospects may continue to be negatively impacted by the pandemic on a limited basis that may vary depending on the context. However, we have begun to observe, and expect to continue to observe, a gradual normalization in patient and health care provider practices, as providers and patients have adapted their behaviors and procedures to the evolving circumstances and as COVID-19 vaccines continue to be administered. With respect to our commercialization activities, while there continues to be some negative impact on demand, new patient starts and treatments for our products arising from the pandemic, primarily due to the inherent limitations of telemedicine and a reprioritization of healthcare resources toward COVID-19, we have seen improvements as healthcare systems have adapted to cope with the ongoing situation. The extent of the impact on our ability to generate sales of approved products, execute on new product launches, our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time.

Our business has been substantially dependent on Xyrem and while we expect that our business will continue to be substantially dependent on oxybate product sales from both Xyrem and Xywav, there is no guarantee that we can maintain oxybate revenues at or near current levels, or that oxybate revenues will continue to grow. Our ability to maintain or increase oxybate revenues and realize the anticipated benefits from our investment in Xywav are subject to a number of risks and uncertainties including, without limitation, those related to the launch of Xywav for the treatment of IH in adults and adoption in that indication; competition from the near-term introduction of authorized generic versions of sodium oxybate and from generic versions of sodium oxybate and new products for treatment of cataplexy and/or EDS in narcolepsy in the U.S. market and from other competitors; the current and potential impacts of the COVID-19 pandemic, including the current and expected future negative impact on demand for our products; increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including our ability to maintain adequate coverage and reimbursement for Xywav and Xyrem; increased rebates required to maintain access to our products; challenges to our intellectual property around Xywav and/or Xyrem, including pending antitrust and intellectual property litigation; and continued acceptance of Xywav and Xyrem by physicians and patients.

In addition to risks related specifically to Xywav and Xyrem, we are subject to other challenges and risks related to successfully commercializing a portfolio of oncology products and other neuroscience products, and other 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: ongoing clinical research activity and related outcomes, obtaining regulatory approval of our late-stage product candidates; effectively commercializing our approved or acquired products such as Epidiolex, Zepzelca and Rylaze; obtaining and maintaining adequate coverage and reimbursement for our products; contracting and rebates to pharmacy benefit managers that reduces our net revenue; increasing scrutiny of pharmaceutical product pricing and resulting changes in healthcare laws and policy; market acceptance; regulatory concerns with controlled substances generally and the potential for abuse; future legislation, action by the U.S. Drug Enforcement Administration, or DEA, or FDA action authorizing the sale, distribution, use,

and insurance reimbursement of non-FDA approved cannabinoid products; delays or problems in the supply of our products, loss of single source suppliers or failure to comply with manufacturing regulations; delays or problems with third parties that are part of our manufacturing and supply chain; identifying, acquiring or in-licensing additional products or product candidates; pharmaceutical product development and the inherent uncertainty of clinical success; 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.

In May 2021, we acquired GW. The total consideration paid by us for the entire issued share capital of GW was $7.2 billion. We refer to the acquisition of GW as the GW Acquisition. The success of the GW Acquisition will depend, in part, on our ability to realize the anticipated benefits from our and GW's historical businesses. The anticipated benefits to us of the GW Acquisition may not be realized fully within the expected timeframe or at all or may take longer to realize or cost more than expected, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Concentrations of Risk

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

We manage our foreign currency transaction risk and interest rate risk within specified guidelines through the use of derivatives. All of our derivative instruments are utilized for risk management purposes, and we do not use derivatives for speculative trading purposes. As of September 30, 2022, we had foreign exchange forward contracts with notional amounts totaling $608.6 million. As of September 30, 2022, the outstanding foreign exchange forward contracts had a net liability fair value of $34.4 million. 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 economic conditions in certain European countries which may result in variability of the timing of cash receipts and an increase in the average length of time that it takes to collect accounts receivable outstanding. Historically, we have not experienced significant credit losses on our accounts receivable and as of September 30, 2022 and December 31, 2021, allowances on receivables were not material. As of September 30, 2022, three customers accounted for 75% of gross accounts receivable, Express Scripts Specialty Distribution Services, Inc. and its affiliates, or ESSDS, which accounted for 55% of gross accounts receivable, Cardinal Health, Inc., or Cardinal, which accounted for 11% of gross accounts receivable, and McKesson Corporation and affiliates, or McKesson, which accounted for 9% of gross accounts receivable. As of December 31, 2021, three customers accounted for 74% of gross accounts receivable, ESSDS, which accounted for 52% of gross accounts receivable, McKesson, which accounted for 12% of gross accounts receivable, and Cardinal, which accounted for 10% of gross accounts receivable.

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

Recent Accounting Pronouncements

In October 2021, the FASB issued ASU 2021-08, “Business Combinations (Topic 805): Accounting for Contract Assets and Contract Liabilities from Contracts with Customers”, which requires entities to recognize and measure contract assets and contract liabilities acquired in a business combination in accordance with ASC 2014-09, “Revenue from Contracts with Customers (Topic 606)”. The update will generally result in an entity recognizing contract assets and contract liabilities at amounts consistent with those recorded by the acquiree immediately before the acquisition date rather than at fair value. The new standard is effective on a prospective basis for fiscal years beginning after December 15, 2022, with early adoption permitted. The new guidance is not expected to have a material impact on our results of operations, financial position, or cash flows.

2. Disposition and License Agreements

Sunosi U.S. Disposition

In March 2022, we entered into a definitive agreement to divest Sunosi to Axsome Therapeutics, or Axsome. In May 2022, we completed the U.S. divestiture of Sunosi and expect to complete the ex-U.S. divestiture later this year. Under the terms of the sale agreement, Axsome received the rights to Sunosi in all of the existing territories available to us. We received an upfront payment of $53.0 million, and have the right to receive a high single-digit royalty on Axsome's U.S. net sales of Sunosi in current indications and a mid-single-digit royalty on Axsome's U.S. net sales of Sunosi in future indications.

Upon closing, we recognized a loss on disposal of $40.8 million within selling, general and administrative expenses in our condensed consolidated statements of income (loss) in the nine months ended September 30, 2022. We are accounting for the contingent consideration in the form of the future royalty as it is earned.

We determined that the disposal of Sunosi does not qualify for reporting as a discontinued operation since it does not represent a strategic shift that has or will have a major effect on our operations and financial results.

License Agreements

In the second quarter of 2022, we entered into a licensing agreement with Werewolf Therapeutics, Inc., or Werewolf, to acquire exclusive global development and commercialization rights to Werewolf's investigational WTX-613, now referred to as JZP898. JZP898 is a differentiated, conditionally-activated interferon alpha (IFNα) INDUKINE™ molecule. Under the terms of the agreement, we made an upfront payment of $15.0 million to Werewolf, which was recorded as acquired in-process research and development, or IPR&D, expense in our condensed consolidated statements of income (loss) in the nine months ended September 30, 2022. Werewolf is eligible to receive development, regulatory and commercial milestone payments of up to $1.26 billion and, if JZP898 is approved, a tiered, mid-single-digit percentage royalty on net sales of JZP898.

In the second quarter of 2022, we entered into a licensing agreement with Sumitomo Pharma Co., Ltd, or Sumitomo, to acquire exclusive development and commercialization rights in the U.S., Europe and other territories for DSP-0187, now referred to as JZP441. JZP441 is a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. Under the terms of the agreement, we made an upfront payment of $50.0 million to Sumitomo, which was recorded as acquired IPR&D expense in our condensed consolidated statements of income (loss) in the nine months ended September 30, 2022. Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to $1.09 billion and, if JZP441 is approved, a tiered, low double-digit royalty on Jazz's net sales of JZP441.

3. Cash and Available-for-Sale Securities

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

	September 30, 2022					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 296,686	$ —	$ —	$ 296,686	$ 296,686	$ —
Time deposits	60,000	—	—	60,000	—	60,000
Money market funds	542,672	—	—	542,672	542,672	—
Totals	$ 899,358	$ —	$ —	$ 899,358	$ 839,358	$ 60,000

	December 31, 2021					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	$ 510,747	$ —	$ —	$ 510,747	$ 510,747	$ —
Money market funds	80,701	—	—	80,701	80,701	—
Totals	$ 591,448	$ —	$ —	$ 591,448	$ 591,448	$ —

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 (loss). Our investment balances represent time deposits with original maturities of greater than three months and less than one year. Interest income from available-for-sale securities was $3.5 million and $4.4 million

in the three and nine months ended September 30, 2022, respectively, and $0.1 million and $1.7 million in the three and nine months ended September 30, 2021, respectively.

4. Fair Value Measurement

The following table summarizes, by major security type, our available-for-sale securities and derivative contracts as of September 30, 2022 and December 31, 2021 that were measured at fair value on a recurring basis and were categorized using the fair value hierarchy (in thousands):

	September 30, 2022			December 31, 2021		
	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:						
Money market funds	$ 542,672	$ —	$ 542,672	$ 80,701	$ —	$ 80,701
Time deposits	—	60,000	60,000	—	—	—
Foreign exchange forward contracts	—	3,388	3,388	—	580	580
Totals	$ 542,672	$ 63,388	$ 606,060	$ 80,701	$ 580	$ 81,281
Liabilities:						
Cross-currency interest rate contracts	$ —	$ —	$ —	$ —	$ 15,232	$ 15,232
Foreign exchange forward contracts	—	37,742	37,742	—	3,187	3,187
Totals	$ —	$ 37,742	$ 37,742	$ —	$ 18,419	$ 18,419

As of September 30, 2022, our available-for-sale securities included money market funds and time deposits and their carrying values were approximately equal to their fair values. Money market funds were measured using quoted prices in active markets, which represent Level 1 inputs and time deposits were measured at fair value using Level 2 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 foreign exchange derivatives that are measured at fair value using observable market inputs such as forward rates and based on these inputs, the derivative assets and liabilities are classified within Level 2 of the fair value hierarchy. The cross-currency interest rate swap contract matured on March 31, 2022.

There were no transfers between the different levels of the fair value hierarchy in 2022 or 2021.

As of September 30, 2022, the carrying amount of investments measured using the measurement alternative for equity investments without a readily determinable fair value was $5.5 million. The carrying amount, which is recorded within other non-current assets, is based on the latest observable transaction price.

As of September 30, 2022, the estimated fair values of the 2024 Notes, the 2026 Notes, the 4.375% senior secured notes, due 2029, or the Secured Notes, and the seven-year $3.1 billion term loan B facility, or the Dollar Term Loan, were approximately $545 million, $1.1 billion, $1.3 billion and $2.7 billion respectively. The fair values of each of these debt facilities was estimated using quoted market prices obtained from brokers (Level 2).

5. Derivative Instruments and Hedging Activities

We are exposed to certain risks arising from operating internationally, including fluctuations in foreign exchange rates primarily related to the translation of sterling and 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.

In order to hedge our exposure to foreign currency exchange risk associated with our seven-year €625.0 million term loan B facility, or the Euro Term Loan, we entered into a cross-currency interest rate swap contract in May 2021, which matured on March 31, 2022, and was de-designated as a fair value hedge. The terms of this contract converted the principal repayments and interest payments on the Euro Term Loan into U.S. dollars. The carrying amount of the Euro Term Loan and the fair value

of the cross-currency interest rate swap contract were remeasured on a monthly basis, with changes in the euro to U.S. dollar foreign exchange rates recognized within foreign exchange gain (loss) in the condensed consolidated statements of income (loss).

The impact on accumulated other comprehensive income (loss) and earnings from the cross-currency interest rate swap contract was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
Cross-Currency Interest Rate Contract:	**2022**	**2021**	**2022**	**2021**
Loss recognized in accumulated other comprehensive income (loss), net of tax	$ —	$ —	$ —	$ (375)
Loss reclassified from accumulated other comprehensive income (loss) to foreign exchange gain (loss), net of tax	—	84	128	84
Loss recognized in foreign exchange gain (loss)	—	(13,750)	(2,646)	(26,115)

We also enter into foreign exchange forward contracts, with durations of up to 12 months, designed to limit the exposure to fluctuations in foreign exchange rates related to the translation of certain non-U.S. dollar denominated liabilities, including intercompany balances. Hedge accounting is not applied to these derivative instruments as gains and losses on these hedge transactions are designed to offset gains and losses on underlying balance sheet exposures. As of September 30, 2022 and December 31, 2021, the notional amount of foreign exchange contracts where hedge accounting is not applied was $608.6 million and $347.2 million, respectively.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
Foreign Exchange Forward Contracts:	**2022**	**2021**	**2022**	**2021**
Loss recognized in foreign exchange gain (loss)	$ (40,331)	$ (8,231)	$ (95,536)	$ (18,264)

The cash flow effects of our derivative contracts for the nine months ended September 30, 2022 and 2021 are included within net cash provided by operating activities in the condensed consolidated statements of cash flows, except for the settlement of notional amounts of the cross-currency interest rate contract, which are included in net cash provided by (used in) financing activities.

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. In May 2021, we repaid the term loan to which these interest rate swap agreements related, at which point the interest rate swap contracts were de-designated as cash flow hedges. The interest rate swap agreements matured in July 2021.

The impact on accumulated other comprehensive income (loss) and earnings from interest rate swap contracts for the three and nine months ended September 30, 2021 was as follows (in thousands):

	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2021
Interest Rate Contracts:		
Loss recognized in accumulated other comprehensive income (loss), net of tax	$ —	$ (14)
Gain reclassified from accumulated other comprehensive income (loss) to interest expense, net of tax	153	2,482

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

	Classification	September 30, 2022	December 31, 2021
Assets			
Derivatives not designated as hedging instruments:			
Foreign exchange forward contracts	Other current assets	$ 3,388	$ 580
Liabilities			
Derivatives not designated as hedging instruments:			
Foreign exchange forward contracts	Accrued liabilities	$ 37,742	$ 3,187
Derivatives designated as hedging instruments:			
Cross-currency interest rate contract	Accrued liabilities	—	15,232
Total fair value of derivative liability instruments		$ 37,742	$ 18,419

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 cross-currency interest rate contracts and foreign exchange forward contracts subject to such provisions (in thousands):

	September 30, 2022					
				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	$ 3,388	$ —	$ 3,388	$ (3,388)	$ —	$ —
Derivative liabilities	(37,742)	—	(37,742)	3,388	—	(34,354)

	December 31, 2021					
				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	$ 580	$ —	$ 580	$ (567)	$ —	$ 13
Derivative liabilities	(18,419)	—	(18,419)	567	—	(17,852)

6. Inventories

Inventories consisted of the following (in thousands):

	September 30, 2022	December 31, 2021
Raw materials	$ 20,284	$ 21,550
Work in process	557,233	886,849
Finished goods	150,557	164,322
Total inventories	$ 728,074	$ 1,072,721

As of September 30, 2022 and December 31, 2021 inventories included $487.3 million and $811.3 million, respectively, related to the purchase accounting inventory fair value step-up on inventory acquired in the GW Acquisition.

7. Goodwill and Intangible Assets

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

Balance at December 31, 2021	$ 1,827,609
Goodwill allocated to divestiture of Sunosi [(1)]	(12,927)
Foreign exchange	(222,047)
Balance at September 30, 2022	$ 1,592,635

[(1)] See Note 2 for further information relating to this divestiture.

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

		September 30, 2022			December 31, 2021		
	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	10.7	$ 7,050,958	$ (1,480,564)	$ 5,570,394	$ 8,195,675	$ (1,198,333)	$ 6,997,342
Manufacturing contracts	—	10,435	(10,435)	—	12,124	(12,124)	—
Trademarks	—	2,852	(2,852)	—	2,893	(2,893)	—
Total finite-lived intangible assets		7,064,245	(1,493,851)	5,570,394	8,210,692	(1,213,350)	6,997,342
Acquired in-process research and development assets		—	—	—	154,986	—	154,986
Total intangible assets		$ 7,064,245	$ (1,493,851)	$ 5,570,394	$ 8,365,678	$ (1,213,350)	$ 7,152,328

The decrease in the gross carrying amount of intangible assets as of September 30, 2022 compared to December 31, 2021 primarily reflects the negative impact of foreign currency translation adjustments due to the weakening of sterling and euro against the U.S. dollar, the impairment of our acquired IPR&D asset of $133.8 million as a result of the decision to discontinue our nabiximols program and the sale of the Sunosi acquired developed technology asset to Axsome.

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

Based on finite-lived intangible assets recorded as of September 30, 2022, 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
2022 (remainder)	$ 133,157
2023	532,628
2024	532,628
2025	532,628
2026	532,628
Thereafter	3,306,725
Total	$ 5,570,394

8. Certain Balance Sheet Items

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

	September 30, 2022	December 31, 2021
Manufacturing equipment and machinery	$ 67,201	$ 69,079
Construction-in-progress	67,088	86,511
Land and buildings	60,720	64,008
Leasehold improvements	60,315	66,318
Computer software	32,876	25,646
Computer equipment	15,769	16,234
Furniture and fixtures	10,341	14,412
Subtotal	314,310	342,208
Less accumulated depreciation and amortization	(97,971)	(85,371)
Property, plant and equipment, net	$ 216,339	$ 256,837

Other current assets consisted of the following (in thousands):

	September 30, 2022	December 31, 2021
Deferred charge for income taxes on intercompany profit	$ 204,652	$ 203,480
Other	45,364	48,912
Total other current assets	$ 250,016	$ 252,392

Accrued liabilities consisted of the following (in thousands):

	September 30, 2022	December 31, 2021
Rebates and other sales deductions	$ 266,389	$ 215,397
Employee compensation and benefits	152,049	158,870
Derivative instrument liabilities	37,742	18,419
Clinical trial accruals	24,036	25,612
Sales return reserve	22,637	15,814
Consulting and professional services	21,858	22,507
Accrued interest	21,371	48,640
Accrued royalties	20,831	20,345
Current portion of lease liabilities	14,877	15,763
Selling and marketing accruals	13,532	21,566
Inventory-related accruals	6,237	16,166
Accrued construction-in-progress	3,978	2,894
Accrued milestones	750	25,000
Other	62,103	59,311
Total accrued liabilities	$ 668,390	$ 666,304

9. Debt

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

	September 30, 2022	December 31, 2021
2024 Notes	$ 575,000	$ 575,000
Unamortized - debt issuance costs	(3,178)	(4,401)
Unamortized discount - equity component	—	(66,836)
2024 Notes, net	571,822	503,763
2026 Notes	1,000,000	1,000,000
Unamortized - debt issuance costs	(9,611)	(11,407)
Unamortized discount - equity component	—	(139,323)
2026 Notes, net	990,389	849,270
Secured Notes	1,476,000	1,473,810
Term Loan [(1)]	2,688,603	3,223,100
Total debt	5,726,814	6,049,943
Less current portion	31,000	31,000
Total long-term debt	$ 5,695,814	$ 6,018,943

(1) In May 2021, we entered into a credit agreement that provided for (i) the Dollar Term Loan, (ii) the Euro Term Loan, together with the Dollar Term Loan, collectively known as the Term Loan and (iii) a five-year $500.0 million revolving credit facility. In 2021, we made voluntary prepayments on the Euro Term Loan totaling €416.7 million, or $502.0 million, and in March 2022 we repaid the remaining outstanding principal of €208.3 million, or $251.0 million. In September 2022, we made a voluntary repayment on the Dollar Term Loan totaling $300.0 million.

Exchangeable Senior Notes Due 2026

In 2020, we completed a private placement of $1.0 billion principal amount of the 2026 Notes. Interest on the 2026 Notes is payable semi-annually in cash in arrears on June 15 and December 15 of each year, beginning on December 15, 2020, at a rate of 2.00% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2026 Notes. The 2026 Notes mature on June 15, 2026, unless earlier exchanged, repurchased or redeemed.

The holders of the 2026 Notes have the ability to require us to repurchase all or a portion of their 2026 Notes for cash in the event we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution or the delisting of our ordinary shares from any of The New York Stock Exchange, The Nasdaq Global Market, The Nasdaq Global Select Market or The Nasdaq Capital Market (or any of their respective successors). Additionally, the terms and covenants in the indenture related to the 2026 Notes include certain events of default after which the 2026 Notes may be due and payable immediately. Prior to June 15, 2026, we may redeem the 2026 Notes, in whole but not in part, subject to compliance with certain conditions, if we have, or on the next interest payment date would, become obligated to pay to the holder of any 2026 Notes additional amounts as a result of certain tax-related events. We also may redeem the 2026 Notes on or after June 20, 2023 and prior to March 15, 2026, in whole or in part, if the last reported sale price per ordinary share has been at least 130% of the exchange price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide the notice of redemption.

The 2026 Notes are exchangeable at an initial exchange rate of 6.4182 ordinary shares per $1,000 principal amount of 2026 Notes, which is equivalent to an initial exchange price of approximately $155.81 per ordinary share. Upon exchange, the 2026 Notes may be settled in cash, ordinary shares or a combination of cash and ordinary shares, at our election. Our intent and policy is to settle the principal amount of the 2026 Notes in cash upon exchange. The exchange rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain make-whole fundamental changes occurring prior to the maturity date of the 2026 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2026 Notes who elect to exchange

their 2026 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to March 15, 2026, the 2026 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

Following the adoption of ASU 2020-06, the 2026 Notes are accounted for as a single liability measured at its amortized cost. The total liability is reflected net of issuance costs of $15.3 million which will be amortized over the term of the 2026 Notes. The effective interest rate of the 2026 Notes is 2.26%. During the three and nine months ended September 30, 2022, we recognized interest expense of $5.7 million and $16.8 million, respectively, of which $5.0 million and $15.0 million, related to the contractual coupon rate and $0.7 million and $1.8 million, related to the amortization of debt issuance costs. Please see Note 1 for further information on the adoption of ASU 2020-06.

Exchangeable Senior Notes Due 2024

In 2017, we completed a private placement of $575.0 million principal amount of 2024 Notes. Interest on the 2024 Notes is payable semi-annually in cash in arrears on February 15 and August 15 of each year, beginning on February 15, 2018, at a rate of 1.50% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2024 Notes. The 2024 Notes mature on August 15, 2024, unless earlier exchanged, repurchased or redeemed.

The holders of the 2024 Notes have the ability to require us to repurchase all or a portion of their 2024 Notes for cash in the event we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution or the delisting of our ordinary shares from The Nasdaq Global Select Market. Prior to August 15, 2024, we may redeem the 2024 Notes, in whole but not in part, subject to compliance with certain conditions, if we have, or on the next interest payment date would, become obligated to pay to the holder of any 2024 Notes additional amounts as a result of certain tax-related events. We also may redeem the 2024 Notes on or after August 20, 2021, in whole or in part, if the last reported sale price per ordinary share has been at least 130% of the exchange price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide the notice of redemption.

The 2024 Notes are exchangeable at an initial exchange rate of 4.5659 ordinary shares per $1,000 principal amount of 2024 Notes, which is equivalent to an initial exchange price of approximately $219.02 per ordinary share. Upon exchange, the 2024 Notes may be settled in cash, ordinary shares or a combination of cash and ordinary shares, at our election. Our intent and policy is to settle the principal amount of the 2024 Notes in cash upon exchange. The exchange rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain make-whole fundamental changes occurring prior to the maturity date of the 2024 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2024 Notes who elect to exchange their 2024 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to May 15, 2024, the 2024 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

Following adoption of ASU 2020-06, the 2024 Notes are accounted for as a single liability measured at its amortized cost. The total liability is reflected net of issuance costs of $11.4 million which will be amortized over the term of the 2024 Notes. The effective interest rate of the 2024 Notes is 1.79%. During the three and nine months ended September 30, 2022, we recognized interest expense of $2.5 million and $7.6 million, respectively, of which $2.1 million and $6.4 million related to the contractual coupon rate and $0.4 million and $1.2 million, related to the amortization of debt issuance costs. Please see Note 1 for further information on the adoption of ASU 2020-06.

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.

Maturities

Scheduled maturities with respect to our long-term debt principal balances outstanding as of September 30, 2022 were as follows (in thousands):

Year Ending December 31,	Scheduled Long-Term Debt Maturities
2022 (remainder)	$ 7,750
2023	31,000
2024	606,000
2025	31,000
2026	1,031,000
Thereafter	4,129,500
Total	$ 5,836,250

10. Commitments and Contingencies

Indemnification

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

We have agreed to indemnify our executive officers, directors and certain other employees for losses and costs incurred in connection with certain events or occurrences, including advancing money to cover certain costs, subject to certain limitations. The maximum potential amount of future payments we could be required to make under the indemnification obligations is unlimited; however, we maintain insurance policies that may limit our exposure and may enable us to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits and other policy provisions, we believe the fair value of these indemnification obligations is not significant. Accordingly, we did not recognize any liabilities relating to these obligations as of September 30, 2022 and December 31, 2021. 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.

Other Commitments

As of September 30, 2022, we had $49.5 million of noncancelable purchase commitments due within one year, primarily related to agreements with third party manufacturers.

Legal Proceedings

We are involved in legal proceedings, including the following matters:

Xyrem Class Action

From June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with generic drug manufacturers who had filed Abbreviated New Drug Applications, or ANDA, violate state and federal antitrust and consumer protection laws, as follows:

On June 17, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of Illinois by Blue Cross and Blue Shield Association, or BCBS, against Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., and Jazz Pharmaceuticals Ireland Limited, or, collectively, the Company Defendants (hereinafter referred to as the BCBS Lawsuit). The BCBS Lawsuit also names Roxane Laboratories, Inc., Hikma Pharmaceuticals USA Inc., Eurohealth (USA), Inc., Hikma Pharmaceuticals plc, Amneal Pharmaceuticals LLC, Par Pharmaceuticals, Inc., Lupin Ltd., Lupin Pharmaceuticals Inc., and Lupin Inc., or, collectively, the BCBS Defendants.

On June 18 and June 23, 2020, respectively, two additional class action lawsuits were filed against the Company Defendants and the BCBS Defendants: one by the New York State Teamsters Council Health and Hospital Fund in the United States District Court for the Northern District of California, and another by the Government Employees Health Association Inc. in the United States District Court for the Northern District of Illinois (hereinafter referred to as the GEHA Lawsuit).

On June 18, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of California by the City of Providence, Rhode Island, on behalf of itself and all others similarly situated, against Jazz Pharmaceuticals plc, and Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Hikma Labs Inc., Hikma Pharmaceuticals USA Inc., and Hikma Pharmaceuticals plc, or, collectively, the City of Providence Defendants.

On June 30, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of Illinois by UFCW Local 1500 Welfare Fund on behalf of itself and all others similarly situated, against Jazz Pharmaceuticals Ireland Ltd., Jazz Pharmaceuticals, Inc., Roxane Laboratories, Inc., Hikma Pharmaceuticals plc, Eurohealth (USA), Inc. and West-Ward Pharmaceuticals Corp., or collectively the UFCW Defendants (hereinafter referred to as the UFCW Lawsuit).

On July 13, 2020, the plaintiffs in the BCBS Lawsuit and the GEHA Lawsuit dismissed their complaints in the United States District Court for the Northern District of Illinois and refiled their respective lawsuits in the United States District Court for the Northern District of California. On July 14, 2020, the plaintiffs in the UFCW Lawsuit dismissed their complaint in the United States District Court for the Northern District of Illinois and on July 15, 2020, refiled their lawsuit in the United States District Court for the Northern District of California.

On July 31, 2020, a class action lawsuit was filed in the United States District Court for the Southern District of New York by the A.F. of L.-A.G.C. Building Trades Welfare Plan on behalf of itself and all others similarly situated, against Jazz Pharmaceuticals plc (hereinafter referred to as the AFL Plan Lawsuit). The AFL Plan Lawsuit also names Roxane Laboratories Inc., West-Ward Pharmaceuticals Corp., Hikma Labs Inc., Hikma Pharmaceuticals plc, Amneal Pharmaceuticals LLC, Par Pharmaceuticals Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc.

On August 14, 2020, an additional class action lawsuit was filed in the United States District Court for the Southern District of New York by the Self-Insured Schools of California on behalf of itself and all others similarly situated, against the Company Defendants, as well as Hikma Pharmaceuticals plc, Eurohealth (USA) Inc., Hikma Pharmaceuticals USA, Inc., West-Ward Pharmaceuticals Corp., Roxane Laboratories, Inc., Amneal Pharmaceuticals LLC, Endo International, plc, Endo Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals Inc., Lupin Inc., Sun Pharmaceutical Industries Ltd., Sun Pharmaceutical Holdings USA, Inc., Sun Pharmaceutical Industries, Inc., Ranbaxy Laboratories Ltd., Teva Pharmaceutical Industries Ltd., Watson Laboratories, Inc., Wockhardt Ltd., Morton Grove Pharmaceuticals, Inc., Wockhardt USA LLC, Mallinckrodt plc, and Mallinckrodt LLC (hereinafter referred to as the Self-Insured Schools Lawsuit).

On September 16, 2020, an additional class action lawsuit was filed in the United States District Court for the Northern District of California, by Ruth Hollman on behalf of herself and all others similarly situated, against the same defendants named in the Self-Insured Schools Lawsuit.

In December 2020, the above cases were centralized and transferred to the United States District Court for the Northern District of California, where the multidistrict litigation will proceed for the purpose of discovery and pre-trial proceedings.

On March 18, 2021, United Healthcare Services, Inc. filed a lawsuit in the United States District Court for the District of Minnesota against the Company Defendants, Hikma Pharmaceuticals plc, Roxane Laboratories, Inc., Hikma Pharmaceuticals USA Inc., Eurohealth (USA) Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical Inc., Lupin Ltd., and Lupin Pharmaceuticals, Inc., raising similar allegations, or the UHS Lawsuit. On March 24, 2021, the U.S. Judicial Panel on Multidistrict Litigation conditionally transferred the UHS Lawsuit to the United States District Court for the Northern District of California, where it was consolidated for discovery and pre-trial proceedings with the other cases.

On August 13, 2021, the United States District Court for the Northern District of California granted in part and denied in part the Company Defendants" motion to dismiss the complaints in the cases referenced above.

On October 8, 2021, Humana Inc. filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On October 8, 2021, Molina Healthcare Inc. filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On February 17, 2022, Health Care Service Corporation filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA

Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On May 9, 2022, Aetna Inc., or Aetna, filed a lawsuit in the Superior Court of California for the County of Alameda against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations. On November 7, 2022, the court in the Aetna case issued a tentative ruling granting in part and denying in part our motion to dismiss. A hearing is scheduled for November 29, 2022.

A hearing on class certification in the consolidated multi-district litigation referenced above is scheduled for April 2023. A trial date will be set following a ruling on class certification.

The plaintiffs in certain of these lawsuits are seeking to represent a class of direct purchasers of Xyrem, and the plaintiffs in the remaining lawsuits are seeking to represent a class of indirect purchasers of Xyrem. Each of the lawsuits generally alleges violations of U.S. federal and state antitrust, consumer protection, and unfair competition laws in connection with the Company Defendants' conduct related to Xyrem, including actions leading up to, and entering into, patent litigation settlement agreements with each of the other named defendants. Each of the lawsuits seeks monetary damages, exemplary damages, equitable relief against the alleged unlawful conduct, including disgorgement of profits and restitution, and injunctive relief. It is possible that additional lawsuits will be filed against the Company Defendants making similar or related allegations. If the plaintiffs were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

GW Acquisition Litigation

On March 15, 2021, GW filed a definitive proxy statement, or Proxy Statement, with the Securities and Exchange Commission in connection with the GW Acquisition.

Since the filing of the Proxy Statement, Jazz Pharmaceuticals plc has been named in two lawsuits filed in state and federal courts in New York on March 17, 2021 by purported GW shareholders in connection with the GW Acquisition. The first was filed in the United States District Court for the Southern District of New York by James Farrell (hereinafter referred to as the Farrell Lawsuit) and an additional suit was filed in New York state court by Brian Levy (hereinafter referred to as the Levy Lawsuit). In addition to Jazz Pharmaceuticals plc, Jazz Pharmaceuticals U.K. Holdings Ltd., GW Pharmaceuticals plc, and the GW board of directors are named as defendants in the Farrell Lawsuit. In the Levy Lawsuit, GW Pharmaceuticals plc, the GW board of directors, Centerview Partners LLC, and Goldman Sachs & Co. LLC are named as defendants. In addition to the Farrell Lawsuit and the Levy Lawsuit, ten additional suits have been filed in New York, California, and Pennsylvania federal courts by purported GW shareholders against GW Pharmaceuticals plc and its board of directors, but which do not name any Jazz Pharmaceuticals parties (hereinafter referred to as the GW Litigation, and collectively with the Farrell Lawsuit and the Levy Lawsuit, as the Transaction Litigation). In the Transaction Litigation, the plaintiffs allege that the Proxy Statement omitted material information and contained misrepresentations, and that the individual members of the GW board of directors breached their fiduciary duties, in violation of state and federal laws, including the Securities Exchange Act of 1934. The plaintiffs in the Transaction Litigation sought various remedies, including injunctive relief to prevent the consummation of the GW Acquisition unless certain allegedly material information was disclosed, or in the alternative, rescission or damages.

On April 14, 2021, GW filed a Form 8-K containing supplemental disclosures related to the GW Acquisition. Pursuant to a memorandum of understanding between the parties, the Levy Lawsuit was dismissed on April 14, 2021.

On May 27, 2021, a class action lawsuit was filed in the United States District Court for the Southern District of California by plaintiff Kurt Ziegler against GW and its former Directors asserting claims under Sections 14(a) and 20(a) of the Securities Exchange Act of 1934, referred to as the Ziegler Lawsuit. The allegations in the Ziegler Lawsuit are similar to those in the previously dismissed Transaction Litigation.

Patent Infringement Litigation

Avadel Patent Litigation

On May 13, 2021, we filed a patent infringement suit against Avadel Pharmaceuticals plc, or Avadel, and several of its corporate affiliates in the United States District Court for the District of Delaware. The suit alleges that Avadel's product candidate FT218 will infringe five of our patents related to controlled release formulations of oxybate and the safe and effective distribution of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe these patents, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents. Avadel filed a motion for partial judgment on the pleadings on its counterclaim that one of our patents should be delisted from the Orange Book. The Court scheduled a hearing on that motion for November 15, 2022.

On August 4, 2021, we filed an additional patent infringement suit against Avadel in the United States District Court for the District of Delaware. The second suit alleges that Avadel's product candidate FT218 will infringe a newly-issued patent related to sustained-release formulations of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe this patent, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents.

On November 10, 2021, we filed an additional patent infringement suit against Avadel in the United States District Court for the District of Delaware. The third suit alleges that Avadel's product candidate FT218 will infringe a newly-issued patent related to sustained-release formulations of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe this patent, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents.

On April 14, 2022, Avadel sued us in the United States District Court for the District of Delaware. Avadel's new suit alleges that we misappropriated trade secrets related to Avadel's once-nightly sodium oxybate development program and breached certain contracts between the parties. Avadel seeks monetary damages, an injunction preventing us from using Avadel's confidential information, and an order directing the United States Patent and Trademark Office to modify the inventorship of one of our oxybate patents.

On June 7, 2022 we received notice from Avadel that it had filed a "paragraph IV certification" regarding one patent listed in the Orange Book for Xyrem. A paragraph IV certification is a certification by a generic applicant that alleges that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product. On July 15, 2022, we filed an additional lawsuit against Avadel asserting infringement of that patent. The suit alleges that the filing of Avadel's application for approval of FT218 is an act of infringement, and that Avadel's product would infringe the patent if launched. The suit seeks an injunction to prevent Avadel from launching a product that would infringe the patent, and an award of damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patent is invalid, that its product, if approved, would not infringe, and that by listing the patent in the Orange Book, we engaged in unlawful monopolization in violation of the Sherman Act.

On July 21, 2022, Avadel filed a lawsuit against FDA in the United States District Court for the District of Columbia, challenging FDA's determination that Avadel was required to file a paragraph IV certification regarding one of our Orange Book listed patents. Avadel filed a motion for preliminary injunction, or in the alternative, summary judgment, seeking relief including a declaration that FDA's decision requiring patent certification was unlawful, an order setting aside that decision, an injunction prohibiting FDA from requiring such certification as a precondition to approval of its application for FT218, and an order requiring FDA to take final action on Avadel's application for approval of FT218 within 14 days of the Court's ruling. On July 27, 2022, we filed a motion to intervene in that case, which the Court granted. The Court held a hearing on the parties' respective motions for summary judgment on October 7, 2022. On November 3, 2022, the Court granted our and FDA's motions for summary judgment and denied Avadel's motion.

Canopy Patent Litigation

In December 2020, Canopy Growth Corporation filed a complaint against our subsidiary, GW, in the United States District Court for the Western District of Texas, alleging infringement of its patent, U.S. Patent No. 10,870,632. Canopy claims that our extraction process used to produce material used to produce Epidiolex infringes its patent. Canopy seeks a judgment that we have infringed their patent and an award of monetary damages. In July 2021, we filed an answer to the amended complaint, and counterclaims seeking judgment that the '632 patent is invalid and that we have not infringed the patent. In October 2021, the United States District Court for the Western District of Texas held a claim construction hearing regarding the disputed term of the '632 patent. In November 2021, the Court issued a claim construction order. On February 23, 2022, the parties filed a Joint Motion and Stipulation to Enter Final Judgment in favor of GW. On February 25, 2022, the Court granted the parties' motion and entered final judgment in favor of GW. Pursuant to the stipulation, Canopy filed a notice of appeal of the Court's ruling on the disputed term in March 2022.

Lupin Patent Litigation

In June 2021, we received notice from Lupin Inc., or Lupin, that it has filed with FDA an ANDA, for a generic version of Xywav. The notice from Lupin included a paragraph IV certification with respect to ten of our patents listed in FDA's Orange Book for Xywav on the date of our receipt of the notice. The asserted patents relate generally to the composition and method of use of Xywav, and methods of treatment when Xywav is administered concomitantly with certain other medications.

In July 2021, we filed a patent infringement suit against Lupin in the United States District Court for the District of New Jersey. The complaint alleges that by filing its ANDA, Lupin has infringed ten of our Orange Book listed patents. We are seeking a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patents.

As a result of this lawsuit, we expect that a stay of approval of up to 30 months will be imposed by FDA on Lupin's ANDA. In June 2021, FDA recognized seven years of Orphan Drug Exclusivity for Xywav through July 21, 2027. On October 4, 2021, Lupin filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents.

In April 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On May 11, 2022, we filed an additional lawsuit against Lupin in the United States District Court for the District of New Jersey alleging that by filing its ANDA, Lupin infringed the newly-issued patent related to a method of treatment when Xywav is administered concomitantly with certain other medications. The suit seeks a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patent. On June 22, 2022, the court consolidated the two lawsuits we filed against Lupin. No trial date has been set in the consolidated case.

Otsuka Patent Litigation

In October 2021, Otsuka Pharmaceutical Co., Ltd., or Otsuka, filed claims against GW Pharma Limited and GW Pharmaceuticals Limited, or collectively, the GW Parties, in the English High Court, Patents Court. Otsuka alleges that under a now-expired Research Collaboration and License Agreement between Otsuka and the GW Parties, Otsuka and the GW Parties jointly own certain patents and other intellectual property, that Epidiolex is covered by that intellectual property, and that Otsuka is therefore due a royalty on net sales of Epidiolex.

In December 2021, GW filed an application contesting the jurisdiction of the Patents Court. On May 3, 2022, the Patents Court denied GW's application. GW has filed papers with the Court of Appeal seeking leave to challenge the Patents Court's decision. The Court of Appeal held a hearing on GW's appeal on October 12, 2022. On November 8, 2022, the Court of Appeal ruled against GW on the jurisdictional challenge, so the case will continue in the Patents Court.

In January 2022, we filed a lawsuit against Otsuka in the Supreme Court of the State of New York, County of New York, seeking a declaration that Otsuka is not entitled to any royalties on sales of Epidiolex under the Research Collaboration and License Agreement.

The Company vigorously enforces its intellectual property rights, but cannot predict the outcome of these matters.

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

11. Shareholders' Equity

Accumulated Other Comprehensive Loss

The components of accumulated other comprehensive loss as of September 30, 2022 and December 31, 2021 were as follows (in thousands):

	Net Unrealized Loss From Hedging Activities	Foreign Currency Translation Adjustments	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2021	$ (128)	$ (400,232)	$ (400,360)
Other comprehensive loss before reclassifications	—	(1,217,414)	(1,217,414)
Amounts reclassified from accumulated other comprehensive loss	128	—	128
Other comprehensive income (loss), net	128	(1,217,414)	(1,217,286)
Balance at September 30, 2022	$ —	$ (1,617,646)	$ (1,617,646)

During the nine months ended September 30, 2022, other comprehensive loss primarily reflects foreign currency translation adjustments, primarily due to the weakening of the sterling and the euro against the U.S. dollar.

12. Net Income (Loss) per Ordinary Share

Basic net income (loss) per ordinary share is based on the weighted-average number of ordinary shares outstanding. Diluted net income (loss) 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 (loss) per ordinary share were computed as follows (in thousands, except per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Numerator:				
Net income (loss)	$ (19,648)	$ (52,833)	$ 16,664	$ (294,317)
Denominator:				
Weighted-average ordinary shares used in per share calculations - basic	62,785	61,284	62,365	59,084
Dilutive effect of employee equity incentive and purchase plans	—	—	1,023	—
Weighted-average ordinary shares used in per share calculations - diluted	62,785	61,284	63,388	59,084
Net income (loss) per ordinary share:				
Basic	$ (0.31)	$ (0.86)	$ 0.27	$ (4.98)
Diluted	$ (0.31)	$ (0.86)	$ 0.26	$ (4.98)

Potentially dilutive ordinary shares from our employee equity incentive and purchase plans 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, and Performance-based restricted stock units, or PRSUs, and the assumed issuance of ordinary shares under our employee stock purchase plan, or ESPP. Potentially dilutive ordinary shares from the Exchangeable Senior Notes are determined by applying the if-converted method to the assumed issuance of ordinary shares upon exchange of the Exchangeable Senior Notes. The potential issue of ordinary shares upon exchange of the Exchangeable Senior Notes was anti-dilutive and had no impact on diluted net income (loss) per ordinary share for the three and nine months ended September 30, 2022.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Exchangeable Senior Notes	9,044	9,579	9,044	9,952
Employee equity incentive and purchase plans	2,194	4,302	1,904	3,375

13. Revenues

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Xyrem	$ 256,039	$ 307,333	$ 772,957	$ 977,065
Xywav	255,936	153,063	677,041	352,643
Total Oxybate	511,975	460,396	1,449,998	1,329,708
Epidiolex/Epidyolex[1]	196,218	160,378	529,400	269,859
Sativex[1]	3,220	6,097	12,104	8,058
Sunosi[2]	—	19,251	28,844	42,981
Total Neuroscience	711,413	646,122	2,020,346	1,650,606
Zepzelca	70,320	71,714	197,943	181,972
Rylaze	73,513	20,674	200,687	20,674
Vyxeos	30,067	34,688	97,714	99,296
Defitelio/defibrotide	49,452	57,705	153,637	155,420
Erwinaze/Erwinase	—	—	—	69,382
Total Oncology	223,352	184,781	649,981	526,744
Other	1,001	3,344	3,576	8,768
Product sales, net	935,766	834,247	2,673,903	2,186,118
Royalties and contract revenues	4,886	3,868	13,348	11,389
Total revenues	$ 940,652	$ 838,115	$ 2,687,251	$ 2,197,507

1. Net product sales for Epidiolex/Epidyolex and Sativex are included from the acquisition of GW on May 5, 2021.
2. Net product sales for Sunosi U.S. are included until the date of divestment to Axsome of May 9, 2022.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
United States	$ 867,835	$ 757,227	$ 2,466,758	$ 1,996,419
Europe	60,024	70,730	181,831	164,540
All other	12,793	10,158	38,662	36,548
Total revenues	$ 940,652	$ 838,115	$ 2,687,251	$ 2,197,507

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
ESSDS	57 %	57 %	56 %	62 %
McKesson	10 %	11 %	11 %	12 %

Financing and payment

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

Contract Liabilities - Deferred Revenue

The deferred revenue balance as of September 30, 2022 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 $0.5 million and $1.6 million during the three and nine months ended September 30, 2022, 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 nine months ended September 30, 2022 (in thousands):

	Contract Liabilities
Balance as of December 31, 2021	$ 2,556
Amount recognized within royalties and contract revenues	(1,569)
Balance as of September 30, 2022	$ 987

14. Share-Based Compensation

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Selling, general and administrative	$ 37,435	$ 39,117	$ 108,453	$ 97,296
Research and development	16,000	11,866	43,338	31,749
Cost of product sales	3,246	2,256	8,647	6,842
Total share-based compensation expense, pre-tax	56,681	53,239	160,438	135,887
Income tax benefit from share-based compensation expense	(10,669)	(10,917)	(30,632)	(25,848)
Total share-based compensation expense, net of tax	$ 46,012	$ 42,322	$ 129,806	$ 110,039

Share Options

There were no share options granted in the three and nine months ended September 30, 2022 and the three months ended September 30, 2021. 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 for the nine months ended September 30, 2021:

	Nine Months Ended September 30, 2021
Shares underlying options granted (in thousands)	110
Grant date fair value	$ 51.39
Black-Scholes option pricing model assumption information:	
Volatility	37 %
Expected term (years)	4.5
Range of risk-free rates	0.4-0.8%
Expected dividend yield	— %

Nominal Strike Price Options

During the second quarter of 2021, we issued nominal strike price share options to replace certain unvested GW awards in connection with the GW Acquisition. There were no nominal strike price share options granted in the three and nine months ended September 30, 2022.

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

	Nine Months Ended September 30, 2021
Nominal strike price share options granted (in thousands)	124
Grant date fair value	$ 170.82

Restricted Stock Units

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
RSUs granted (in thousands)	64	75	2,014	1,707
Grant date fair value	$ 153.75	$ 161.91	$ 152.45	$ 169.69

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.

Performance-Based Restricted Stock Units

The Compensation & Management Development Committee of our board of directors approved awards of PRSUs to certain employees of the Company, subject to vesting on the achievement of certain commercial and pipeline performance criteria to be assessed over a performance period from the date of the grant to December 31, 2023 and December 31, 2024, respectively. Following the determination of the Company's achievement with respect to the performance criteria, the amount of shares awarded will be subject to adjustment based on the application of a relative total shareholder return, or TSR modifier. The number of shares that may be earned ranges between 0% and 200% of the target number of PRSUs granted based on the degree of achievement of the applicable performance metric and the application of the relative TSR modifier.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
PRSUs granted (in thousands)	2	—	287	224
Grant date fair value	$ 176.58	$ —	$ 179.10	$ 190.81

As the PRSUs granted in 2021 and 2022 are subject to a market condition, the grant date fair value for such PRSUs was based on a Monte Carlo simulation model. The Company evaluated the performance targets in the context of its current long-range financial plan and its product candidate development pipeline and recognized expense based on the probable number of awards that will ultimately vest.

As of September 30, 2022, compensation cost not yet recognized related to unvested share options, RSUs and PRSUs was $16.5 million, $342.0 million and $45.2 million, respectively, which is expected to be recognized over a weighted-average period of 1.2 years, 2.8 years and 1.8 years, respectively.

15. Income Taxes

Our income tax benefit was $43.0 million and $58.6 million for the three and nine months ended September 30, 2022, respectively, compared to an income tax benefit of $18.1 million and an income tax expense of $228.6 million for the same periods in 2021. Our income tax benefit for the three and nine months ended September 30, 2022 included the tax impacts of

the impairment of our acquired IPR&D asset and restructuring costs. Our income tax expense for the nine months ended September 30, 2021 included an expense of $250.6 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory rate in the U.K. following enactment of the U.K. Finance Act 2021. Excluding these impacts, the decrease in the income tax benefit in the three months ended September 30, 2022 compared to the same period in 2021 resulted primarily from the mix of pre-tax income and losses incurred across tax jurisdictions. The income tax benefit in the nine months ended September 30, 2022 is in line with the prior period. 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 is primarily related to acquired intangible assets, and is net of deferred tax assets related to 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 deferred tax assets. Each reporting period, we evaluate the need for a valuation allowance on our deferred tax assets by jurisdiction and adjust our estimates as more information becomes available.

We are required to recognize the financial statement effects of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained upon examination. As a result, we have recorded an unrecognized tax benefit for certain tax benefits which we judge may not be sustained upon examination. Our most significant tax jurisdictions are Ireland, the U.S. (both at the federal level and in various state jurisdictions) and the U.K. In Ireland we are no longer subject to income tax audits by taxing authorities for the years prior to 2017. The U.S. jurisdictions generally have statute 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), carryforwards that were generated in 2017 and earlier may still be adjusted upon examination by the tax authorities. In the U.K., we are no longer subject to income tax audits by taxing authorities for the years prior to 2018. Certain of our Luxembourg subsidiaries are currently under examination by the Luxembourg taxing authorities for the years ended December 31, 2017 and 2018. Certain of our German subsidiaries are currently under examination by the German taxing authorities for the years ended December 31, 2017, 2018 and 2019.

16. Subsequent Events

In October 2022, we announced an exclusive licensing agreement with Zymeworks Inc., or Zymeworks, under which we have the right to acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the U.S., Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. Zanidatamab is a bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Under the terms of the agreement, following clearance relating to the U.S Hart-Scott Rodino Antitrust Improvements Act of 1976, or HSR Clearance, Zymeworks is eligible to receive an upfront payment of $50.0 million, and should we decide to continue the collaboration following readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of $325 million. Zymeworks is also eligible to receive regulatory and commercial milestone payments of up to $1.4 billion, for total potential payments of $1.76 billion. Pending approval, Zymeworks is eligible to receive tiered royalties between 10% and 20% on our net sales. Subject to HSR Clearance, the upfront payment of $50.0 million would be expensed to acquired IPR&D in the fourth quarter of 2022.

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 whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases - often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we strive to identify new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science.

Our strategy for growth is rooted in executing commercial launches and ongoing commercialization initiatives; advancing robust research and development, or R&D, programs and delivering impactful clinical results; effectively deploying capital to strengthen the prospects of achieving our short- and long-term goals through strategic corporate development; and delivering strong financial performance. We focus on patient populations with high unmet needs. We identify and develop differentiated therapies for these patients that we expect will be long-lived assets and that we can support with an efficient commercialization model. In addition, we leverage our efficient, scalable operating model and integrated capabilities across our global infrastructure to effectively reach patients around the world.

At the 40th Annual J.P. Morgan Healthcare Conference in January 2022, we announced our Vision 2025, which aims to deliver sustainable growth and enhanced value, driving our continued transformation to an innovative, high-growth global pharmaceutical leader. The three core components of our Vision 2025 focus on commercial execution, pipeline productivity and operational excellence.

Commercial Achievements

Our marketed products are approved in countries around the world to improve patient care.

Product	Indications	Initial Approval Date	Markets
NEUROSCIENCE			
Xywav® (calcium, magnesium, potassium, and sodium oxybates)	Treatment of cataplexy or excessive daytime sleepiness, or EDS, in patients seven years of age and older with narcolepsy.	July 2020	U.S.
	Treatment of idiopathic hypersomnia, or IH, in adults.	August 2021	U.S.
Xyrem® (sodium oxybate)	Treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy.	July 2002	U.S.
	For the treatment of cataplexy in patients with narcolepsy.	August 2005	Canada
	Treatment of narcolepsy with cataplexy in adult patients, adolescents and children from age of 7 years.	October 2005	EU, Great Britain, other markets (through licensing agreement)

Epidiolex® (cannabidiol)	Treatment of seizures associated with Lennox-Gastaut syndrome, or LGS, Dravet syndrome, or DS, or tuberous sclerosis complex, or TSC, in patients 1 year of age and older.	June 2018	U.S.
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older.*	September 2019	EU, Great Britain, other markets
	For adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.**	April 2021	EU, Great Britain, other markets
Sunosi® (solriamfetol)***	Improve wakefulness and reduce EDS in adult patients with narcolepsy (with or without cataplexy) or adult patients with obstructive sleep apnea, or OSA, whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure, or CPAP.	January 2020	EU, Great Britain, other markets
	Treatment of EDS in adult patients with narcolepsy or OSA.	May 2021	Canada
Sativex® (nabiximols)	Treatment for adult patients with moderate to severe spasticity due to multiple sclerosis, or MS, who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy.	June 2010	U.K. (other markets through licensing agreements with partners)
ONCOLOGY			
Zepzelca® (lurbinectedin)	Treatment of adult patients with metastatic small cell lung cancer, or SCLC, with disease progression on or after platinum-based chemotherapy.	June 2020	U.S. (licensed from PharmaMar)****
	Treatment of adults with Stage III or metastatic SCLC who have progressed on or after platinum-containing therapy.	September 2021	Canada (licensed from PharmaMar)*****
Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)	A component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia, or ALL, and lymphoblastic lymphoma, or LBL, in adult and pediatric patients 1 month or older who have developed hypersensitivity to *E. coli*-derived asparaginase.	June 2021	U.S.
	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL, in adults and pediatric patients 1 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.	September 2022	Canada

Vyxeos® (daunorubicin and cytarabine) liposome for injection	Treatment of newly-diagnosed therapy-related acute myeloid leukemia, or t-AML or AML-MRC in adults and pediatric patients one year and older.	August 2017	U.S.
Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion	Treatment of adults with newly-diagnosed t-AML or AML-MRC.	August 2018	EU, Great Britain, other markets
Vyxeos® Daunorubicin and cytarabine liposome for injection Powder, 44 mg daunorubicin and 100 mg cytarabine per vial, intravenous infusion	Treatment of adults with newly diagnosed therapy-related t-AML or AML with AML-MRC.	April 2021	Canada
Defitelio® (defibrotide sodium)	Treatment of adult and pediatric patients with hepatic veno-occlusive disease, or VOD, also known as sinusoidal obstruction syndrome, or SOS, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT.	March 2016	U.S.
Defitelio® (defibrotide)	Treatment of severe hepatic VOD, also known as SOS, following HSCT therapy.	October 2013	EU, Great Britain, other markets

*Clobazam restriction limited to EU and Great Britain

**TSC approval in certain markets

***In May 2022, we completed the U.S. divestiture of Sunosi to Axsome Therapeutics, or Axsome; we expect to complete the ex-U.S. divestiture to Axsome later this year. For more information, see Note 2, Disposition and License Agreements, of the Notes to Condensed Consolidated Financial Statements, included in Part I of this Quarterly Report on Form 10-Q.

****Accelerated approval received from the U.S. Food and Drug Administration, or FDA

*****Conditional approval received from Health Canada

Neuroscience

We are the global leader in the development and commercialization of oxybate therapy for patients with sleep disorders. Xyrem was approved by FDA in 2002, and has become a standard of care for treating EDS and cataplexy in narcolepsy. In 2020, we received FDA approval for Xywav for the treatment of cataplexy or EDS, in patients seven years of age and older with narcolepsy. In August 2021, Xywav became the first and only therapy approved by FDA for the treatment of IH in adults. Xywav is an oxybate therapy that contains 92% less sodium than Xyrem.

Since there is no cure for narcolepsy and long-term disease management is needed, we believe that Xywav represents an important new therapeutic option for patients with this sleep disorder. Our commercial efforts are focused on educating patients and physicians about the lifelong impact of high sodium intake, and how the use of Xywav enables them to address what is a modifiable risk factor.

In June 2021, FDA recognized seven years of Orphan Drug Exclusivity, or ODE, for Xywav in narcolepsy. ODE extends through July 2027. In connection with granting ODE, FDA stated that "Xywav is clinically superior to Xyrem by means of greater safety because Xywav provides a greatly reduced chronic sodium burden compared to Xyrem. "FDA's summary also stated that "the differences in the sodium content of the two products at the recommended doses will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated."

We view the adoption of Xywav in narcolepsy as a positive indication that physicians and patients appreciate the benefits of a lower sodium oxybate option. We continue to see Xywav adoption among existing Xyrem patients, as well as the majority of new-to-oxybate narcolepsy patients.

On August 12, 2021, FDA approved Xywav for the treatment of IH in adults. Xywav is the first and only FDA-approved therapy to treat IH. We initiated the U.S. commercial launch of Xywav for the treatment of IH in adults on November 1, 2021. In January 2022, FDA recognized seven years of ODE for Xywav in IH that extends through August 2028. IH is a debilitating neurologic sleep disorder characterized by chronic EDS, the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness. An estimated 37,000 people in the U.S. have been diagnosed with IH and are actively seeking healthcare.

We now have agreements in place for Xywav with all three major pharmacy benefit managers, or PBMs, in the U.S. To date, we have entered into agreements with various entities and have achieved benefit coverage for Xywav in both narcolepsy and IH indications for approximately 90% of commercial lives.

We have seen strong adoption of Xywav in narcolepsy since its launch in November 2020, and increasing adoption in IH since its launch in November 2021. Exiting the third quarter of 2022, there were approximately 9,500 patients taking Xywav, including approximately 8,050 patients with narcolepsy and approximately 1,450 patients with IH. With respect to Xywav and Xyrem in the aggregate, the average number of active oxybate patients on therapy was approximately 17,600 in the third quarter of 2022.

We acquired Epidiolex (Epidyolex outside the U.S.) in May 2021 as part of the acquisition of GW Pharmaceuticals plc, or GW, which we refer to as the GW Acquisition, which expanded our growing neuroscience business with a global, high-growth childhood-onset epilepsy franchise. Epidiolex was approved in the U.S. in June 2018 for the treatment of seizures associated with two rare and severe forms of epilepsy, LGS and DS, in patients two years of age and older, and subsequently approved in July 2020 for the treatment of seizures associated with TSC in patients one year of age and older. FDA also approved the expansion of all existing indications, LGS and DS, to patients one year of age and older. The rolling European launch of Epidyolex is also underway following European Commission approval in September 2019 for use as adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients two years of age and older. We successfully completed the pricing and reimbursement process for Epidyolex in France; after commercial launch in France, expected by the end of 2022, Epidyolex will be commercially available and fully reimbursed in all five key European markets: United Kingdom, Germany, Italy, Spain and France. The clobazam restriction is limited to EU and Great Britain. Epidyolex was also approved for adjunctive therapy of seizures associated with TSC for patients 2 years of age and older in the EU in April 2021 and Great Britain in August 2021, and is approved or under review for this indication in other markets. Outside the U.S. and Europe, Epidiolex/Epidyolex is approved in Israel and Australia.

Sativex (nabiximols) is approved in 29 countries outside the U.S. for the treatment of adult patients with moderate to severe spasticity due to MS who have not responded adequately to other anti-spasticity medication. We support the availability of Sativex directly in the U.K. and through licensing agreements with partners in other countries.

In addition to our currently-marketed products, we previously marketed Sunosi® (solriamfetol) in the U.S. and, pending the completion of the ex-U.S. divestiture of Sunosi to Axsome Therapeutics, or Axsome, we continue to market Sunosi in Europe and Canada. In this regard, in March 2022, we entered into a definitive agreement to divest Sunosi to Axsome. In May 2022, we completed the U.S. divestiture of Sunosi to Axsome and we expect to complete the ex-U.S. divestiture to Axsome later this year. Under the terms of the sale agreement with Axsome, Axsome received the rights to Sunosi in all of the existing territories available to us. We received an upfront payment of $53.0 million, and have the right to receive a high single-digit royalty on Axsome's U.S. net sales of Sunosi in current indications and a mid-single-digit royalty on Axsome's U.S. net sales of Sunosi in future indications. The divestiture of Sunosi to Axsome is intended to enable us to sharpen our focus on our highest strategic priorities designed to deliver sustainable growth and enhanced shareholder value. In assessing the positioning of Sunosi in the overall treatment landscape, we believe that Axsome is well positioned to deliver access to this important medicine and to maximize the value of Sunosi to us through future growth.

Oncology

We acquired U.S. development and commercialization rights to Zepzelca in early 2020, and launched six months thereafter, with an indication for treatment of patients with SCLC with disease progression on or after platinum-based chemotherapy. Our education and promotional efforts are focused on SCLC-treating physicians. We are continuing to raise awareness of Zepzelca across academic and community cancer centers, and see continued opportunities for growth in second-line share and overall demand, reflecting the significant unmet need and favorable Zepzelca product profile. In collaboration with F. Hoffmann-La Roche Ltd (Roche), we have initiated a Phase 3 pivotal clinical trial in first-line extensive stage SCLC of Zepzelca in combination with Tecentriq® (atezolizumab). We are also developing Zepzelca in additional indications.

Rylaze was approved by FDA in June 2021 under the Real-Time Oncology Review, or RTOR, program, and was launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL or LBL in pediatric and adult patients one month and older who have developed hypersensitivity to *E. coli*-derived asparaginase. Rylaze is the only recombinant *erwinia* asparaginase manufactured product that maintains a clinically meaningful level of asparaginase activity throughout the entire duration of treatment. We developed Rylaze to address the needs of patients and health care providers for an innovative, high-quality *erwinia* asparaginase with reliable supply. The current indication is for an intramuscular, or IM, dosing regimen of 25 mg/m^2 every 48 hours. We submitted a supplemental Biologics License Application, or sBLA, with additional data in support of a Monday/Wednesday/Friday, or M/W/F, IM dosing schedule in January 2022 and submitted a separate sBLA for intravenous, or IV, administration in April 2022, both of which have been granted review under the RTOR program with Prescription Drug User Fee Act, or PDUFA, action dates in 2022 and 2023, respectively. We also completed a Marketing Authorization Application, or MAA, submission to the European Medicines Agency, or EMA, in May 2022 for M/W/F and every 48-hour dosing schedules and IV and IM administration, with potential for approval in 2023. We are also advancing the program for potential submission, approval and launch in Japan, as well as planning additional submissions in other markets.

Vyxeos is a treatment for adults with newly-diagnosed t-AML, or AML-MRC. In March 2021, FDA approved a revised label to include a new indication to treat newly-diagnosed t-AML, or AML-MRC, in pediatric patients aged one year and older. We have a number of ongoing development activities and continue to expand into new markets internationally. Despite an ongoing trend in the U.S. towards lower-intensity treatments and away from Vyxeos that accelerated due to the COVID-19 pandemic, we continue to see recovery in demand for Vyxeos and expect future demand for appropriate secondary AML patients to remain steady. In Europe, we continue to expect a negative impact on demand for and utilization of Vyxeos compared to historical periods due to COVID-19.

Defitelio is the first and only approved treatment for patients with VOD following HSCT. There was a significant decline in the number of patients receiving HSCT due to the effects of the COVID-19 pandemic. We anticipate the use of Defitelio will increase to the extent that hospital systems globally are able to continue moving forward with HSCT procedures.

Research and Development Progress

Our research and development activities encompass all stages of development and currently include clinical testing of new product candidates and activities related to clinical improvements of, or additional indications or new clinical data for, our existing marketed products. We also have active preclinical programs for novel therapies, including precision medicines in hematology and oncology and the GW cannabinoid platform. We are increasingly leveraging our growing internal research and development function, and we have also entered into collaborations with third parties for the research and development of innovative early-stage product candidates and have supported additional investigator-sponsored trials, or ISTs, that are anticipated to generate additional data related to our products. We also seek out investment opportunities in support of the development of early- and mid-stage technologies in our therapeutic areas and adjacencies. We have a number of licensing and collaboration agreements with third parties, including biotechnology companies, academic institutions and research-based companies and institutions, related to preclinical and clinical research and development activities in hematology and in precision oncology, as well as in neuroscience.

With the approvals and launches of Rylaze for the treatment ALL or LBL in pediatric and adult patients one month and older who have developed hypersensitivity to *E. coli*-derived asparaginase and Xywav for IH in 2021, we accomplished our goal to deliver five product launches through 2020 and 2021. We have taken both Rylaze and Xywav from concept to commercialization.

Our neuroscience R&D efforts include the initiation in August 2022 of an ongoing pivotal Phase 3 clinical trial of Epidiolex for the treatment of Epilepsy with Myoclonic-Atonic Seizures, or EMAS, also known as Doose syndrome. This trial is evaluating Epidiolex in a fourth childhood-onset epileptic encephalopathy with high unmet need. EMAS is characterized by generalized myoclonic-atonic seizures, and this trial is designed to provide the first randomized, controlled clinical data with Epidiolex in this syndrome type. Seizure types including atonic, tonic, clonic, tonic-clonic and partial onset seizures are seen in LGS, DS, and TSC. We enrolled the first patient in a Phase 3 trial of Epidyolex for LGS, DS and TSC in Japan in October 2022.

In October 2022, we announced an exclusive licensing agreement with Zymeworks Inc., or Zymeworks, under which we have the right to acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. Zanidatamab is a bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Under the terms of the agreement, following clearance relating to the U.S. Hart-Scott Rodino Antitrust Improvements Act of 1976, or HSR Clearance, Zymeworks is eligible to receive an upfront payment of $50.0 million, and should we decide to continue the collaboration following readout of the top-line clinical data from HERIZON-BTC-01, a

second, one-time payment of $325 million. Zymeworks is also eligible to receive regulatory and commercial milestone payments of up to $1.4 billion, for total potential payments of $1.76 billion. Pending approval, Zymeworks is eligible to receive tiered royalties between 10% and 20% on our net sales. Subject to HSR Clearance, the upfront payment of $50.0 million would be expensed to acquired IPR&D in the fourth quarter of 2022.

On June 28, 2022, we announced the nabiximols Phase 3 RELEASE MSS1 trial in multiple sclerosis (MS)-related spasticity did not meet the primary endpoint of change in Lower Limb Muscle Tone-6 between baseline and Day 21, as measured by the Modified Ashworth Scale. The analysis of the MSS1 trial has been completed. We have assessed the nabiximols program's potential to support regulatory approval for MS-related spasticity in the U.S., as well as in the context of our broader pipeline opportunities, and have made the decision to discontinue the program. Sativex (nabiximols) was approved outside the U.S. for the treatment of MS-related spasticity based on a comprehensive clinical trial program, including multiple late-stage randomized, controlled trials completed in Europe. We will continue to support the availability of Sativex in the 29 markets outside the U.S. where it is approved. We remain committed to the GW Cannabinoid Platform and are working to advance multiple early-stage cannabinoid programs with the potential to address critical unmet patient needs.

In December 2021 we initiated Phase 2 clinical trials for suvecaltamide, or JZP385, for essential tremor, or ET, and for JZP150 for post-traumatic stress disorder, or PTSD. Additionally, in November 2022, we initiated a Phase 2 trial of suvecaltamide in patients with Parkinson's disease tremor. These patient populations suffer significant impacts to their quality of life and there are limited current treatment options. We are also pursuing early-stage activities related to the development of JZP324, an extended-release low sodium, oxybate formulation that we believe could provide a clinically meaningful option for narcolepsy patients.

Within our oncology R&D program, there is a robust development plan being executed for Zepzelca. We are collaborating with Roche on a pivotal Phase 3 clinical trial evaluating Zepzelca in combination with Tecentriq in first-line extensive stage SCLC. In December 2021, our licensor PharmaMar initiated a confirmatory trial in second-line SCLC. This is a three-arm trial comparing Zepzelca as either monotherapy or in combination with irinotecan to investigator's choice of irinotecan or topotecan. Data from this trial could confirm the benefit of Zepzelca in the treatment of SCLC when patients progress following first-line treatment with a platinum-based regimen.

In 2022, we initiated a Phase 2 basket trial to explore Zepzelca monotherapy in patients with select advanced or metastatic solid tumors. Cohorts include advanced urothelial cancer, large cell neuroendocrine tumor of the lung and homologous recombination deficient, or HRD, cancers. In addition, we have initiated a Phase 4 observational study to collect real world safety and outcome data in adult Zepzelca monotherapy patients with SCLC who progress on or after prior platinum-containing chemotherapy.

For Rylaze, in January 2022 we submitted an sBLA with data in support of a M/W/F IM dosing schedule and submitted a separate sBLA for intravenous administration in April 2022, both of which have been granted review under the RTOR program. We completed a MAA submission to the EMA in May 2022.

In June 2022, we announced the FDA had cleared our Investigational New Drug, or IND, application for JZP815 and in October 2022, we enrolled the first patient in a Phase 1 trial. JZP815 is an investigational, pre-clinical stage pan-RAF kinase inhibitor that targets specific components of the mitogen-activated protein kinase, or MAPK, pathway that, when activated by oncogenic mutations, can be a frequent driver of human cancer.

In the second quarter of 2022, we acquired development and commercialization rights to two early-stage molecules, consistent with our objective to expand our pipeline. In April 2022, we announced that we had entered into a licensing agreement with Werewolf Therapeutics, Inc., or Werewolf, to acquire exclusive global development and commercialization rights to Werewolf's investigational WTX-613, now referred to as JZP898. JZP898 is a differentiated, conditionally-activated interferon alpha, or IFNα, INDUKINE™ molecule. Under the terms of the agreement, we made an upfront payment of $15.0 million to Werewolf, and Werewolf is eligible to receive development, regulatory and commercial milestone payments of up to $1.26 billion. If approved, Werewolf is eligible to receive a tiered, mid-single-digit percentage royalty on net sales of JZP898. This transaction underscores our commitment to enhancing our pipeline to deliver novel oncology therapies to patients, and also provides us with an opportunity to expand into immuno-oncology.

In May 2022, we announced that we had entered into a licensing agreement with Sumitomo Pharma Co., Ltd, or Sumitomo, to acquire exclusive development and commercialization rights in the United States, Europe and other territories for DSP-0187, now referred to as JZP441, a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. Under the terms of the agreement, we made an upfront payment of $50 million to Sumitomo, and Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to $1.09 billion. If approved, Sumitomo is eligible to receive a tiered, low double-digit royalty on Jazz's net sales of JZP441.

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

Product Candidates	Description
NEUROSCIENCE	
Phase 3	
Epidiolex	EMAS, also known as Doose syndrome (ongoing trial) LGS, TSC and DS (ongoing trial in Japan)
Phase 2b	
Suvecaltamide (JZP385)	ET (ongoing trial)
Phase 2	
JZP150	PTSD (ongoing trial)
Suvecaltamide (JZP385)	Parkinson's disease tremor (ongoing trial)
Additional cannabinoids	Autism spectrum disorders (ongoing trial)
Phase 1	
JZP324	Oxybate extended-release formulation (planned trial)
JZP441*	Potent, highly selective oral orexin-2 receptor agonist (ongoing trial in Japan)
Additional cannabinoids	Neonatal hypoxic-ischemic encephalopathy (ongoing trial) Neuropsychiatry targets (ongoing trial)
Preclinical	
Undisclosed targets	Neuroscience Cannabinoids
ONCOLOGY	
Regulatory Review	
Rylaze	ALL/LBL FDA approval in June 2021; submitted sBLA in January 2022 seeking approval for M/W/F IM dosing schedule; submitted separate sBLA seeking approval for intravenous administration; completed MAA submission to EMA in May 2022
Phase 3	
Zepzelca	First-line extensive stage SCLC in combination with Tecentriq (collaboration with Roche) (ongoing trial) Confirmatory Study (PharmaMar trial) (ongoing trial)
Zanidatamab**	HER2-positive gastroesophageal adenocarcinoma, or GEA (ongoing trial)
Vyxeos	AML or high-risk Myelodysplastic Syndrome, or MDS (AML18) (cooperative group studies) (ongoing trial) Newly diagnosed adults with standard- and high-risk AML (AML Study Group cooperative group study) (ongoing trial) Newly diagnosed pediatric patients with AML (Children's Oncology Group cooperative group study) (ongoing trial)
Pivotal Phase 2	
Zanidatamab**	Previously treated, advanced HER2-expressing biliary tract cancer, or BTC (ongoing trial)
Phase 2	
Zepzelca	Basket trial including urothelial cancer, large cell neuroendocrine tumor of the lung, and HRD cancers (ongoing trial)
Vyxeos	High-risk MDS (European Myelodysplastic Syndromes (cooperative group study) (ongoing trial) Newly diagnosed untreated patients with high-risk AML (cooperative group study) (planned trial)
Vyxeos + venetoclax	De novo or relapsed/refractory, or R/R, AML (MD Anderson collaboration study) (ongoing trial)
Zanidatamab**	HER2-expressing GEA, BTC or colorectal cancer in combination with standard first-line chemotherapy (ongoing trial)
Phase 2a	
Zanidatamab**	Previously treated HER2+HR+ breast cancer in combination with palbociclib

Product Candidates	Description
Phase 1b/2	
Zanidatamab**	First line breast cancer and GEA (BeiGene trial) (ongoing trial)
Zanidatamab**	HER2-expressing breast cancer in combination with ALX148 (ongoing trial)
Phase 1	
Vyxeos	Low intensity dosing for higher risk MDS (MD Anderson collaboration study) (ongoing trial)
Vyxeos + other approved therapies	R/R AML or hypomethylating agent failure MDS (MD Anderson collaboration study) (ongoing trial) First-line, fit AML (Phase 1b study) (ongoing trial) Low intensity therapy for first-line, unfit AML (Phase 1b study) (ongoing trial)
JZP815	Raf and Ras mutant tumors (acquired from Redx) (ongoing trial)
Zanidatamab**	In previously treated metastatic HER2-expressing cancers in combination with select antineoplastic therapies (ongoing trial)
Preclinical	
CombiPlex®	Hematology/oncology exploratory activities
JZP341 (long-acting *Erwinia* asparaginase)	ALL and other hematological malignancies (collaboration with Ligand)
JZP898	Conditionally-activated IFNα INDUKINE™ molecule
Undisclosed target	Ras/Raf/MAPK pathway (collaboration with Redx) Oncology
Exosome targets (up to 3 targets)	Hematological malignancies/solid tumors (collaboration with Codiak BioSciences, Inc., or Codiak)
Undisclosed targets	Oncology

*Also known as DSP-0187

**Pending transaction close

Operational Excellence

We remain focused on continuing to build excellence in areas that we believe will give us a competitive advantage, including building an increasingly agile and adaptable commercialization engine and strengthening our customer-focused market expertise across patients, providers and payors. We are refining our approach to engaging our customers by strengthening alignment and integration across functions and across regions. This includes a more integrated approach to brand planning, a heightened focus on launch and operational excellence and multichannel customer engagement. We have fully adapted to reaching our key audiences through both in-person and virtual initiatives. This includes maintaining a virtual presence at scientific congresses, when appropriate, designed to ensure we can continue to provide promotional and non-promotional interactions and supporting our field-based teams with virtual customer interaction tools, training and content. These initiatives mark a significant operational evolution that is directly linked to our corporate strategy and are designed to better enable our teams to work collaboratively on an aligned and shared agenda through both virtual and in-person interactions. In most geographies, our teams are increasing the frequency of in-person interactions as medical congresses and healthcare practices begin to resume in-person activities, taking into account applicable public health authority and local government guidelines which are designed to ensure community and employee safety.

COVID-19 Business Update

We have implemented a comprehensive response strategy designed to manage the impact of the COVID-19 pandemic on our employees, patients and our business. The prolonged nature of the pandemic is negatively impacting our business in a varied manner due to the emergence of variants with increased transmissibility, even in vaccinated people, including limited access to health care provider offices and institutions and the willingness of patients or parents of patients to seek treatment or change existing treatments. We expect that our business, financial condition, results of operations and growth prospects may continue to be negatively impacted by the pandemic on a limited basis that may vary depending on the context. However, we have begun to observe, and expect to continue to observe, a gradual normalization in patient and health care provider practices, as providers and patients have adapted their behaviors and procedures to the evolving circumstances and as COVID-19 vaccines continue to be administered.

Workplace and Employees

We support broad public health strategies designed to prevent the spread of COVID-19 and are focused on the health and welfare of our employees. Our global organization has mobilized to enable our employees to accomplish our most critical goals through a combination of virtual and in-person work. In addition to rolling out new technologies and collaboration tools, we have implemented processes and resources to support our employees in the event an employee receives a positive COVID-19 diagnosis. We have reopened our sites to enable our employees to return to our global offices, which takes into account applicable public health authority and local government guidelines, and which is designed to ensure community and employee safety. We have moved to a more flexible mix of virtual and in-person working designed to advance our culture, drive innovation and agility and enable greater balance and well-being for our workforce. This should also enable us to reconfigure our physical workspaces to optimize the footprint of our company-owned or leased office spaces.

Commercialization

There continues to be some negative impact on demand, new patient starts and treatments for our products arising from the pandemic, primarily due to the inherent limitations of telemedicine and a reprioritization of healthcare resources toward COVID-19. As healthcare systems have adapted to cope with the ongoing situation, we have seen improvements. We are utilizing technology to continue to engage healthcare professionals and other customers virtually to support patient care. As more clinics and institutions begin to allow in-person interactions pursuant to local health authority and government guidelines, our field teams continue to resume in-person interactions with healthcare professionals and clinics combined with virtual engagement. The level of renewed in-person engagement varies by account, region and country and may be adversely impacted in the future as a result of the continuing impact of the COVID-19 pandemic. The lack of access to health care providers has caused, and may continue to cause, delays in appropriate diagnosis, treatment and ongoing care for some patients, which has negatively impacted, and could continue to impact, prescribing and use of our products.

Supply Chain

Our manufacturing facilities in Athlone, Ireland, which produces Xywav and Xyrem, Villa Guardia, Italy, which produces defibrotide, and Kent Science Park, U.K., which produces Epidiolex/Epidyolex and Sativex, are operational with staff onsite and office-based staff working onsite and virtually as business needs require. We currently expect to have adequate global supply of all of our products for 2022.

Research and Development

With respect to our clinical trial activities, we have taken measures to implement remote and virtual approaches, including remote data monitoring where possible, to maintain patient safety and trial continuity and to preserve study integrity. We have seen some COVID-19-related impact to our mid- and late-stage clinical trial activity. We rely on contract research organizations or other third parties to assist us with clinical trials, and we cannot guarantee that they will perform their contractual duties in a timely and satisfactory manner as a result of the evolving effects of the COVID-19 pandemic. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as health care providers, have heightened exposure to COVID-19, is adversely impacting our clinical trial operations. Supply chain disruptions related to the pandemic have also impacted our ability to initiate clinical trials as originally planned.

Corporate Response

The COVID-19 pandemic has caused a significant burden on health systems globally and has highlighted the need for companies to evaluate existing therapies to assess if they can be utilized beyond their current indications to treat COVID-19 as well as consider developing new therapies. To this end, we have granted requests for several ISTs to evaluate the use of defibrotide in COVID-19 patients experiencing respiratory distress.

In addition, we are supporting our local communities and patient-focused organizations in COVID-19 relief efforts including through corporate donations to charitable organizations providing food and medical relief to communities in which we operate, and other localities where the needs related to the impact of COVID-19 are greatest. We are engaging with patient advocacy organizations to better understand the impact of COVID-19 and working to enable patients living with sleep disorders, epilepsies and oncology conditions with access to treatments and that their other needs are addressed given the impact of COVID-19 on the healthcare system. We are committed to enabling our employees to give back, including allowing licensed healthcare practitioners employed by us to support local response efforts.

Other Challenges, Risks and Trends Related to Our Business

Our business has been substantially dependent on Xyrem. Our future plans assume that Xywav, with 92% lower sodium compared to Xyrem, depending on the dose, absence of a sodium warning and dosing titration option, will become the treatment of choice for patients who can benefit from oxybate treatment, including current Xyrem patients and patients who previously were not prescribed Xyrem for whom sodium content is a concern. In June 2021, FDA recognized seven years of

ODE for Xywav in narcolepsy through July 21, 2027 stating that Xywav is clinically superior to Xyrem by means of greater safety due to reduced chronic sodium burden. While we expect that our business will continue to be substantially dependent on oxybate product sales from both Xywav and Xyrem, there is no guarantee that we can maintain oxybate sales at or near historical levels, or that oxybate sales will continue to grow.

Our ability to successfully commercialize Xywav will depend on, among other things, our ability to maintain adequate coverage and reimbursement for Xywav and acceptance of Xywav by payors, physicians and patients, including of Xywav for the treatment of IH in adults. In an effort to support strong adoption of Xywav, we are focused on providing robust patient copay and savings programs and facilitating payor coverage for Xywav. Moreover, we have increasingly experienced pressure from third party payors to agree to discounts, rebates or restrictive pricing terms, and we cannot guarantee we will be able to agree to commercially reasonable terms with PBMs and other third party payors, or that we will be able to ensure patient access and acceptance on institutional formularies. Entering into agreements with PBMs and payors to ensure patient access has and will likely continue to result in higher gross to net deductions. In addition to the COVID-19-related impacts described above, we expect our oxybate products to face competition from the near-term introduction of authorized generic versions of sodium oxybate and from generic versions of sodium oxybate pursuant to the settlement agreements we have entered into with multiple abbreviated new drug application, or ANDA, filers. Generic competition can decrease the prices at which Xywav and Xyrem are sold and the number of prescriptions written for Xywav and Xyrem. Xywav and Xyrem may also face increased competition from new branded products for treatment of cataplexy and/or EDS in narcolepsy in the U.S. market.

Our financial condition, results of operations and growth prospects are also dependent on our ability to maintain or increase sales of Epidiolex/Epidyolex in the U.S. and Europe, which is subject to many risks and there is no guarantee that we will be able to continue to successfully commercialize Epidiolex/Epidyolex for its approved indications. The commercial success of Epidiolex depends on the extent to which patients and physicians accept and adopt Epidiolex as a treatment for seizures associated with LGS, DS and TSC, and we do not know whether our or others' estimates in this regard will be accurate. Physicians may not prescribe Epidiolex and patients may be unwilling to use Epidiolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex in the market, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex. Thus, significant uncertainty remains regarding the commercial potential of Epidiolex.

In addition to our neuroscience products and product candidates, we are commercializing a portfolio of oncology products, including Defitelio, Vyxeos, Rylaze and Zepzelca. An inability to effectively commercialize Defitelio, Vyxeos, Rylaze and Zepzelca and to maximize their potential where possible through successful research and development activities could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

A key aspect of our growth strategy is our continued investment in our evolving and expanding research and development activities. If we are not successful in the clinical development of these or other 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.

In addition to continued investment in our R&D pipeline, we intend to continue 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. Failure to identify and acquire, in-license or develop additional products or product candidates, 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, such as the GW Acquisition, could have a material adverse effect on our business, results of operations and financial condition.

The success of the GW Acquisition will depend, in part, on our ability to realize the anticipated benefits from our and GW's businesses. Nonetheless, Epidiolex and the other products and technologies acquired may not be successful or continue to grow at the same rate as if our companies operated independently or they may require significantly greater resources and investments than originally anticipated. As a result, the anticipated benefits of the GW Acquisition may not be realized fully within the expected timeframe or at all or may take longer to realize or cost more than expected, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our industry has been, and is expected to continue to be, subject to healthcare cost containment and drug pricing scrutiny by regulatory agencies in the U.S. and internationally. If new 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 may be affected, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted. For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 into law, which, among other things, requires the U.S. Department of Health and Human

Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under the program, that could negatively affect our business and financial condition. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are currently capped at 100 percent of average manufacturer price, but, effective January 1, 2024, this cap will be lifted, which could adversely affect our rebate liability. We are also subject to increasing pricing pressure and restrictions on reimbursement imposed by payors. If we fail to obtain and maintain adequate formulary positions and institutional access for our products and future approved products, we will not be able to achieve a return on our investment and our business, financial condition, results of operations and growth prospects would be materially adversely affected.

While certain preparations of cannabis remain Schedule I controlled substances, if such products are approved by FDA for medical use in the U.S. they are rescheduled to Schedules II-V, since approval by FDA satisfies the "accepted medical use" requirement; or may be removed from control under the Controlled Substances Act entirely. If any of our product candidates receive FDA approval, the Department of Health and Human Services, or HHS, and the U.S. Drug Enforcement Administration, or DEA, will make a scheduling determination. U.S. or foreign regulatory agencies may request additional information regarding the abuse potential of our products which may require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse potential, which could increase the cost, delay the approval and/or delay the launch of that product. In addition, there are non-FDA approved cannabidiol preparations being made available from companies through the state-enabled medical marijuana industry, which might attempt to compete with Epidiolex. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

Finally, business practices by pharmaceutical companies, including product formulation improvements, patent litigation settlements, and risk evaluation and mitigation strategy, or REMS, programs, have increasingly drawn public scrutiny from legislators and regulatory agencies, 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 our business practices, including as they relate to the Xywav and Xyrem REMS, the launch of Xywav, our Xyrem patent litigation settlement agreements or otherwise, we could incur significant monetary charges to resolve these matters and could be distracted from operation of our business and execution of our strategy. For example, in July 2022, we received a subpoena from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to Xyrem and U.S. Patent No. 8,772,306 ("Method of Administration of Gamma Hydroxybutyrate with Monocarboxylate Transporters"), product labeling changes for Xyrem, communications with FDA and the U.S. Patent and Trademark Office, pricing of Xyrem, and other related documents. For more information, see the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products*" in Part II, Item 1A. We may also become subject to similar investigations by other state or federal governmental agencies. The investigation by the U.S. Attorney's Office and any additional investigations or litigation related to the subject matter of this investigation may result in damages, fines, penalties, financial charges to resolve the matter or administrative sanctions against us, negative publicity or other negative actions that could harm our reputation, reduce demand for Xyrem and/or reduce coverage of Xyrem, including by federal health care programs and state health care programs. In addition, from June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with certain generic companies violate state and federal antitrust and consumer protection laws. For additional information on these lawsuits, see Note 10, Commitments and Contingencies-Legal Proceedings of the Notes to Condensed Consolidated Financial Statements, included in Part I of this Quarterly Report on Form 10-Q. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages. Moreover, we are, and expect to continue to be, the subject of various claims, legal proceedings, and government investigations apart from those set forth above that have arisen in the ordinary course of business that have not yet been fully resolved and that could adversely affect our business and the execution of our strategy.

Any of the foregoing risks and uncertainties could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In addition, to the extent the COVID-19 pandemic continues to adversely affect our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described above. All of these risks and uncertainties are discussed in greater detail, along with other risks and uncertainties, in "Risk Factors" in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Results of Operations

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

	Three Months Ended September 30,		Increase/	Nine Months Ended September 30,		Increase/
	2022	2021	(Decrease)	2022	2021 [1]	(Decrease)
Product sales, net	$ 935,766	$ 834,247	12 %	$ 2,673,903	$ 2,186,118	22 %
Royalties and contract revenues	4,886	3,868	26 %	13,348	11,389	17 %
Cost of product sales (excluding amortization of acquired developed technologies)	133,661	145,224	(8)%	373,153	304,607	23 %
Selling, general and administrative	358,478	363,682	(1)%	1,033,764	1,053,221	(2)%
Research and development	148,870	141,036	6 %	417,898	350,305	19 %
Intangible asset amortization	141,232	159,804	(12)%	461,782	368,476	25 %
Acquired in-process research and development	—	—	—	69,148	—	N/A(2)
Impairment charge	133,648	—	N/A(2)	133,648	—	N/A(2)
Interest expense, net	80,244	93,372	(14)%	214,117	190,168	13 %
Foreign exchange loss (gain)	4,649	2,631	N/A(2)	16,532	(1,262)	N/A(2)
Income tax expense (benefit)	(43,027)	(18,057)	N/A(3)	(58,603)	228,583	N/A(3)
Equity in loss (gain) of investees	2,545	3,256	(22)%	9,148	(2,274)	(502)%

(1) The results of operations of the GW business have been included from the closing of the acquisition of GW on May 5, 2021.
(2) Comparison to prior period not meaningful.
(3) The fluctuations in the income tax expense (benefit) for the three and nine months ended September 30, 2022 and 2021 are primarily due to the impacts in 2022 of the impairment of our acquired IPR&D asset, costs related to restructuring and the impact in 2021 of the change in the statutory tax rate in the U.K..

Revenues

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

	Three Months Ended September 30,		Increase/	Nine Months Ended September 30,		Increase/
	2022	2021	(Decrease)	2022	2021[1]	(Decrease)
Xyrem	$ 256,039	$ 307,333	(17)%	$ 772,957	$ 977,065	(21)%
Xywav	255,936	153,063	67 %	677,041	352,643	92 %
Total Oxybate	511,975	460,396	11 %	1,449,998	1,329,708	9 %
Epidiolex/Epidyolex	196,218	160,378	22 %	529,400	269,859	N/A(3)
Sativex	3,220	6,097	(47)%	12,104	8,058	N/A(3)
Sunosi[2]	—	19,251	N/A(3)	28,844	42,981	(33)%
Total Neuroscience	711,413	646,122	10 %	2,020,346	1,650,606	22 %
Zepzelca	70,320	71,714	(2)%	197,943	181,972	9 %
Rylaze	73,513	20,674	256 %	200,687	20,674	N/A(3)
Vyxeos	30,067	34,688	(13)%	97,714	99,296	(2)%
Defitelio/defibrotide	49,452	57,705	(14)%	153,637	155,420	(1)%
Erwinaze/Erwinase	—	—	—	—	69,382	N/A(3)
Total Oncology	223,352	184,781	21 %	649,981	526,744	23 %
Other	1,001	3,344	(70)%	3,576	8,768	(59)%
Product sales, net	935,766	834,247	12 %	2,673,903	2,186,118	22 %
Royalties and contract revenues	4,886	3,868	26 %	13,348	11,389	17 %
Total revenues	$ 940,652	$ 838,115	12 %	$ 2,687,251	$ 2,197,507	22 %

(1) The results of operations of the GW business have been included from the closing of the acquisition of GW on May 5, 2021.
(2) Net product sales for Sunosi U.S. are included until the date of divestment to Axsome of May 9, 2022.
(3) Comparison to prior period not meaningful.

Product Sales, Net

Total oxybate product sales increased by $51.6 million and $120.3 million in the three and nine months ended September 30, 2022, respectively, compared to the same periods in 2021. Total oxybate revenue bottle volume increased by 7% and 5% in the three and nine months ended September 30, 2022, respectively, compared to the same periods in 2021. Average active oxybate patients on therapy were approximately 17,600 in the third quarter of 2022, an increase of approximately 10% compared to the same period in 2021. Xyrem product sales decreased in the three and nine months ended September 30, 2022 compared to the same periods in 2021 primarily due to a decrease in sales volume, reflecting the continued adoption of Xywav by existing Xyrem patients, partially offset by a higher average net selling price. Price increases were instituted in January 2021 and January 2022. Xywav product sales increased in the three and nine months ended September 30, 2022 compared to the same periods in 2021 primarily due to higher sales volume, with bottle volume increasing by 61% and 87%, respectively. Xywav product sales were positively impacted by the launch of Xywav for IH and continued strong adoption in narcolepsy driven by educational initiatives around the benefit of lowering sodium intake. Epidiolex/Epidyolex product sales increased by $35.8 million in the three months ended September 30, 2022 compared to the same period in 2021 primarily due to an increase in commercial sales volume and a higher average net selling price, partially offset by higher gross to net deductions. On a pro forma basis, Epidiolex/Epidyolex product sales increased by 14% in the nine months ended September 30, 2022 compared to the same period in 2021 primarily due to an increase in commercial sales volume and a higher average net selling price, partially offset by higher gross to net deductions. Price increases were instituted in January 2021 and January 2022. We completed the U.S. divestiture of Sunosi in May 2022.

Zepzelca product sales in the three months ended September 30, 2022 decreased compared to the same period in 2021, primarily due to higher gross to net deductions, as a result of a returns accrual release in the three months ended September 30, 2021, partially offset by the impact of a higher average net selling price. Zepzelca product sales increased in the nine months ended September 30, 2022 compared to the same period in 2021 primarily due to a higher average net selling price and an increase in sales volume, partially offset by the impact of higher gross to net deductions. Price increases were instituted in July 2021, January 2022 and July 2022. Rylaze product sales were $73.5 million and $200.7 million in the three and nine months ended September 30, 2022, respectively, following product launch in July 2021. Rylaze net product sales increased in the three months ended September 30, 2022 compared to the same period in 2021 primarily due to higher sales volume reflecting the significant unmet patient need for a high-quality, reliable supply of Erwinia asparaginase for patients with ALL. A price increase was instituted in July 2022. Vyxeos product sales decreased in the three months ended September 30, 2022 compared to the same period in 2021 due to higher gross to net deductions, partially offset by an increase in sales volume. Vyxeos product sales decreased in the nine months ended September 30, 2022 compared to the same period in 2021 primarily due to higher gross to net deductions and the negative impact of foreign exchange rates, partially offset by increased sales volume. Price increases were instituted in August 2021, January 2022 and July 2022. Defitelio/defibrotide product sales decreased in the three months ended September 30, 2022 compared to the same period in 2021 primarily due to the negative impact of foreign exchange rates and a decrease in sales volume. Defitelio/defibrotide product sales in the nine months ended September 30, 2022 were in line with the same period in 2021 as the impact of a higher average net selling price and increased sales volume were offset by the negative impact of foreign exchange rates. Price increases were instituted in July 2021, January 2022 and July 2022. We distributed our final Erwinaze inventory in June 2021 following expiration of our license and supply agreement.

We expect total product sales, net will increase in 2022 over 2021, primarily due to an increase in product sales of Xywav partially offset by a decrease in Xyrem, as patients continue to transition to Xywav, expected growth in, and the inclusion of a full year sales of, Epidiolex and Rylaze, and expected growth in Zepzelca, partially offset by a reduction in Erwinaze following expiration of our license and supply agreement and a reduction in Sunosi following completion of the sale to Axsome.

Cost of Product Sales

Cost of product sales decreased in the three months ended September 30, 2022 compared to the same period in 2021 primarily due to a decrease in the acquisition accounting inventory fair value step-up expense, or fair value step-up expense, of $11.7 million. Cost of product sales increased in the nine months ended September 30, 2022 compared to the same period in 2021 primarily due to the cost of product sales acquired in the acquisition of GW, including an increase in the fair value step-up expense of $54.6 million. Gross margin as a percentage of net product sales was 85.7% for the three months ended September 30, 2022 compared to 82.6% for the same period in 2021 primarily due to the reduction in the fair value step-up expense. Gross margin as a percentage of net product sales of 86.0% for the nine months ended September 30, 2022 was in line

with the same period in 2021. We expect our cost of product sales to increase in 2022 compared to 2021 primarily driven by the inclusion of a full year of fair value step-up expense.

Selling, General and Administrative Expenses

Selling, general and administrative expenses decreased in the three months ended September 30, 2022 compared to the same period in 2021, primarily due to lower transaction and integration expenses related to the acquisition of GW, lower Sunosi related spend offset by restructuring costs and costs related to program terminations and increased marketing expenses relating to Xywav. Selling, general and administrative expenses decreased in the nine months ended September 30, 2022 compared to the same period in 2021, primarily due to lower transaction and integration expenses, lower Sunosi related costs partially offset by restructuring costs and costs related to program terminations, the loss on disposal of Sunosi and an increase in compensation related expenses driven by the inclusion of GW related headcount costs for the full period in 2022.

We expect selling, general and administrative expenses in 2022 to decrease compared to 2021, primarily due to a reduction in transaction and integration expenses, together with synergies expected to be realized in connection with the acquisition of GW, partially offset by the inclusion of a full year of expense related to the acquired GW business, the loss on disposal of Sunosi and restructuring costs.

Research and Development Expenses

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Clinical studies and outside services	$ 57,115	$ 63,929	$ 170,694	$ 162,140
Personnel expenses	59,123	54,523	170,728	138,678
Restructuring expenses	11,891	—	11,891	—
Milestone expense	752	3,000	6,252	5,000
Other	19,989	19,584	58,333	44,487
Total	$ 148,870	$ 141,036	$ 417,898	$ 350,305

Research and development expenses increased by $7.8 million and $67.6 million in the three and nine months ended September 30, 2022, respectively, compared to the same periods in 2021. Clinical studies and outside services costs decreased in the three months ended September 30, 2022, compared to the same period in 2021, primarily due to a reduction in costs related to JZP458 (Rylaze) and solriamfetol related expenses and increased in the nine months ended September 30, 2022 compared to the same period in 2021, primarily due to additional costs related to clinical programs for Epidiolex, nabiximols and cannabinoids and an increase in costs related to JZP150. Personnel expenses increased in the three months ended September 30, 2022, compared to the same period in 2021, primarily due to share-based compensation related expenses. Personnel expenses in the nine months ended September 30, 2022 increased compared to the same period in 2021 due to the inclusion of GW-related headcount costs for the full period in 2022. There were restructuring costs of $11.9 million in the three and nine months ended September 30, 2022. Other costs for the three months ended September 30, 2022 were in line with the same period in 2021 and increased in the nine months ended September 30, 2022 compared to the same period in 2021 primarily due to the inclusion of GW-related costs for the full period in 2022.

For 2022, we expect that our research and development expenses will continue to increase from previous levels due to the inclusion of a full year of expense with respect to the acquired GW business and initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates.

Intangible Asset Amortization

Intangible asset amortization decreased by $18.6 million in the three months ended September 30, 2022, compared to the same period in 2021 due to movements in foreign exchange rates and increased by $93.3 million in the nine months ended September 30, 2022, compared to the same period in 2021 primarily due to the inclusion of the amortization of the intangible assets arising from the acquisition of GW, primarily related to Epidiolex, offset by a decrease relating to the Erwinaze intangible asset that was fully amortized in June 2021. Intangible asset amortization is expected to increase in 2022 compared to 2021 primarily as a result of the inclusion of a full years amortization on the intangible assets acquired in the acquisition of GW.

Acquired In-Process Research and Development

Acquired in-process research and development, or IPR&D, expense in the nine months ended September 30, 2022 primarily related to the upfront payments made in connection with our licensing agreements with Sumitomo and Werewolf of $50.0 million and $15.0 million, respectively.

Impairment charge

In the three and nine months ended September 30, 2022, we recorded an IPR&D asset impairment charge of $133.8 million as a result of the decision to discontinue our nabiximols program.

Interest Expense, Net

Interest expense, net in the three months ended September 30, 2022, decreased by $13.1 million, compared to the same period in 2021, primarily driven by a decrease in non-cash interest expense relating to the 1.50% exchangeable senior notes due 2024, or the 2024 Notes, and the 2.00% exchangeable senior notes due 2026, or the 2026 Notes, following the adoption of ASU No. 2020-06, “Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging— Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity”, or ASU 2020-06, on January 1, 2022. Interest expense, net, increased by $23.9 million in the nine months ended September 30, 2022, compared to the same period in 2021, primarily due to higher interest expense from the seven-year $3.1 billion term loan B facility, or the Dollar Term Loan and the 4.375% senior secured notes, due 2029, or the Secured Notes, offset by a decrease in non-cash interest expense relating to the 2024 and 2026 Notes. We expect interest expense, net for 2022 to be broadly in line with 2021.

Foreign Exchange Loss (Gain)

The foreign exchange loss (gain) is primarily related to the translation of sterling and 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.

Income Tax Expense (Benefit)

Our income tax benefit was $43.0 million and $58.6 million for the three and nine months ended September 30, 2022, respectively, compared to an income tax benefit of $18.1 million and an income tax expense of $228.6 million for the same periods in 2021. Our income tax benefit for the three and nine months ended September 30, 2022 included the tax impacts of the impairment of our acquired IPR&D asset and restructuring costs. Our income tax expense for the three and nine months ended September 30, 2021 included an expense of $250.6 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory rate in the U.K. following enactment of the U.K. Finance Act 2021. Excluding these impacts, the decrease in the income tax benefit in the three months ended September 30, 2022 compared to the same period in 2021 resulted primarily from the mix of pre-tax income and losses incurred across tax jurisdictions. The income tax benefit in the nine months ended September 30, 2022 is in line with the prior period. 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.

Liquidity and Capital Resources

As of September 30, 2022, we had cash, cash equivalents and investments of $899.4 million, borrowing availability under our revolving credit facility of $500.0 million and long-term debt principal balance of $5.8 billion. Our long-term debt included $2.8 billion in aggregate principal amount of the Dollar Term Loan, $1.5 billion in aggregate principal amount of the Secured Notes, $1.0 billion principal amount of the 2026 Notes and $575.0 million principal amount of the 2024 Notes. We generated cash flows from operations of $930.0 million during the nine months ended September 30, 2022, and we expect to continue to generate positive cash flows from operations which will enable us to operate our business and de-lever our balance sheet over time.

In 2022, we made voluntary repayments of $300.0 million of the Dollar Term Loan principal outstanding and €208.3 million, or $251.0 million, of the seven-year €625.0 million term loan B facility, or the Euro Term Loan, which represented the remaining principal amount. We have made voluntary repayments of €625.0 million, or $753.0 million, relating to Euro Term Loan and voluntary and mandatory repayments of $300.0 million and $38.2 million, respectively, relating to the Dollar Term Loan since the closing of the acquisition of GW in May 2021.

We have a significant amount of debt outstanding on a consolidated basis. For a more detailed description of our debt arrangements, including information relating to our scheduled maturities with respect to our long-term debt, see Note 9, Debt, of the notes to the condensed consolidated financial statements, included in Part I, Item 1 of this Quarterly Report on Form 10-Q. This substantial level of debt could have important consequences to our business, including, but not limited to the factors set forth in “Risk Factors” of this Quarterly Report on Form 10-Q under the heading “We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.”

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 in Part II, Item 1A “Risk Factors” of this Quarterly Report on Form 10-Q under the headings “Risks Related to our Lead Products and Product Candidates” 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 and grow 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. We regularly evaluate the performance of our products and product candidates to ensure fit within our portfolio and support efficient allocation of capital. 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. However, global economic conditions have been worsening, with disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures, the COVID-19 pandemic and otherwise. If these conditions persist and deepen, we could experience an inability to access additional capital or our liquidity could otherwise be impacted, which could in the future negatively affect our capacity for certain corporate development transactions or our ability to make other important, opportunistic investments. In addition, under Irish law we must have authority from our shareholders to issue any ordinary shares, including ordinary shares that are part of our authorized but unissued share capital. Moreover, as a matter of Irish law, when an Irish public limited company issues ordinary shares to new shareholders for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders on a pro-rata basis, unless this statutory pre-emption obligation is dis-applied, or opted-out of, by approval of its shareholders. At our annual general meeting of shareholders in July 2022, our shareholders voted to approve our proposal to dis-apply the statutory pre-emption obligation on terms that are substantially more limited than our general pre-emption opt-out authority that had been in effect prior to August 4, 2021. This current pre-emption opt-out authority is due to expire in December 2023. If we are unable to obtain further pre-emption authorities from our shareholders in the future, or otherwise continue to be limited by the terms of new pre-emption authorities approved by our shareholders in the future, our ability to use our unissued share capital to fund in-licensing, acquisition or other business opportunities, or to otherwise raise capital, could be adversely affected. In any event, an inability to borrow or raise additional capital in a timely manner and on attractive terms could prevent us from expanding our business or taking advantage of acquisition opportunities, and could otherwise have a material adverse effect on our business and growth prospects. 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. Furthermore, any equity financing would be dilutive to our shareholders, and could require the consent of the lenders under the Credit Agreement and the indenture for the Secured Notes for certain financings.

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

	Nine Months Ended September 30,	
	2022	2021
Net cash provided by operating activities	$ 930,006	$ 600,752
Net cash used in investing activities	(121,852)	(5,202,051)
Net cash (used in) provided by financing activities	(549,087)	4,217,131
Effect of exchange rates on cash and cash equivalents	(11,157)	(1,821)
Net increase (decrease) in cash and cash equivalents	$ 247,910	$ (385,989)

Operating activities

Net cash provided by operating activities increased by $329.3 million in the nine months ended September 30, 2022 compared to the same period in 2021, primarily due to increased cash received on sales of our products and decreased transaction and integration-related costs associated with the GW Acquisition.

Investing activities

Net cash used in investing activities decreased by $5,080.2 million in the nine months ended September 30, 2022 compared to the same period in 2021, primarily due to the following:

- $6,234.8 million outflow related to the net cash paid for the GW Acquisition in the nine months ended September 30, 2021; and
- $53.0 million upfront payment from Axsome relating to the Sunosi U.S. disposition in the nine months ended September 30, 2022; offset by

- $1,129.3 million decrease in net proceeds from maturity of investments, primarily time deposits in the nine months ended September 30, 2022; and
- $69.1 million in upfront payments for acquired IPR&D primarily driven by the $50.0 million and $15.0 million payments to Sumitomo and Werewolf, respectively, in connection with our licensing agreements in the nine months ended September 30, 2022.

Financing activities

Net cash (used in) provided by financing activities decreased by $4,766.2 million in the nine months ended September 30, 2022 compared to the same period in 2021, primarily due to:

- Net proceeds from issuance of borrowings under the Credit Agreement of $3,719.9 million and the Secured Notes of $1,471.5 million in the nine months ended September 30, 2021; and
- A decrease of $49.2 million in proceeds from employee equity incentive and purchase plans; offset by
- Payments for repurchase of the 2021 Notes of $218.8 million in the nine months ended September 30, 2021; and
- Repayments of long-term debt of $574.3 million in the nine months ended September 30, 2022, compared to $843.0 million in the nine months ended September 30, 2021.

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. During the nine months ended September 30, 2022, there were no changes to the credit agreement, as set forth in Note 12, Debt, of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2021.

Contractual Obligations

During the nine months ended September 30, 2022, 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, 2021.

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 and also with respect to the acquisition and valuation of intangibles and income taxes. 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, 2021. 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, 2021.

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 nine months ended September 30, 2022, 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, 2021.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures. We have carried out an evaluation under the supervision and with the participation of management, including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e) of the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on their evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of September 30, 2022.

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

Changes in Internal Control over Financial Reporting. During the quarter ended September 30, 2022, other than continuing changes to our internal control process resulting from the integration of GW, there have been no changes to our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings

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

Item 1A. Risk Factors

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

Summary Risk Factors

Below is a summary of material factors that make an investment in our ordinary shares speculative or risky. Importantly, this summary does not address all of the risks and uncertainties that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, as well as other risks and uncertainties that we face, immediately follows this risk factor summary. The below risk factor summary is qualified in its entirety by that more complete discussion of such risks and uncertainties. You should consider carefully the risks and uncertainties described below as part of your evaluation of an investment in our ordinary shares.

- Our inability to maintain or increase sales from our oxybate franchise would have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products and product candidates would adversely affect sales of our oxybate products and product candidates.
- The distribution and sale of our oxybate products are subject to significant regulatory restrictions, including the requirements of a REMS and safety reporting requirements, and these regulatory and safety requirements subject us to risks and uncertainties, any of which could negatively impact sales of Xywav® and Xyrem®.
- Our inability to maintain or increase sales of Epidiolex®/Epidyolex® would have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- While we expect our oxybate products and Epidiolex/Epidyolex to remain the largest parts of our business, our success also depends on our ability to effectively commercialize other products in our neuroscience and oncology therapeutic areas.
- We face substantial competition from other companies, including companies with larger sales organizations and more experience working with large and diverse product portfolios, and face competition from generic drugs and potentially from non-FDA approved cannabidiol preparations.
- Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and other organizations; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement, either of which could diminish our sales or adversely affect our ability to sell our products profitably.
- The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy, including recently enacted changes to Medicare in the U.S., 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 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.
- 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.

- Our future success depends on our ability to successfully develop and obtain and maintain regulatory approvals for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.
- 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 transactions.
- 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.
- We may not realize the anticipated benefits and synergies from the GW Acquisition.
- It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.
- 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 business is currently adversely affected and could be materially and adversely affected in the future by the evolving effects of the COVID-19 pandemic and related global economic slowdown, including with respect to our commercialization efforts, clinical trial activity, research and development activities, supply chain and corporate development activities and other business operations.
- Significant disruptions of information technology systems or data security breaches could adversely affect our business.
- We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations or penalties and may result in significant additional expense and limit our ability to commercialize our products.
- If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.
- 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 and grow our business.

Risks Related to Our Lead Products and Product Candidates

Our inability to maintain or increase sales from our oxybate franchise would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our business has been substantially dependent on Xyrem® (sodium oxybate) oral solution, and our financial results have been significantly influenced by sales of Xyrem. Our future plans assume that Xywav®, our oxybate product launched in November 2020, will become the treatment of choice for patients who can benefit from oxybate treatment, current Xyrem patients, and patients who previously were not prescribed Xyrem, including those patients for whom sodium content is a concern. Xywav has 92%, or approximately 1,000 to 1,500 milligrams per day, less sodium than Xyrem, depending on the dose, the absence of a sodium warning and a dosing titration option. In June 2021, U.S. Food and Drug Administration, or FDA, recognized seven years of Orphan Drug Exclusivity through July 21, 2027 for Xywav in narcolepsy stating that Xywav is clinically superior to Xyrem by means of greater safety due to reduced chronic sodium burden. However, our ability to successfully commercialize Xywav will continue to depend on, among other things, our ability to maintain adequate coverage and reimbursement for Xywav and acceptance of Xywav by payors, physicians and patients.

In addition, our ability to maintain or increase oxybate product sales and realize the anticipated benefits from our investment in Xywav is subject to a number of additional risks and uncertainties as discussed in greater detail below, including those related to the near-term introduction of authorized generic versions of sodium oxybate and generic versions of sodium oxybate and new products for treatment of cataplexy and/or excessive daytime sleepiness, or EDS, in narcolepsy in the U.S. market; the current and potential impacts of the COVID-19 pandemic, including the current and expected future negative impact on demand for our products and the uncertainty with respect to our ability to meet commercial demand in the future;

increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including our ability to maintain adequate coverage and reimbursement for Xywav; and challenges to our intellectual property around Xyrem and/or Xywav. While we expect that our business will continue to be substantially dependent on oxybate product sales, there is no guarantee that we can maintain oxybate sales at or near historical levels, or that oxybate sales will continue to grow. A significant decline in oxybate sales could cause us 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 new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products and product candidates would adversely affect sales of our oxybate products and product candidates.

While Xywav and Xyrem are currently the only products approved by FDA and marketed in the U.S. for the treatment of both cataplexy and EDS in both adult and pediatric patients with narcolepsy, new treatment options for cataplexy and EDS in narcolepsy have launched, and in the future, other products may be launched that are competitive with or disrupt the market for our oxybate products.

For example, in the future, we expect Xywav and Xyrem to face competition from authorized generic versions of sodium oxybate and generic versions of sodium oxybate. 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, FDA has approved or tentatively approved four of these ANDAs, and we believe that it is likely that FDA will approve or tentatively approve some or all of the others. In our patent litigation settlement with the first filer, West-Ward Pharmaceuticals Corp. (a wholly owned subsidiary of Hikma Pharmaceuticals PLC and now known as Hikma in the U.S.), or Hikma, we granted Hikma the right to sell an authorized generic product, or AG Product, with royalties back to us, in the U.S. beginning on January 1, 2023, or earlier under certain circumstances. Hikma has a right to elect to continue to sell the Hikma AG Product for a total of up to five years. We also granted Hikma a license to launch its own generic sodium oxybate product as early as six months after it has the right to sell the Hikma AG Product, but if it elects to launch its own generic product, Hikma will no longer have the right to sell the Hikma 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, and ending on December 31, 2025, with royalties back to us. AG Products will be distributed through the same risk evaluation and mitigation strategy, or REMS, as Xywav and Xyrem. 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 the circumstance where Hikma elects to launch its own generic product. If Amneal, Lupin or Par elects to launch its own generic product under such circumstance, it will no longer have the right to sell an AG Product. 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 circumstances where Hikma launches 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. 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.

Any ANDA holder launching an AG Product or another generic sodium oxybate product will independently 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 will likely 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 royalties and other revenue based on sales of an AG Product in accordance with the terms of our settlement agreements.

Other companies may develop sodium oxybate products for treatment of narcolepsy, using an alternative formulation or a different delivery technology, and seek approval in the U.S. using a new drug application, or NDA, approval pathway under Section 505(b)(2) and referencing the safety and efficacy data for Xyrem. In February 2021, FDA accepted for filing an NDA submitted by Avadel Pharmaceuticals plc, or Avadel, for FT218, an extended-release formulation of sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy. In May 2022, Avadel reported that FDA requested Avadel certify to our REMS patent and in July 2022, Avadel announced that it had received tentative approval of FT218 pending disposition of the REMS patent. Accordingly, Avadel stated that it is pursuing all options to accelerate full approval on or before the expiration of our REMS patent on June 17, 2023. Moreover, Avadel has announced that it has obtained an orphan drug designation from FDA for its extended-release sodium oxybate formulation. To obtain approval in light of the prior approval of our oxybate products and to obtain its own Orphan Drug Exclusivity for FT218 if approved, Avadel will have to show clinical superiority to Xywav and Xyrem, which requires establishing that FT218 has

greater effectiveness, greater safety, or otherwise makes a major contribution to patient care when compared to our products. We cannot predict the timing of full approval of Avadel's sodium oxybate product or how FDA will evaluate any clinical superiority arguments that either we or Avadel may make, but in any event, we expect to face competition from Avadel.

Xyrem and Xywav also face increased competition from new branded entrants to treat EDS in narcolepsy such as pitolisant. Other companies have announced that they have product candidates in various phases of development to treat the symptoms of narcolepsy, such as Axsome Therapeutics, Inc.'s reboxetine, and various companies are performing research and development on orexin agonists for the treatment of sleep disorders.

We expect that Xywav for the treatment of both cataplexy and EDS in patients with narcolepsy will face competition from generic or authorized generic sodium oxybate products or new branded entrants in narcolepsy notwithstanding FDA recognizing Orphan Drug Exclusivity for Xywav. For example, we received notice in June 2021 that Lupin filed an ANDA for a generic version of Xywav. Additional companies may file ANDAs seeking to market a generic version of Xywav which could lead to additional patent litigation or challenges with respect to Xywav.

Moreover, non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy or idiopathic hypersomnia, or IH, including new market entrants, even if not directly competitive with Xywav or Xyrem, could have the effect of changing treatment regimens and payor or formulary coverage of Xywav or Xyrem in favor of other products, and indirectly materially and adversely affect sales of Xywav and Xyrem. Examples of such new market entrants include pitolisant, a drug that was approved by FDA in 2019 for the treatment of EDS in adult patients with narcolepsy and approved by FDA in 2020 pursuant to a complete response resubmission for an adult cataplexy indication in the U.S. Pitolisant has also been approved and marketed in Europe to treat adult patients with narcolepsy, with or without cataplexy, and to treat EDS in obstructive sleep apnea, or OSA. Pitolisant is also in late stage development for the treatment of IH. In addition, we are also aware that prescribers often prescribe branded or generic medications for cataplexy, before or instead of prescribing oxybate therapy in Xywav and Xyrem, and that payors often require patients to try such medications before they will cover Xywav or Xyrem, even if they are not approved for this use. Examples of such products are described in "Business—Competition" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2021.

We expect that the approval and launch of an AG Product or other generic version of Xyrem could have a material adverse effect on our sales of Xywav and Xyrem and on our business, financial condition, results of operations and growth prospects. We also expect that sales of Xywav will, and the approval and launch of any other sodium oxybate (including Avadel's extended-release sodium oxybate formulation) or alternative product that treats narcolepsy could, have a material adverse effect on our sales of Xyrem, which could have the additional impact of potentially triggering acceleration of market entry of AG Products or other generic sodium oxybate products under our patent litigation settlement agreements.

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

The active pharmaceutical ingredient, or API, of Xywav and Xyrem, is a form 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, FDA requires that we maintain a REMS with elements to assure safe use, or ETASU, for Xywav and 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 Xywav and Xyrem that we are responsible for implementing. Any failure to demonstrate our substantial compliance with our REMS obligations, including as a result of business or other interruptions resulting from the evolving effects of the COVID-19 pandemic, or a determination by FDA that the REMS is not meeting its goals, could result in enforcement action by FDA, lead to changes in our REMS obligations, negatively affect sales of Xywav or 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.

FDA will evaluate the Xywav and Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. We cannot predict whether FDA will request, seek to require or ultimately require modifications to, or impose additional requirements on, the Xywav and Xyrem REMS, including in connection with the submission of new oxybate products or indications, the introduction of authorized generics, or to accommodate generics, or whether FDA will approve modifications to the Xywav and Xyrem REMS that we consider warranted. Any modifications approved, required or rejected by FDA could change the safety profile of Xywav or Xyrem, and have a significant negative impact in terms of product liability, public acceptance of Xywav or Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our oxybate business. Modifications approved, required or rejected by FDA could also make it more difficult or expensive for us to distribute Xywav or Xyrem, make distribution easier for oxybate competitors, disrupt continuity of care for Xywav or Xyrem patients and/or negatively affect sales of Xywav or Xyrem.

We depend on outside vendors, including Express Scripts Specialty Distribution Services, Inc., the central certified pharmacy, to distribute Xywav and Xyrem in the U.S., provide patient support services and implement the requirements of the Xywav and Xyrem REMS. If the central pharmacy fails to meet the requirements of the Xywav and Xyrem REMS applicable to the central pharmacy or otherwise does not fulfill its contractual obligations to us, moves to terminate our agreement, refuses or fails to adequately serve patients, or fails to promptly and adequately address operational challenges or challenges in implementing REMS modifications, whether due to business or other interruptions resulting from the evolving effects of the COVID-19 pandemic or otherwise, the fulfillment of Xywav or 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 Xywav or 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 under the REMS and would also need to implement the particular processes, procedures and activities necessary to distribute under the Xywav and Xyrem REMS. Transitioning to a new pharmacy could result in product shortages, which would negatively affect sales of Xywav and 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.

In its approval of Hikma's ANDA, FDA waived the requirement of a single shared REMS between the brand drug and generic versions, approving Hikma's ANDA with a generic sodium oxybate REMS separate from the Xywav and Xyrem REMS, except for the requirement that the generic sodium oxybate REMS program pharmacies contact the Xywav and Xyrem REMS by phone to verify and report certain information. The generic sodium oxybate REMS was approved with the condition that it be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. A sodium oxybate distribution system that is less restrictive than the Xywav and Xyrem REMS, such as the generic sodium oxybate REMS or another branded sodium oxybate REMS, could increase the risks associated with 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 Xywav or Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our oxybate business.

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

REMS programs have increasingly drawn public scrutiny from the U.S. Congress, the Federal Trade Commission, or FTC, and FDA, with allegations that such programs are used as a means of improperly blocking or delaying competition. In December 2019, as part of the Further Consolidated Appropriations Act of 2020, the U.S. Congress passed legislation known as the Creating and Restoring Equal Access To Equivalent Samples Act, or CREATES. CREATES is intended to prevent companies from using REMS and other restricted distribution programs as a means to deny potential competitors access to product samples that are reasonably necessary to conduct testing in support of an application that references a listed drug or biologic, and provides such potential competitors a potential private right of action if the innovator fails to timely provide samples upon request. CREATES also grants FDA additional authority regarding approval of generic products with REMS.

It is possible that the FTC, FDA or other governmental authorities 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, FDA expressed concern that we were aware that the Xyrem REMS is blocking competition. From June 2020 to May 2022, we were served with a number of lawsuits that included allegations that we had used the Xyrem REMS to delay approval of generic sodium oxybate. In December 2020, these cases were centralized and transferred to the United States District Court for the Northern District of California, where the multidistrict litigation will proceed for the purpose of discovery and pre-trial proceedings. For additional information on these lawsuits, see Note 10, Commitments and Contingencies-Legal Proceedings of the Notes to Condensed Consolidated Financial Statements, included this Quarterly Report on Form 10-Q. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs were to be successful in their claims, they

may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Pharmaceutical companies, including their agents and employees, are required to monitor adverse events occurring during the use of their products and report them to FDA. The patient counseling and monitoring requirements of the Xywav and Xyrem REMS provide more extensive information about adverse events experienced by patients taking Xywav and Xyrem, including deaths, than is generally available for other products that are not subject to similar REMS requirements. As required by FDA and other regulatory agencies, the adverse event information that we collect for Xywav and Xyrem is regularly reported to FDA and could result in FDA requiring changes to Xywav and/or 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 Xywav and Xyrem. As required by FDA, Xywav's and 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 FDA or another regulatory authority could result in such regulatory authorities taking actions in the future which could have a material adverse effect on oxybate product sales and therefore on our business, financial condition, results of operations and growth prospects.

Our inability to maintain or increase sales of Epidiolex/Epidyolex would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our ability to maintain or increase sales of Epidiolex/Epidyolex (cannabidiol) is subject to many risks. There are many factors that could cause the commercialization of Epidiolex to be unsuccessful, including a number of factors that are outside our control. The commercial success of Epidiolex depends on the extent to which patients and physicians accept and adopt Epidiolex as a treatment for seizures associated with Lennox-Gastaut syndrome, or LGS, Dravet syndrome and Tuberous Sclerosis Complex, and we do not know whether our or others' estimates in this regard will be accurate. Physicians may not prescribe Epidiolex and patients may be unwilling to use Epidiolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex in the market, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex.

While we expect our oxybate products and Epidiolex/Epidyolex to remain the largest parts of our business, our success also depends on our ability to effectively commercialize other products in our neuroscience and oncology therapeutic areas.

In addition to Xywav, Xyrem, Epidiolex/Epidyolex and our other neuroscience products and product candidates, we are commercializing a portfolio of products, including our other lead marketed products, Zepzelca, Rylaze, Vyxeos and Defitelio. An inability to effectively commercialize our other lead marketed products and to maximize their potential where possible through successful research and development activities could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Zepzelca

Our ability to realize the anticipated benefits from our investment in Zepzelca® (lurbinectedin) is subject to a number of risks and uncertainties, including our ability to successfully commercialize Zepzelca in the U.S.; adequate supply of Zepzelca to meet demand; availability of favorable pricing and adequate coverage and reimbursement; the limited experience of, and need to educate, physicians in the use of Zepzelca for the treatment of metastatic small cell lung cancer, or SCLC; the potential for negative trial data read-outs in ongoing or future Zepzelca clinical trials; our and Pharma Mar, S.A., or PharmaMar's, ability to maintain accelerated approval or successfully complete a confirmatory study of Zepzelca; and the impact of the evolving effects of the COVID-19 pandemic on our ability to educate health care providers about Zepzelca in the treatment of relapsed, metastatic SCLC in the U.S. and on patients' access to lung cancer screening, diagnosis and treatment. If we are unable to successfully commercialize Zepzelca in the U.S. and Canada, or if sales of Zepzelca do not reach the levels we expect, our anticipated revenue from Zepzelca will be negatively affected, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Rylaze

Our ability to realize the anticipated benefits from our investments in Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) is subject to a number of uncertainties, including our ability to successfully commercialize Rylaze in the U.S. including creating awareness among health care professionals and ensuring that patients with acute lymphoblastic leukemia, or ALL, or lymphoblastic lymphoma, or LBL, will be given the appropriate course of therapy based on current FDA approval. In addition, there continues to be the potential of a competitive erwinia product being reintroduced into the marketplace that could create uncertainty in demand and utilization of Rylaze moving forward.

Vyxeos

Our ability to realize the anticipated benefits from our investment in Vyxeos® (daunorubicin and cytarabine) liposome for injection by successfully and sustainably growing sales is subject to a number of risks and uncertainties, including our ability to differentiate Vyxeos from other liposomal chemotherapies and generically available chemotherapy combinations with which physicians and treatment centers are more familiar; acceptance by hospital pharmacy and therapeutics committees in the U.S., the EU and other countries; the increasing complexity of the acute myeloid leukemia, or 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 increasing use of venetoclax, which received full FDA approval in October 2020 for AML treatment; the limited size of the population of high-risk AML patients who may potentially be indicated for treatment with Vyxeos, particularly as a result of the shift of healthcare resources toward less intensive outpatient AML treatments in the U.S. in light of the COVID-19 pandemic which is directly negatively impacting, or delaying, the use of Vyxeos, as well as the limited return of in-person interactions with healthcare professionals at several institutions due to COVID-19 pandemic restrictions that have not been fully lifted; the availability of adequate coverage, pricing and reimbursement approvals; and competition from new and existing products and potential competition from products in development. If sales of Vyxeos do not reach the levels we expect, our anticipated revenue from the product would be negatively affected, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Defitelio

Our ability to maintain and grow sales and to realize the anticipated benefits from our investment in Defitelio® (defibrotide sodium) is subject to a number of risks and uncertainties, including continued acceptance by hospital pharmacy and therapeutics committees in the U.S., the EU and other countries; the continued availability of favorable pricing and adequate coverage and reimbursement; the limited experience of, and need to educate, physicians and other health care providers in recognizing, diagnosing and treating hepatic veno-occlusive disease, or 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; and the limited size of the population of VOD patients who are indicated for treatment with Defitelio (particularly if changes in hematopoietic stem cell transplantation, or HSCT, treatment protocols reduce the incidence of VOD diagnosis and demand for Defitelio).

If sales of Defitelio do not reach the levels we expect, our anticipated revenue from the product would be negatively affected and our business, financial condition, results of operations and growth prospects would be adversely affected. For example, the number of patients receiving HSCT due to the effects of the COVID-19 pandemic is only starting to return to pre-pandemic levels. In addition, 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.

We face substantial competition from other companies, including companies with larger sales organizations and more experience working with large and diverse product portfolios, and face competition from generic drugs and potentially from non-FDA approved cannabidiol preparations.

Our products compete, and our product candidates may in the future compete, with currently existing therapies, including generic drugs, product candidates currently under development by us and others and/or future product candidates, including new chemical entities that may be safer or more effective or more convenient 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. Many of our competitors, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources 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. In addition, many of our competitors deploy more personnel to market and sell their products than we do, and we compete with other companies to recruit, hire, train and retain pharmaceutical sales and marketing personnel. 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. In any event, 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. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

There is a substantial amount of change occurring in the U.S. regarding the use of medical and recreational marijuana products. While federal law prohibits the sale and distribution of most marijuana products not approved or authorized by FDA,

46 states and the District of Columbia have legalized either cannabidiol, or CBD, or marijuana for either recreational or medical use, or both. Under the U.S. Farm Bill, enacted in late 2018, certain extracts and other material derived from cannabis are no longer controlled under the Federal Controlled Substances Act, or CSA. Although the marketing of such products as a food, dietary supplement, or for medical purposes remains subject to FDA requirements, FDA continues to evaluate regulatory pathways to permit CBD in conventional foods and dietary supplements. In addition, Congressional efforts related to legalization of marijuana continue. Although our business is distinct from that of entities marketing FDA-unapproved marijuana and CBD-containing dietary supplement, future legislation or federal government action authorizing the sale, distribution, use, and insurance reimbursement of non-FDA approved marijuana or cannabinoid products could increase competition for and adversely affect our ability to generate sales of Epidiolex and our cannabinoid product candidates.

In addition, Epidiolex competes with product offerings from a variety of companies. FDA approved Zogenix, Inc.'s low-dose fenfluramine, or Fintepla, in Dravet syndrome in June 2020, and for LGS in March 2022. In March 2022, UCB S.A. announced that it had completed its acquisition of Zogenix. Ovid Therapeutics Inc./Takeda Pharmaceutical Company Limited, Eisai Company Limited, and Marinus Pharmaceuticals, Inc. are developing therapies for treating Developmental and Epileptic Encephalopathies (includes Dravet and LGS). Stiripentol has been approved in Europe for several years to treat Dravet syndrome and was approved in 2018 by FDA. Zynerba Pharmaceuticals, Inc. is developing a topical formulation of CBD, for which it is working with FDA on a path forward on CONNECT-FX data for Zygel in Fragile X syndrome. There are a number of public and private companies in the early stages of developing genetic therapies for the underlying causes of Dravet syndrome, including Stoke Therapeutics, Inc., which has an antisense oligonucleotide, STK-001, in early clinical trials. Other companies, including those with greater resources than us may announce similar plans in the future. In addition, there are non-FDA approved CBD preparations being made available from companies in the medical marijuana industry, which might attempt to compete with Epidiolex. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

For a description of the competition that our lead marketed products and most advanced product candidates face or may face, see the discussion in "Business—Competition" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2021 and the risk factor under the heading "*The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products and product candidates would adversely affect sales of our oxybate products and product candidates"* in this Part II, Item 1A.

Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and other organizations; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement, either of which could diminish our sales or adversely 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, including governmental payors (such as the Medicare and Medicaid programs in the U.S.), managed care organizations and private health insurers. Without third party payor reimbursement, patients may not be able to obtain or afford prescribed medications. In addition, reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a significant impact on the prescribing physicians' willingness and ability to prescribe our products. The demand for, and the profitability of, our products could be materially harmed if state Medicaid programs, the Medicare program, other healthcare programs in the U.S. or elsewhere, or third party commercial 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. In particular, we cannot predict to what extent the evolving effects of the COVID-19 pandemic may disrupt global healthcare systems and access to our products or result in a widespread loss of individual health insurance coverage due to unemployment, a shift from commercial payor coverage to government payor coverage, or an increase in demand for patient assistance and/or free drug programs, any of which could adversely affect net revenue.

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. 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.

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. If our competitors offer their products at prices that provide purportedly 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 benefit coverage and reimbursement and co-pay policies. Because some of our products compete in a market with both branded and generic products, obtaining and maintaining access and reimbursement coverage for our products may be more challenging than for products that are new chemical entities for which no therapeutic alternatives exist.

Third party pharmacy benefit managers, or PBMs, other similar organizations and payors can 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, make a complex and time-intensive request for medical exemptions, or pay 100% of the cost of a drug. In addition, in many instances, certain PBMs, other similar organizations and third party payors may exert negotiating leverage by requiring incremental rebates, discounts or other concessions from manufacturers in order to maintain formulary positions, which could continue to result in higher gross to net deductions for affected products. In this regard, we have entered into agreements with PBMs and payor accounts to provide rebates to those entities related to formulary coverage for our products, but we cannot guarantee that we will be able to agree to coverage terms with other PBMs and other third party payors. Payors could decide to exclude our products from formulary coverage lists, impose step edits that require patients to try alternative, including generic, treatments before authorizing payment for our products, limit the types of diagnoses for which coverage will be provided or impose a moratorium on coverage for products while the payor makes a coverage decision. An inability to maintain adequate formulary positions could increase patient cost-sharing for our products and cause some patients to determine not to use our products. Any delays or unforeseen difficulties in reimbursement approvals could limit patient access, depress therapy adherence rates, and adversely impact our ability to successfully commercialize our products. If we are unsuccessful in maintaining broad coverage for our products, our anticipated revenue from and growth prospects for our products could be negatively affected.

In many countries outside the U.S., procedures to obtain price approvals, coverage and reimbursement can take considerable time after the receipt of marketing authorization. Many European countries periodically review their reimbursement of medicinal products, which could have an adverse impact on reimbursement status. In addition, we expect that legislators, policymakers and healthcare insurance funds in the EU member states will continue to propose and implement cost-containing measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative to branded products, and/or branded products available through parallel import to keep healthcare costs down. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU member states, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. 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 national laws in each EU member state, is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA 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 beginning in January 2025, the EU HTA regulation will apply; this regulation aims to harmonize the clinical benefit assessment of HTA across the EU. If we are unable to maintain favorable pricing and reimbursement status in EU member states that represent significant markets, our anticipated revenue from and growth prospects for our products in the EU could be negatively affected. For example, the European Commission, or EC, granted marketing authorization for Vyxeos in August 2018 and for Epidyolex in September 2019, and, as part of our rolling launches of Vyxeos and Epidyolex in Europe, we are making pricing and reimbursement submissions in European countries. If we experience setbacks or unforeseen difficulties in obtaining favorable pricing and reimbursement decisions, including as a result of regulatory review delays, planned launches in the affected EU member states would be delayed, which could negatively impact anticipated revenue from and growth prospects for Vyxeos and Epidyolex.

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, including recently enacted changes to Medicare, 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, as governmental oversight and scrutiny of biopharmaceutical companies is increasing. For example, we anticipate that the U.S. Congress, state legislatures, and federal and state regulators may adopt or accelerate adoption of new

healthcare policies and reforms intended to curb healthcare costs, such as federal and state controls on reimbursement for drugs (including under Medicare, Medicaid and commercial health plans), new or increased requirements to pay prescription drug rebates and penalties to government health care programs, and additional pharmaceutical cost transparency policies that aim to require drug companies to justify their prices through required disclosures. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under the program, that could negatively affect our business and financial condition. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are currently capped at 100 percent of average manufacturer price, but, effective January 1, 2024, this cap will be lifted, which could adversely affect our rebate liability.

Legislative and regulatory proposals that have recently been considered include, among other things, proposals to limit the terms of patent litigation settlements with generic sponsors, to define certain conduct around patenting and new product development as unfair competition, to address the scope of orphan drug exclusivity and to facilitate the importation of drugs into the U.S. from other countries. Legislative and regulatory proposals to reform the regulation of the pharmaceutical industry and reimbursement for pharmaceutical drugs are continually changing, and all such considerations may adversely affect our business and industry in ways that we cannot accurately predict.

There is also ongoing activity related to health care coverage. The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers. These changes impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment-for-performance initiatives. Further, federal policy makers have taken and are expected to continue to try to take steps towards expanding health care coverage beyond the Affordable Care Act, which could have ramifications for the pharmaceutical industry. Additional legislative changes, regulatory changes, or guidance could be adopted, which may impact the marketing approvals and reimbursement for our products and product candidates. For example, there has been increasing legislative, regulatory, and enforcement interest in the U.S. with respect to drug pricing practices. There have been several Congressional inquiries and proposed and enacted federal and state legislation and regulatory initiatives designed to, among other things, bring more transparency to product pricing, evaluate the relationship between pricing and manufacturer patient programs, and reform government healthcare program reimbursement methodologies for drug products beyond the changes enacted by the IRA.

If new 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 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 Xywav and Xyrem, most recently in January 2022, and there is no guarantee that we will make similar price adjustments to Xywav and Xyrem in the future or that price adjustments we have taken or may take in the future will not negatively affect Xywav or Xyrem sales volumes and revenues. We also have made and may in the future make price adjustments 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 Xywav and Xyrem, limit the commercial opportunities for our products and/or negatively impact revenues from sales of our products.

If we become the subject of any government investigation or U.S. Congressional oversight 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 example, in July 2022, we received a subpoena from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to Xyrem and U.S. Patent No. 8,772,306 ("Method of Administration of Gamma Hydroxybutyrate with Monocarboxylate Transporters"), product labeling changes for Xyrem, communications with FDA and the U.S. Patent and Trademark Office, pricing of Xyrem, and other related documents. For more information, see the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products*" in this Part II, Item 1A.

We expect that legislators, policymakers and healthcare insurance funds in Europe will continue to propose and implement cost-containing measures to keep healthcare costs down; particularly due to the financial strain that the COVID-19 pandemic has placed on their healthcare systems and the volatile economic environment brought about by the ongoing military conflict in Ukraine and Russia's curtailment of energy supplies. These measures could include limitations on the prices we will be able to charge for our products or the level of reimbursement available for these products from governmental authorities or third party payors as well as clawbacks and revenue caps. Further, an increasing number of European and other foreign

countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

In addition 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 or equivalent obligation imposed in a European or other foreign country, patient registry requirements or labeling restrictions;
- the prevalence of the disease or condition for which the product is approved and its diagnosis;
- the efficacy of the product in regular use;
- the severity of side effects and other risks in relation to the benefits of our products;
- unanticipated serious adverse events;
- acceptance by physicians and patients of each product as a safe and effective treatment;
- availability of sufficient product inventory to meet demand;
- physicians' decisions relating to treatment practices based on availability of product;
- perceived clinical superiority and/or advantages over alternative treatments;
- overcoming negative publicity surrounding illicit use of
    - GHB or
    - cannabinoid and marijuana products

  and the view of patients, law enforcement agencies, physicians and regulators of our products as being the same or similar to illicit products;
- relative convenience and ease of administration;
- with respect to Xywav and Xyrem, physician and patient assessment of the burdens associated with obtaining or maintaining the certifications required under the Xywav and 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 any 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.

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 the supply of manufacturing materials, 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 FDA's current Good Manufacturing Practices, or cGMP, requirements, DEA regulations and equivalent rules and regulations prescribed by non-U.S. regulatory authorities. If we or any of our suppliers encounter manufacturing, quality or compliance difficulties with respect to any of our products, whether due to the ongoing military conflict in Ukraine and related sanctions imposed against Russia (including as a result of disruptions of global shipping, the transport of products, energy supply, cybersecurity incidents and banking systems as well as of our ability to control input costs) or otherwise, 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, we could be subject to enforcement

action by regulatory authorities for our failure to comply with cGMP with respect to the products we manufacture in our facilities as well as for our failure to adequately oversee compliance with cGMP by any of our third party suppliers operating under contract. Moreover, failure to comply with applicable legal and regulatory requirements subjects us and our suppliers to possible 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.

We have a manufacturing and development facility in Athlone, Ireland where we manufacture Xywav and Xyrem, a manufacturing plant in Villa Guardia, Italy where we produce the defibrotide drug substance and a manufacturing and development facility in the U.K. at Kent Science Park, where we produce Epidiolex/Epidyolex and Sativex and have capability to develop product candidates. We currently do not have our own commercial manufacturing or packaging capability for our other products, their APIs or product candidates outside of those developed at Kent Science Park. As a result, our ability to develop and supply products in a timely and competitive manner depends primarily on third party suppliers being able to meet our ongoing commercial and clinical trial needs for API, other raw materials, packaging materials and finished products.

In part due to the limited market size for our products and product candidates, we have a single source of supply for most of our marketed products, product candidates and their APIs. Single sourcing puts us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties. 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. FDA and similar international or national regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and certain packaging materials used in our products. 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.

We are responsible for the manufacture and supply of Sativex to our collaboration partners and for the manufacture and supply of Epidiolex/Epidyolex and other cannabinoid product candidates for commercial use and for use in clinical trials. The manufacturing of Epidiolex/Epidyolex and our product candidates necessitates compliance with Good Manufacturing Practice, or GMP, and other regulatory requirements in jurisdictions internationally. Our ability to successfully manufacture Epidiolex/Epidyolex and other cannabinoid product candidates involves cultivation of botanical raw material from specific cannabinoid plants, extraction and purification processes, manufacture of finished products and labeling and packaging, which includes product information, tamper evidence and anti-counterfeit features, under tightly controlled processes and procedures. In addition, we must ensure chemical consistency among our batches, including clinical batches and, if approved, marketing batches. Demonstrating such consistency may require typical manufacturing controls as well as clinical data. We must also ensure that our batches conform to complex release specifications. We have a second site at which we can grow the specific cannabinoid plants that produce the CBD used in Epidiolex/Epidyolex, a second site at which we can extract CBD from botanical raw material and a second site at which we can crystallize the purified CBD from the liquid plant extract. A number of our product candidates (excluding Epidiolex/Epidyolex) consist of a complex mixture manufactured from plant materials, and because the release specifications may not be identical in all countries, certain batches may fail release testing and not be able to be commercialized. If we are unable to manufacture Epidiolex/Epidyolex or other product candidates in accordance with regulatory specifications, including GMP or if there are disruptions in our manufacturing process due to damage, loss or otherwise, or failure to pass regulatory inspections of our manufacturing facilities, we may not be able to meet current demand or supply sufficient product for use in clinical trials, and this may also harm our ability to commercialize Epidiolex/Epidyolex and our product candidates on a timely or cost-competitive basis, if at all. Our manufacturing program requires significant time and resources and may not be successful, may lead to delays, interruptions to supply or may prove to be more costly than anticipated.

Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. There have been batch failures due to mechanical, component, raw materials and other issues in the production of Vyxeos, and batches have been produced that have otherwise not been in compliance with applicable specifications. We are continuing to work with Baxter and others to address manufacturing complexities related to Vyxeos. 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, our sales of 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.

Rylaze drug substance is manufactured by AGC Biologics at its facility in Copenhagen, Denmark and the drug product is manufactured and packaged by Patheon at its facility in Greenville, North Carolina. Both sites have ample capacity to support forecast demand and we have secured supply for more than one year's forecast demand. To successfully manufacture Rylaze, the manufacturer must have an adequate master and working cell bank. If we fail to obtain a sufficient supply of Rylaze in

accordance with applicable specifications on a timely basis, our sales of Rylaze, our future maintenance and potential growth of the market for this product, our competitive advantage over competing products that have supply constraints, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

In addition, in order to conduct our ongoing and any future clinical trials of, complete marketing authorization submissions for, and potentially launch our other product candidates, we also need to have sufficient quantities of product manufactured.

Moreover, to obtain approval from FDA or a similar international or national regulatory body of any product candidate, we or our suppliers for that product must obtain approval by the applicable regulatory body to manufacture and supply product, in some cases based on qualification data provided to the applicable body as part of our regulatory submission. Any delay in generating, or failure to generate, data required in connection with submission of the chemistry, manufacturing and controls portions of any regulatory submission could negatively impact our ability to meet our anticipated submission dates, and therefore our anticipated timing for obtaining FDA or similar international or national regulatory body approval, or our ability to obtain regulatory approval at all. In addition, any failure of us or a supplier to obtain approval by the applicable regulatory body 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.

If the effects of the COVID-19 pandemic become more severe and begin to impact supply of manufacturing materials or essential distribution systems such as general delivery services, or require us or our suppliers to again cease or restrict operations at our respective manufacturing facilities, we could experience disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of our products, which would adversely impact our ability to generate sales of our approved products and our business, financial condition, results of operations and growth prospects would be materially adversely affected. For example, supply chain interruptions and shortage of construction materials could lead to delays and rising costs associated with our planned construction project at our commercial manufacturing facility in the U.K. at Kent Science Park. In addition, energy prices have spiked recently due to global macro-economic issues, which has directly impacted CO2 prices and availability. CO2 is a critical raw material for manufacturing our cannabinoid products. Further, energy price rises have also increased costs many other areas of manufacturing and supply in recent months and these could worsen in future periods.

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 approvals for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.

The testing, manufacturing and marketing of our products require regulatory approvals, including approval from FDA and similar bodies in Europe and other countries. If FDA, the European Medicines Agency, or EMA, or the competent authorities of the EU member states or other European countries 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. Our inability to obtain and maintain regulatory approval for our product candidates in the U.S. and internationally and to successfully commercialize new products that are approved would prevent us from receiving a return on our investments and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Even if we receive regulatory approval of a product, regulatory authorities may impose significant labeling restrictions or requirements, including limitations on the dosing of the product, requirements around the naming or strength of a product, restrictions on 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 or equivalent obligation imposed in a European or other foreign country to ensure that the benefits of the drug outweigh the risks. FDA requires a REMS and a boxed warning for Xywav and Xyrem, and similar restrictions could be imposed on other products in the future. Our receipt of approval for narrower indications than sought, restrictions on marketing through a REMS or equivalent obligation imposed in a European or other foreign country, or significant labeling restrictions or requirements in an approved label such as a boxed warning, could have a negative impact on our ability to recoup our research and development costs and to successfully commercialize that product, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Regulatory authorities may also impose post-marketing obligations as part of their approval, which may lead to additional costs and burdens associated with commercialization of the product and may pose a risk to maintaining approval of the product. We are subject to certain post-marketing requirements and commitments in connection with the approval of certain of our products, including Epidiolex, Defitelio, Vyxeos, Rylaze and Zepzelca. These post-marketing requirements and commitments include satisfactorily conducting multiple post-marketing clinical trials and safety studies. For example, FDA granted

accelerated approval to Zepzelca for relapsed SCLC based on data from a Phase 2 trial, which approval is contingent upon verification and description of clinical benefit in a post-marketing clinical trial. We and our licensor PharmaMar are committed to the further study of lurbinectedin, both as a single agent and in combination, and have reached agreement with FDA regarding a confirmatory clinical development program. Our inability to confirm its clinical benefit could result in the withdrawal of approval of Zepzelca, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. With respect to FDA's and EC's approvals of Epidiolex/Epidyolex, we are subject to certain post-marketing requirements. Failure to comply with these post-marketing requirements could result in withdrawal of our marketing approvals for Epidiolex/Epidyolex and/or other civil or criminal penalties. In any event, if we are unable to comply with our post-marketing obligations imposed as part of the marketing approvals in the U.S., the EU, or other countries, our approval may be varied, suspended or revoked, product supply may be delayed and our sales of our products could be materially adversely affected.

We are pursuing activities related to the development of additional 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 Ligand Pharmaceuticals Incorporated, or Ligand. We developed Rylaze, a recombinant Erwinia asparaginase product for the treatment of patients with ALL and LBL who have hypersensitivity to E. coli-derived asparaginase, under our Ligand agreement. We also have clinical development efforts in a variety of other areas, including those focused on expanding the potential of Epidiolex, Vyxeos, Rylaze and Xywav, as well as clinical development efforts focused on suvecaltamide (JZP385) for the treatment of essential tremor and JZP150 for post-traumatic stress disorder. Epidiolex has been administered only to a limited number of patients and in limited populations in clinical trials. While FDA and EC granted approval of Epidiolex/Epidyolex based on the data included in GW's NDA, supplemental NDA and marketing authorization application, we do not know whether the results will be consistent with those resulting from administration of the drug to a large number of patients. New data relating to Epidiolex/Epidyolex, including from adverse event reports and post-marketing studies in the U.S. and Europe, and from other ongoing clinical trials, may result in changes to the product label and/or imposition of a REMS and may adversely affect sales, or result in withdrawal of Epidiolex/Epidyolex from the market. FDA, EMA and regulatory authorities in other jurisdictions may also consider the new data in reviewing Epidiolex/Epidyolex marketing applications for indications other than our approved uses in other jurisdictions or impose additional post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales of Epidiolex/Epidyolex. 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 transactions.

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. However, we may be unable to identify or consummate suitable acquisition or in-licensing opportunities, and this inability could impair our ability to grow our business. Other companies, many of which may have substantially greater financial, sales and marketing resources, compete with us for these opportunities. 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.

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. Further, while we seek to mitigate risks and liabilities of potential acquisitions and in-licensing transactions through, among other things, due diligence, there may be risks and liabilities that such due diligence efforts fail to discover, that are not disclosed to us, or that we inadequately assess. Any failure in identifying and managing these risks, liabilities and uncertainties effectively, could have a material adverse effect on our business, results of operations and financial condition. In addition, product and product candidate acquisitions, particularly when the acquisition takes the form of a merger or other business consolidation such as our acquisition of GW, have required, and any similar future transactions also will require, significant efforts and expenditures, including with respect to transition and integration activities. We may encounter unexpected difficulties, or incur substantial costs, in connection with potential acquisitions and similar transactions, which include:

- the need to incur substantial debt and/or engage in dilutive issuances of equity securities to pay for acquisitions;
- the need to comply with regulatory requirements, including in some cases clearance from the Federal Trade Commission;
- 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 integrating acquired products and product candidates into our portfolio;
- the difficulties in assimilating employees and corporate cultures;
- the failure to retain key managers and other personnel;
- 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.

As a result of these or other factors, products or product candidates we acquire, or obtain licenses to, may not produce the revenues, earnings or business synergies that we anticipated, may not result in regulatory approvals, and may not perform as expected. Failure to manage effectively our growth through acquisitions or in-licensing transactions could adversely affect our growth prospects, business, results of operations and financial condition.

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 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. If FDA determines that the safety or efficacy data included in any marketing application we submit do not warrant marketing approval for the affected product or product candidate, we may be required to conduct additional preclinical studies or clinical trials, which could be challenging to perform, costly and time-consuming. Even if we believe we have successfully completed testing, FDA or any equivalent non-U.S. regulatory agency may determine our data is not sufficiently compelling to warrant marketing approval for the indication(s) sought, if at all, and may require us to engage in additional clinical trials or provide further analysis which may be costly and time-consuming. 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 FDA or an equivalent 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:

- direct and indirect impacts of the evolving effects of the COVID-19 pandemic on various aspects and stages of the clinical development process, including the inherent limitations of remote and virtual approaches, and interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel, quarantines or social distancing protocols imposed or recommended by federal or state governments, employers and others;
- difficulty identifying, recruiting or enrolling eligible patients, often based on the number of clinical trials, particularly with enrollment criteria targeting the same patient population, and in rare diseases with small patient populations;
- 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;
- failure of our clinical trials and clinical investigators, including contract research organizations or other third parties assisting us with clinical trials, to satisfactorily perform their contractual duties, meet expected deadlines and comply with FDA and other regulatory agencies' requirements, including good clinical practices;
- unforeseen safety issues;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites; or
- insufficient funds to complete the trials.

In some jurisdictions such as the EU, initiating phase 3 clinical trials and clinical trials in the pediatric population is subject to a requirement to obtain approval or a waiver from the competent authorities of the EU member states and/or the EMA. If we do not obtain such approval our ability to conduct clinical trials and obtain marketing authorizations or approvals may be severely impaired and our business may be adversely impacted.

Our ability to recruit and retain patients and principal investigators and site staff who, as health care providers, may have heightened exposure to COVID-19, may adversely impact our clinical trial operations. In light of the evolving effects of the COVID-19 pandemic, we have taken measures to implement remote and virtual approaches, including remote data monitoring where possible, to maintain patient safety and trial continuity and to preserve study integrity. To date we have seen some COVID-19-related impact to our mid- and late-stage clinical trial activity causing delays in site initiation, including due to staffing shortages at trial sites. We could also see an impact on the ability to supply study drug, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority employee resources or otherwise. In addition, we rely on contract research organizations or other third parties to assist us with clinical trials, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the evolving effects of the COVID-19 pandemic. If these effects become more severe, we could experience significant disruptions to our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects. In addition, some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services.

Risks Related to the GW Acquisition

We may not realize the anticipated benefits from the GW Acquisition.

On May 5, 2021, we completed the acquisition of GW. The success of the acquisition will depend, in part, on our ability to realize the anticipated benefits from successfully combining our and GW's historical businesses and the integration of our business practices and operations with GW's so that we can fully realize the anticipated benefits of the acquisition. Epidiolex and the other products and technologies acquired may not be successful or grow at the same rate as if our companies operated independently or they may require significantly greater resources and investments than originally anticipated. For example, in the third quarter of 2022, we recorded a $133.6 million asset impairment charge as a result of the decision to discontinue our nabiximols program. We have assessed the nabiximols program's potential to support regulatory approval for MS-related spasticity in the U.S., as well as in the context of our broader pipeline opportunities, and have made the decision to discontinue the program. As a result, the anticipated benefits of the acquisition may not be realized fully or may take longer to realize or cost more than expected, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Risks Related to Our Intellectual Property

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

Our commercial success depends in part on obtaining, 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 degree of protection to be afforded by our proprietary rights is difficult to predict 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 fall outside the exclusive rights granted 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;
- our patents covering certain aspects of our products or the distribution thereof could be delisted from FDA's publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” or Orange Book, as a result of challenges by third parties before FDA or the courts;
- 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.

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. The legal systems of certain countries, particularly certain developing countries, may lack maturity or consistency when it comes to the enforcement of patents and other intellectual property rights, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

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 portfolio. Any patent may be challenged, and potentially invalidated or held unenforceable, including through patent litigation or through administrative procedures that permit challenges to patent validity. Patents can also be circumvented, potentially including by an ANDA or Section 505(b)(2) application that avoids infringement of our intellectual property.

In June 2021, we received notice from Lupin that it has filed with FDA an ANDA for a generic version of Xywav. The notice from Lupin included a “paragraph IV certification” with respect to ten of our patents listed in FDA’s Orange Book for Xywav on the date of our receipt of the notice. A paragraph IV certification is a certification by a generic applicant that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product.

On July 28, 2021, we filed a patent infringement suit against Lupin in the United States District Court for the District of New Jersey. The complaint alleges that by filing its ANDA, Lupin has infringed ten of our Orange Book listed patents. We are seeking a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patents. As a result of this lawsuit, we expect that a stay of approval of up to 30 months will be imposed by FDA on Lupin's ANDA. In June 2021, FDA recognized seven years of Orphan Drug Exclusivity for Xywav through July 21, 2027. On October 4, 2021, Lupin filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents.

In April 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On May 11, 2022, we filed an additional lawsuit against Lupin in the United States District Court for the District of New Jersey alleging that by filing its ANDA, Lupin infringed the newly-issued patent related to a method of treatment when Xywav is administered concomitantly with certain other medications. The suit seeks a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patent.

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 (and in certain cases, an authorized generic version of Xyrem) in advance of the expiration of the last of our patents. Notwithstanding our Xyrem patents and settlement agreements, additional third parties may also attempt to introduce generic versions of Xyrem, Xywav 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. Such third parties 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 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 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 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.

On May 13, 2021, we filed a patent infringement suit against Avadel and several of its corporate affiliates in the United States District Court for the District of Delaware. The suit alleges that Avadel's product candidate FT218 will infringe five of our patents related to controlled release formulations of oxybate and the safe and effective distribution of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe these patents, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents. Avadel filed a motion for partial judgment on the pleadings on its counterclaim that one of our patents should be delisted from the Orange Book. The Court scheduled a hearing on that motion for November 15, 2022.

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 also currently rely on trade secret protection for several of our products, including Defitelio, and product candidates. Trade secret protection does not protect information or inventions if another party develops that information or invention independently, and establishing that a competitor developed a product through trade secret misappropriation rather than through legitimate means may be difficult to prove. 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. Moreover, if a dispute arises with our employees, consultants, advisors or partners over the ownership of rights to inventions, including jointly developed intellectual property, we could lose patent protection or the confidentiality of our proprietary information, and possibly also lose the ability to pursue the development of 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 successfully 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 process, or IPR, or a post grant review 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 through a proceeding before the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office.

There is a risk that a court 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. In addition, the PTAB may invalidate a patent, as happened with six of our patents covering the Xywav and Xyrem REMS, which were invalidated through the IPR process. 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.

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). The U.S. Congress and state legislatures have also identified pharmaceutical patent litigation settlements as potential impediments to generic competition and have introduced, and in states like California passed, legislation to regulate them. Third party payors have also challenged such settlements on the grounds that they increase drug prices. Because there is currently no precise legal standard with respect to the lawfulness of such settlements, many pharmaceutical companies, including us, have faced extensive litigation over whether patent litigation settlements they have entered into are reasonable and lawful. From June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with Hikma and other ANDA filers violate state and federal antitrust and consumer protection laws. For additional information on these lawsuits, see Note 10, Commitments and Contingencies-Legal Proceedings of the Notes to the Condensed Consolidated Financial Statements included in this Quarterly Report on Form 10-Q. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs in the class action complaints were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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 patent 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, 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. 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.

If we were found to infringe upon a patent or other intellectual property right, or if we failed to obtain or renew a license under a patent or other intellectual property right from a third party, or if a third party that we were licensing technologies from was found to infringe upon a patent or other intellectual property rights of another third party, we may be required to pay damages, including damages of up to three times the damages found or assessed, if the infringement is found to be willful, suspend the manufacture of certain products or reengineer or rebrand our products, if feasible, or we may be unable to enter certain new product markets. Litigation, whether filed by us or against us, can be expensive and time consuming to defend and divert management’s attention and resources. Our competitive position could suffer as a result. In addition, if we have declined or failed to enter into a valid assignment agreement for any reason, we may not own the invention or our intellectual property, and our products may not be adequately protected.

With respect to our products and product candidates targeting rare indications, relevant regulatory exclusivities such as orphan drug exclusivity or pediatric exclusivity may not be granted or, if granted, may be limited.

The first NDA applicant with an Orphan Drug Designation for a particular active moiety to treat a specific disease or condition that receives FDA approval is usually entitled to a seven-year exclusive marketing period in the U.S. for that drug, for that indication. We rely in part on this Orphan Drug Exclusivity and other regulatory exclusivities to protect Xywav, Epidiolex, Zepzelca, Defitelio, Vyxeos and, potentially, our other products and product candidates from competitors, and we expect to continue relying in part on these regulatory exclusivities in the future. The duration of our regulatory exclusivity period could be impacted by a number of factors, including FDA’s later determination that our request for orphan designation was materially defective, that the manufacturer is unable to supply sufficient quantities of the drug, that the extension of the exclusivity period established by the Improving Regulatory Transparency for New Medical Therapies Act does not apply, or the possibility that we are unable to successfully obtain pediatric exclusivity. There is no assurance that we will successfully obtain Orphan Drug Designation for other products or product candidates or other rare diseases or that a product candidate for which we receive Orphan Drug Designation will be approved, or that we will be awarded orphan drug exclusivity upon approval as, for example, FDA may reconsider whether the eligibility criteria for such exclusivity have been met and/or maintained. Moreover, a drug product with an active moiety that is different from that in our drug candidate or, under limited circumstances, the same drug product, may be approved by FDA for the same indication during the period of marketing exclusivity. The limited

circumstances include a showing that the second drug is clinically superior to the drug with marketing exclusivity through a demonstration of superior safety or efficacy or that it makes a major contribution to patient care. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for the same indication before us, approval of our product candidate would be blocked during the period of marketing exclusivity unless we could demonstrate that our product candidate is clinically superior to the approved product. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for a different orphan indication, this may negatively impact the market opportunity for our product candidate. There have been legal challenges to aspects of FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, including whether two drugs are the same drug product, and future challenges could lead to changes that affect the protections potentially afforded our products in ways that are difficult to predict. In a successful legal challenge, a court invalidated FDA's denial of orphan exclusivity to a drug on the grounds that the drug was not proven to be clinically superior to a previously approved product containing the same ingredient for the same orphan use. In response to the decision, FDA released a policy statement stating that the court's decision is limited just to the facts of that particular case and that FDA will continue to require the sponsor of a designated drug that is the "same" as a previously approved drug to demonstrate that its drug is clinically superior to that drug upon approval in order to be eligible for orphan drug exclusivity, or in some cases, to even be eligible for marketing approval. In the future, there is the potential for legislative changes or additional legal challenges to FDA's orphan drug regulations and policies, and it is uncertain how such challenges might affect our business.

In the European Union, if a marketing authorization is granted for a medicinal product that is designated an orphan drug, that product is entitled to ten years of marketing exclusivity. We rely in part on this orphan drug exclusivity and other regulatory exclusivities to protect Epidyolex, Vyxeos and Defitelio. During the period of marketing exclusivity, subject to limited exceptions, no similar medicinal product may be granted a marketing authorization for the orphan indication. There is no assurance that we will successfully obtain Orphan Drug Designation for future rare indications or orphan exclusivity upon approval of any of our product candidates that have already obtained designation. Even if we obtain orphan exclusivity for any product candidate, the exclusivity period can be reduced to six years if at the end of the fifth year it is established that the orphan designation criteria are no longer met or if it is demonstrated that the orphan drug is sufficiently profitable that market exclusivity is no longer justified. Further, a similar medicinal product may be granted a marketing authorization for the same indication notwithstanding our marketing exclusivity if we are unable to supply sufficient quantities of our product, or if the second product is safer, more effective or otherwise clinically superior to our orphan drug. In addition, if a competitor obtains marketing authorization and orphan exclusivity for a product that is similar to a product candidate we are pursuing for the same indication, approval of our product candidate would be blocked during the period of orphan marketing exclusivity unless we could demonstrate that our product candidate is safer, more effective or otherwise clinically superior to the approved product.

Other Risks Related to Our Business and Industry

Changes in the market for directors and officers liability insurance could make it more difficult and more expensive for us to obtain directors and officers liability insurance.

In recent years, the market for directors and officers liability insurance for biopharmaceuticals and life sciences companies has changed in ways adverse to us. The premiums charged for such policies have generally increased and the terms of such policies have generally become less favorable. As a result, it is currently expensive and may become significantly more expensive for us to maintain directors and officers liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. In any event, there can be no assurance that directors and officers liability insurance will be adequate to cover our potential liabilities or will be generally available to us in the future or, if available, that the cost of such insurance will be commercially justifiable. The increased cost and decreased availability of directors and officers liability insurance could make it more difficult for us to attract and retain qualified persons to serve on our board of directors or as executive officers, and could also make it more difficult and more expensive for us to negotiate and consummate future corporate development transactions, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our business is currently adversely affected and could be materially and adversely affected in the future by the evolving effects of the COVID-19 pandemic and related global economic slowdown, including with respect to our commercialization efforts, clinical trial activity, research and development activities, supply chain and corporate development activities and other business operations.

The COVID-19 pandemic continues to have a significant impact on the global healthcare delivery system. Many healthcare systems have had to restructure operations to prioritize caring for COVID-19 patients and limit or cease other activities. The severe burden on healthcare systems caused by this pandemic has impaired the ability to diagnose and treat patients with non-COVID-19 related conditions and impaired the ability of many clinical research sites to start new studies,

enroll new patients and monitor patients in clinical trials. Health care provider offices and institutions have experienced workforce disruption, including the inability to hire staff and challenges maintaining appropriate staffing. The lack of access to health care providers has caused, and may continue to cause, delays in appropriate diagnosis, treatment and ongoing care for some patients, which could subsequently impact prescribing and use of our products. The evolving effects of the COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as significant reductions in business related activities have occurred, supply chains have been disrupted, and manufacturing and clinical development activities have been curtailed or suspended.

Continued remote work policies, quarantines, shelter-in-place and similar government orders, shutdowns or other restrictions on the conduct of business operations related to the effects of the COVID-19 pandemic may materially and adversely affect our business, our ability to generate sales of our approved products, our supply chain, regulatory, clinical development and corporate development activities. With respect to our commercialization activities, the COVID-19 pandemic restrictions continue to have some negative impact on demand, new patient starts and treatments for our products. Due to the nature of the pandemic, we are not able to accurately predict the duration or extent of these impacts on demand for our products. Beginning in March 2020, we transitioned our field-based sales, market access, reimbursement and medical employees out of the field and suspended work-related travel and in-person customer interactions. We utilized technology to continue to engage healthcare professionals and other customers virtually to support patient care. As the effects of the pandemic have evolved from 2020 to 2022, some clinics and institutions began to allow in-person interactions pursuant to local health authority and government guidelines. The level of renewed in-person engagement varies by account, region and country and may be adversely impacted in the future as a result of the continuing impact of the COVID-19 pandemic. The limits on full in-person interactions have had a negative impact on our ability to effectively communicate product benefits to physicians, limiting their awareness and understanding and use of our products.

For Xywav and Xyrem, COVID-19 protocols and staffing shortages at sleep labs across the U.S. have resulted in reduced access to sleep testing. The decline in prescribers' ability to diagnose new narcolepsy patients has resulted in an overall decline in new patients starting on therapy. Although patient persistence and compliance with oxybate therapy remained steady during recent quarters, we continue to expect that delays in obtaining a narcolepsy diagnosis could have a negative impact on new Xywav and Xyrem patient enrollments in future quarters. We also anticipate that pricing and reimbursement reviews by certain European regulatory authorities may take longer in certain countries due to the pandemic, which could delay growth prospects for Vyxeos and Epidyolex in those EU member states.

We have also seen an upward trend in demand for patient assistance programs. Depending on the ultimate duration and severity of the COVID-19 pandemic and the extent of a global economic slowdown, widespread unemployment and resulting loss of employer-sponsored insurance coverage or other market dynamics, we may experience an increasing shift from commercial payor coverage to government payor coverage or increasing demand for patient assistance and/or free drug programs, which could adversely affect net product sales.

In addition, the COVID-19 pandemic has resulted in significant volatility in the global financial markets. If this volatility persists and deepens, we could experience an inability to access additional capital or our liquidity could otherwise be impacted, which could in the future negatively affect our capacity for certain corporate development transactions or our ability to make other important, opportunistic investments. In addition, the current recession or additional market corrections resulting from the impact of the evolving effects of the COVID-19 pandemic could materially affect our business and the value of our ordinary shares. While we expect these effects to adversely affect our business operations and financial results, the extent of the impact on our ability to generate sales of our approved products, execute on new product launches, our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time. Such developments include continued spread of variants with increased transmissibility, the ultimate duration and severity of the pandemic, governmental "stay-at-home" orders and travel restrictions, quarantines, social distancing and business closure requirements in the U.S., Ireland and other countries, and the effectiveness of vaccination programs and other actions taken globally to contain and treat the disease. These effects could materially and adversely affect our business, financial condition, results of operations and growth prospects, as further described in the risks and uncertainties described elsewhere in this ''Risk Factors'' section.

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 offices in multiple locations, including the U.S., the U.K., Italy and Canada. We may further expand our international operations into other countries in the future, either organically or by acquisition. Conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including:

- the diverse regulatory, financial and legal requirements in the countries where we are located or do business, and any changes to those requirements;

- the impact of Brexit on trade relations between the EU and the U.K.;
- challenges inherent in efficiently managing employees and commercial partners 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;
- additional exposure to foreign currency exchange risk from non-U.S. operations; and
- public health risks, such as the COVID-19 pandemic and potential related effects on supply chain, travel and employee health and availability.

In addition, there can be no guarantee that we will effectively manage the increasing, global complexity of our business 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 U.K.'s withdrawal from the EU, commonly referred to as Brexit, could increase our cost of doing business, reduce our gross margins or otherwise negatively impact our business and our financial results.

Brexit continues to create uncertainty concerning the future relationship between the U.K. and the EU, following the U.K. withdrawal from the EU in January 2020. We have a commercial manufacturing facility in the U.K. at Kent Science Park, and multiple offices in England. Since a significant portion of the regulatory framework in the U.K. is derived from EU laws, Brexit continues to impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the U.K. or the EU. In this regard, in December 2020, the EU and U.K. reached an agreement in principle on the framework for their future relationship, the EU-U.K. Trade and Cooperation Agreement, or TCA. Among the changes that have had a direct impact are that Great Britain (England, Scotland and Wales) is now treated as a "third country," a country that is not a member of the EU and whose citizens do not enjoy the EU right to free movement. Northern Ireland continues to follow many aspects of the EU regulatory rules, particularly in relation to trade in goods. As part of the TCA, the EU and the U.K. will recognize GMP inspections carried out by the other party and the acceptance of official GMP documents issued by the other party. The TCA also encourages, although it does not oblige, the parties to consult one another on proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The U.K. has unilaterally agreed to accept EU batch testing and batch release for a period of at least 2 years until January 1, 2023. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the U.K. must be retested and re-released when entering the EU market for commercial use. As it relates to marketing authorizations, Great Britain has introduced a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland, however, continues to be covered by the marketing authorizations granted by the EC. Therefore, our medicine candidates require a separate marketing authorization for Great Britain, which involves additional administrative burden. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could prevent us from or delay us commercializing our medicine candidates in the U.K. and/or the European Economic Area, or EEA, and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the U.K. and/or EEA for our medicine candidates, which could harm our business. In addition, the EU's regulatory environment for clinical trials has been harmonized as part of the Clinical Trials Regulation from January 31, 2022, but it is currently unclear as to what extent the U.K. will seek to align its regulations with the EU. Failure of the U.K. to closely align its regulations with the EU may have an effect on the cost of conducting clinical trials in the U.K. as opposed to other countries and/or make it harder to seek a marketing authorization for our medicine candidates in the EEA on the basis of clinical trials conducted in the U.K. In the short term there is a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective U.K. and EU customs agencies that may delay time-sensitive shipments and may negatively impact our product supply chain. All of these changes could increase our costs and otherwise adversely affect our business.

Significant disruptions of information technology systems or data security breaches could adversely affect 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 data. 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, and those of our vendors, 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 and our vendors 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, including in our remote work environment as a result of the COVID-19 pandemic, 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 data), 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 data, including personal data 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 data. This 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.

We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and 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. 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 Xywav and 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 conduct or 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. FDA, the competent authorities of the EU member states on behalf of the EMA, and the competent authorities of other European countries, also periodically inspect our records related to safety reporting. 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.

Defibrotide, Vyxeos, Rylaze, Epidyolex and Sativex are available on a named patient basis or through a compassionate use process 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. Any failure to maintain revenues from sales of products 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 an adverse effect on our business, financial condition, results of operations and growth prospects.

FDA, the competent authorities of the EU member states and other European countries, 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. A determination that we have promoted an approved product for off-label uses could subject us 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 and/or civil or criminal penalties that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

Other Regulatory Authorities

We are also subject to regulation by other regional, national, state and local agencies, including the DEA, the DOJ, the FTC, the United States Department of Commerce, the Office of Inspector General of the U.S. Department of Health and Human Services, or OIG, 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 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. These laws are described in “Business—Government Regulation” in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2021. 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 available statutory exceptions and regulatory safe harbors whenever possible, and otherwise comply with applicable laws, regulations or guidance, 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. For example, in November 2020, the OIG issued a Special Fraud Alert to highlight certain inherent fraud and abuse risks associated with speaker fees, honorariums and expenses paid by pharmaceutical and medical device companies to healthcare professionals participating in company-sponsored events. The Special Fraud Alert sent a clear signal that speaker programs will be subject to potentially heightened enforcement scrutiny.

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 or violations of the federal anti-kickback statute. 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.

On July 11, 2022, we received a subpoena from the U.S. Attorney’s Office for the District of Massachusetts requesting documents related to Xyrem and U.S. Patent No. 8,772,306 (“Method of Administration of Gamma Hydroxybutyrate with Monocarboxylate Transporters”), product labeling changes for Xyrem, communications with FDA and the U.S. Patent and Trademark Office, pricing of Xyrem, and other related documents. We are cooperating with this investigation. We are unable to predict how long this investigation will continue or its outcome, but it is possible that we will incur significant costs in connection with the investigation, regardless of the outcome. We may also become subject to similar investigations by other state or federal governmental agencies. The investigation by the U.S. Attorney’s Office and any additional investigations or litigation related to the subject matter of this investigation may result in damages, fines, penalties or administrative sanctions against us, negative publicity or other negative actions that could harm our reputation, reduce demand for Xyrem and/or reduce coverage of Xyrem, including by federal health care programs and state health care programs. If any or all of these events occur, our business and stock price could be materially and adversely affected.

Public reporting under the Physician Payment Sunshine Act, or Sunshine provisions, and other similar state laws, the requirements of which are discussed in "Business—Government Regulation" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2021, has resulted in increased scrutiny of the financial relationships between industry, teaching hospitals, physicians and other health care providers. Such scrutiny may negatively impact our ability to engage with physicians and other health care providers 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. 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, and administrative penalties, damages or fines.

We have various programs to help patients access our products, including patient assistance programs, which include co-pay coupons for certain of our products, assistance to 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, and some states have imposed restrictions on manufacturer co-pay programs when therapeutic equivalents are available. 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 issued guidance for how pharmaceutical manufacturers can lawfully 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. In April 2019, we finalized our civil settlement agreement with the DOJ and OIG and 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. Although we have structured our programs to follow available guidance and the requirements of our corporate integrity agreement, 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, or 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 of our patient assistance programs or other business practices, which could result in damages, fines, penalties, exclusion from participation in federal health care programs or other criminal, civil or administrative sanctions or enforcement actions, as well as negative publicity, reduction in demand for, or patient access to, our products and/or reduced 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 U.K. Bribery Act of 2010, or the U.K. Bribery Act. 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, the U.K. Bribery Act and equivalent national laws in other countries. As an example, recently the U.S. Securities and Exchange Commission and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. Violation of these laws by us or our suppliers and other third party agents for which we may be liable 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.

Outside the U.S., interactions between pharmaceutical companies and physicians are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

We are also subject to federal, state, national and international laws and regulations governing the privacy and security of health related and other personal data we collect and maintain (e.g., Section 5 of the Federal Trade Commission Act, the California Consumer Privacy Act, or CCPA, and the EU's General Data Protection Regulation, or GDPR). These laws and regulations are evolving and subject to interpretation, and may impose limitations on our activities or otherwise adversely affect our business. Because of the remote work policies we implemented due to the COVID-19 pandemic, information that is normally protected, including company confidential information, may be less secure. Cybersecurity and data security threats continue to evolve and raise the risk of an incident that could affect our operations or compromise our business information or sensitive personal data, including health data. We may also need to collect more extensive health-related information from our employees to manage our workforce. If we or our third party partners fail to comply or are alleged to have failed to comply with applicable data protection and privacy laws and regulations, and related employment rules, or if we were to experience a data breach involving personal data, we could be subject to government enforcement actions or private lawsuits. In addition, 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. For example, in July 2020, the Court of Justice of the European Union, or the Court of Justice, declared the EC's privacy shield framework between the EU and U.S. was invalid, which could adversely impact our ability to transfer personal data from the EU to the U.S. or otherwise may cause us to incur significant costs to do so legally. The Court of Justice further ruled that in order to transfer data outside of the EU, under the existing mechanism known as the Standard Contractual Clauses, or SCCs, the importing country's level of protection must be adequate. If the level of protection in the U.S. or any other importing country is called into question under the SCCs, this could further impact our ability to transfer data outside of the EU or Switzerland. In March 2022, the EC and the U.S. announced that they have agreed in principle on a new Trans-Atlantic Data Privacy Framework, as a successor arrangement to the EU-U.S. Privacy Shield. The two sides are now expected to finalize the details of this agreement in principle and translate it into legal texts that will form the basis of a draft adequacy decision to be proposed by the EC.

Furthermore, following the U.K.'s exit from the EU, the U.K. became a third country to the EU in terms of personal data transfers. The EC has adopted an Adequacy Decision concerning the level of personal data protection in the U.K. under which personal data may now flow freely from the EU to the U.K. However, personal data transfers from the EU to the U.K. may nevertheless be at a greater risk than before because the Adequacy Decision may be suspended.

In addition, numerous other federal, state, national and international laws and regulations govern the privacy and security of the personal data we collect and maintain, including data breach notification laws, state health information and/or genetic privacy laws, federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act, and the CCPA), and laws outside of the United States that may apply to us, such as the GDPR and other country laws. Many of these laws and regimes, across countries but even within the United States, differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Compliance with these laws is difficult, constantly evolving, and time consuming. International regulators, federal regulators, state attorneys general, and plaintiffs' attorneys, including class action attorneys, have been and will likely continue to be active in this space.

In California, the CCPA establishes certain requirements for data use and sharing transparency and creates new data privacy rights for California residents. The CCPA and its implementing regulations have already been amended multiple times since their enactment, including by the California Privacy Rights Act, or CPRA. The CPRA introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency, or CPPA. The amendments introduced by the CPRA go into effect on January 1, 2023, and new implementing regulations are expected to be introduced by the CPPA. Failure to comply with the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with certain types of incidents. These claims may result in significant liability and damages. Other states, including Virginia, Colorado, Utah, and Connecticut have enacted similar privacy laws that impose new obligations or limitations in areas affecting our business and we continue to assess the impact of these state legislation, on our business as additional information and guidance becomes available. These laws and regulations are evolving and subject to interpretation, and may impose limitations on our activities or otherwise adversely affect our business. Similarly, there are legislative proposals in the EU, the U.S. at the federal level as well as in other jurisdictions that could impose new obligations or limitations in areas affecting our business. In addition, some countries are considering or have passed legislation implementing data protection or privacy requirements or requiring local storage and processing of data or similar requirements that could increase the cost and complexity of delivering our services and research activities. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws.

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses, as well as their "business associates" – certain persons or covered entities that create, receive, maintain, or transmit protected health information in connection with providing a specified service or performing a function on behalf of a covered entity. Although we are not directly subject to HIPAA, we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

The FTC also sets expectations for failing to take appropriate steps to keep consumers' personal information secure, or failing to provide a level of security commensurate to promises made to individual about the security of their personal information (such as in a privacy notice) may constitute unfair or deceptive acts or practices in violation of Section 5(a) of the Federal Trade Commission Act, or FTC Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. With respect to privacy, the FTC also sets expectations that companies honor the privacy promises made to individuals about how the company handles consumers' personal information; any failure to honor promises, such as the statements made in a privacy policy or on a website, may also constitute unfair or deceptive acts or practices in violation of the FTC Act. While we do not intend to engage in unfair or deceptive acts or practices, the FTC has the power to enforce promises as it interprets them, and events that we cannot fully control, such as data breaches, may be result in FTC enforcement. Enforcement by the FTC under the FTC Act can result in civil penalties or enforcement actions.

If we or our third party partners fail to comply or are alleged to have failed to comply with these or other applicable data protection and privacy laws and regulations, or if we were to experience a data breach involving personal data, we could be subject to government enforcement actions or private lawsuits. Any associated claims, inquiries, or investigations or other government actions could lead to unfavorable outcomes that have a material impact on our business including through significant penalties or fines, monetary judgments or settlements including criminal and civil liability for us and our officers and directors, increased compliance costs, delays or impediments in the development of new products, negative publicity, increased operating costs, diversion of management time and attention, or other remedies that harm our business, including orders that we modify or cease existing business practices.

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

We participate in the Medicaid Drug Rebate Program, the 340B program, the U.S. Department of Veterans Affairs, Federal Supply Schedule, or FSS, pricing program, and the Tricare Retail Pharmacy program, and have obligations to report the average sales price for certain of our drugs to the Medicare program. All of these programs are described in more detail 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, 2021. For calendar quarters beginning January 1, 2022, manufacturers will need to start reporting the average sales price for drugs under the Medicare program regardless of whether they are enrolled in the Medicaid Drug Rebate Program. In addition, starting in 2023, manufacturers must pay refunds to Medicare for single source drugs or biologicals, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Statutory or regulatory changes or guidance from the Centers for Medicare & Medicaid Services, or CMS, could affect the average sales price calculations for our products and the resulting Medicare payment rate and could negatively impact our results of operations. Further, starting in January 2023, the IRA establishes a Medicare Part B inflation rebate scheme, under which, generally speaking, manufacturers will owe rebates if the average sales price of a Part B drug increases faster than the pace of inflation. Failure to timely pay a Part B inflation rebate is subject to a civil monetary penalty.

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, which can change and evolve over time. 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 generally 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 and give rise to an obligation to refund entities participating in the 340B program for overcharges during past quarters impacted by a price recalculation.

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, 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. CMS could also decide to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS to be incomplete or incorrect. Moreover, once the refund program for

discarded drug takes effect in 2023, manufacturers that fail to pay refunds could be subject to civil monetary penalties of 125 percent of the refund amount.

Our failure to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental programs could negatively impact our financial results. CMS issued a final regulation, which became effective in April 2016, to implement the changes to the Medicaid Drug Rebate Program under the Affordable Care Act. In December 2020, CMS issued a final regulation that modified prior Medicaid Drug Rebate Program regulations to permit reporting multiple best price figures with regard to value-based purchasing arrangements; and to provide definitions for "line extension," "new formulation," and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula. While the regulatory provisions that purported to affect the applicability of the best price and average manufacturer price exclusions of manufacturer-sponsored patient benefit programs, in the context of pharmacy benefit manager "accumulator" programs were invalidated by a court, such programs may continue to negatively affect us in other ways. Regulatory and legislative changes, and judicial rulings relating to the Medicaid Drug Rebate Program and related policies (including coverage expansion), have increased and will continue to increase our costs and the complexity of compliance, have 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 or another agency challenges the approach we take in our implementation. Rebates are currently capped at 100 percent of average manufacturer price, but, effective January 1, 2024, this cap will be lifted.

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 in January 2019. Implementation of this regulation could affect our obligations and potential liability under the 340B program in ways we cannot anticipate. We are also required to report the 340B ceiling prices for our covered outpatient drugs to HRSA, which then publishes them to 340B covered entities. Any charge by HRSA that we have violated this regulation or other requirements of the program could negatively impact our financial results. Moreover, HRSA newly established an administrative dispute resolution, or ADR, process under a final regulation effective January 2021, for claims by covered entities that a manufacturer engaged in overcharging, including claims that a manufacturer limited the ability of a covered entity to purchase the manufacturer's drugs at the 340B ceiling price, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. This ADR regulation has been challenged in separate litigation instituted by PhRMA and by pharmaceutical manufacturers in multiple federal courts. Also, a public notice published in December 2021 by the Office of Management and Budget revealed that HRSA intends to propose a new ADR rule to replace the ADR rule which became effective in January 2021 and that this new rule will propose new requirements and procedures for the 340B program's ADR process. Under the ADR final rule which became effective in January 2021, an ADR proceeding could potentially subject us to discovery by covered entities and other onerous procedural requirements and could result in additional liability. HRSA could also decide to terminate a manufacturer's agreement to participate in the 340B program for a violation of that agreement or other good cause shown, in which case the manufacturer's covered outpatient drugs may no longer be eligible for federal payment under the Medicaid or Medicare Part B program.

Further, legislation may be introduced that, if passed, would, among other things, modify the requirements of the 340B program.

Medicare Part D generally provides coverage to enrolled Medicare patients for self-administered drugs (*i.e.*, drugs that are not administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and, subject to detailed program rules and government oversight, each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time to time. The prescription drug plans negotiate pricing with manufacturers and pharmacies and may condition formulary placement on the availability of manufacturer discounts. In addition, manufacturers, including us, are currently required to provide to CMS a 70% discount on brand name prescription drugs utilized by Medicare Part D beneficiaries when those beneficiaries are in the coverage gap phase of the Part D benefit design. Civil monetary penalties could be due if we fail to offer discounts to beneficiaries under the Medicare Part D coverage gap discount program. The IRA sunsets the coverage gap discount program starting in 2025 and replaces it with a new manufacturer discount program. In addition, starting in October 2022, the IRA establishes a Medicare Part D inflation rebate scheme, under which, generally speaking, manufacturers will owe additional rebates if the average manufacturer price of a Part D drug increases faster than the pace of inflation. Failure to timely pay a Part D inflation rebate is subject to a civil monetary penalty.

The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be capped by reference to, among other things, a specified non-federal average manufacturer price starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and/or a civil monetary penalty. This or any other legislative change could

impact the market conditions for our products. We further expect continued scrutiny on government price reporting from Congress, agencies, and other bodies.

Pursuant to applicable law, knowing provision of false information in connection with price reporting under the U.S. Department of Veterans Affairs, FSS or Tricare Retail Pharmacy, or Tricare, 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.

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 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 FDA, the EC 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 FDA, the EC or the competent authorities of the EU member states could lead to product liability lawsuits as well.

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. 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.

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 Ireland, the U.K. and Italy where we have manufacturing facilities. If an accident or contamination involving pollutants or hazardous substances 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 with sufficient coverage on acceptable terms, or at all. 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.

Risks Related to Controlled Substances

Xyrem and Xywav are controlled substances and certain product candidates we are developing may be subject to U.S. federal and state controlled substance laws and regulations, and our failure to comply with these laws and regulations, or the cost of compliance with these laws and regulations, could materially and adversely affect our business, results of operations, financial condition and growth prospects.

Xyrem and Xywav and certain product candidates we are developing contain controlled substances as defined in the CSA. Controlled substances are subject to a number of requirements and restrictions under the CSA and implementing regulations, including certain registration, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V substances.

Schedule I substances by definition have a high potential for abuse, no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. which contain a controlled substance are listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Schedule I and II drugs are subject to the strictest controls under the CSA, including manufacturing and procurement quotas, heightened security requirements and additional criteria for importation. In addition, dispensing of Schedule II drugs is restricted. For example, they may not be refilled without a new prescription.

Drug products approved for medical use by FDA that contain cannabis or cannabis extracts may be controlled substances and will be rescheduled to Schedules II-V after approval, or, like Epidiolex, removed completely from the schedules by operation of other laws.

Individual states have also established controlled substance laws and regulations. Though state-controlled substances laws often mirror federal law, they may separately schedule our products or our product candidates as well. We or our partners may also be required to obtain separate state registrations, permits or licenses in order to be able to manufacture, distribute, administer or prescribe controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

U.S. facilities conducting research, manufacturing, distributing, importing or exporting, or dispensing controlled substances must be registered (licensed) to perform these activities and must comply with the security, control, recordkeeping and reporting obligations under the CSA, DEA regulations and corresponding state requirements. DEA and state regulatory bodies conduct periodic inspections of certain registered establishments that handle controlled substances. Obtaining and maintaining the necessary registrations and complying with the regulatory obligations may result in delay of the importation, manufacturing, distribution or clinical research of our commercial products and products candidates. Furthermore, failure to maintain compliance with the CSA and DEA and state regulations by us or any of our contractors, distributors or pharmacies can result in regulatory action that could have a material adverse effect on our business, financial condition and results of operations. DEA and state regulatory bodies may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could lead to criminal penalties.

Schedule I and II substances are subject to DEA's annual manufacturing and procurement quota requirements. The annual quota allocated to us or our contract manufacturers for the active ingredients in our products may not be sufficient to complete clinical trials or meet commercial demand. Consequently, any delay or refusal by the DEA in establishing our, or our contract manufacturers', procurement and/or production quota for controlled substances could delay or stop our clinical trials or product launches, which could have a material adverse effect on our business, results of operations, financial condition and growth prospects.

Some of our cannabinoid product candidates are currently controlled substances, the use of which may generate public controversy.

Some of our product candidates derived from botanical marijuana contain controlled substances, their regulatory approval may generate public controversy. Political and social pressures and adverse publicity could lead to challenges in the approval of, and increased expenses for, our product candidates. These pressures could also limit or restrict the introduction and marketing of our product candidates. Adverse publicity from cannabis misuse or adverse side effects from cannabis or other cannabinoid products may adversely affect the commercial success or market penetration achievable by our cannabinoid product candidates. The nature of our business attracts a high level of public and media interest, and in the event of any resultant adverse publicity, our reputation may be harmed.

Our ability to research, develop and commercialize Epidiolex/Epidyolex and certain of our product candidates is dependent on our ability to maintain licenses relating to the cultivation, possession and supply of botanical cannabis, a controlled substance.

Our cannabinoid research and manufacturing facilities are located exclusively in the U.K. In the U.K., licenses to cultivate, possess and supply cannabis for medical research are granted by the Home Office on an annual basis. Although the Home Office has renewed our licenses each year since 1998, it may not do so in the future, in which case we may not be in a position to carry on our research and development program in the U.K. In addition, we are required to maintain our existing commercial licenses to cultivate, produce and supply cannabis. However, if the Home Office were not prepared to renew such licenses, we would be unable to manufacture and distribute our products on a commercial basis in the U.K. or beyond. In order to carry out research in countries other than the U.K., similar licenses to those outlined above are required to be issued by the relevant authority in each country. In addition, we will be required to obtain licenses to export from the U.K. and to import into the recipient country. To date, we have obtained necessary import and export licenses to over 30 countries. Although we have

an established track record of successfully obtaining such licenses as required, this may change in the future, which could materially and adversely affect our business, results of operations, financial condition and growth prospects.

Controlled substance legislation differs between countries and legislation in certain countries may restrict or limit our ability to sell Epidyolex and certain of our product candidates.

Most countries are parties to the Single Convention on Narcotic Drugs 1961, which governs international trade and domestic control of narcotic substances, including cannabis extracts. Countries may interpret and implement their treaty obligations in a way that creates a legal obstacle to our obtaining regulatory approval for Epidyolex and certain of our product candidates in those countries. These countries may not be willing or able to amend or otherwise modify their laws and regulations to permit Epidyolex or certain of our product candidates to be marketed, or achieving such amendments to the laws and regulations may take a prolonged period of time. In the case of countries with similar obstacles, we would be unable to market Epidyolex and certain of our product candidates in countries in the near future or perhaps at all if the laws and regulations in those countries do not change.

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, and our business would be adversely affected if we are unable to service our debt obligations.

As of September 30, 2022, we had total indebtedness of approximately $5.8 billion. Our substantial indebtedness may:

- limit our ability to use our cash flow or borrow additional funds for working capital, capital expenditures, acquisitions, investments 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, or our ability to take specified actions to take advantage of certain business opportunities that may be presented to us;
- expose us to the risk of increased interest rates as certain of our borrowings, including borrowings under the credit agreement, are at variable rates of interest;
- result in dilution to our existing shareholders in the event exchanges of our 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.

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 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. In addition, if we are unable to repay amounts under our secured credit agreement or senior secured notes, the credit agreement lenders and note holders could proceed against the collateral granted to them to secure that debt, which would seriously harm our business.

Covenants in our credit agreement and indenture governing our senior secured notes 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 credit agreement and the indenture governing our senior secured notes contain 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;
- pay dividends or distributions or redeem or repurchase capital stock;
- prepay, redeem or repurchase certain debt;
- make loans, investments, acquisitions (including certain acquisitions of exclusive licenses) and capital expenditures;
- enter into agreements that restrict distributions from our subsidiaries;
- enter into transactions with affiliates;
- enter into sale and lease-back transactions;

- sell, transfer or exclusively license certain assets, including material intellectual property, and capital stock of our subsidiaries; and
- consolidate or merge with or into, or sell substantially all of our assets to, another person.

If we undergo a change of control triggering event, we would be required to make an offer to purchase all of the senior secured notes at a purchase price in cash equal to 101% of their principal amount, plus accrued and unpaid interest, subject to certain exceptions. If we engage in certain asset sales, we will be required under certain circumstances to make an offer to purchase the senior secured notes at 100% of the principal amount, plus accrued and unpaid interest.

The credit agreement also includes certain financial covenants that require us to maintain a maximum secured leverage ratio and a minimum interest coverage ratio as long as we have drawn funds under the revolving credit facility (or letters of credit in excess of $50 million have been issued and remain undrawn).

As a result of these restrictions, we may be:

- limited in how we conduct our business;
- unable to raise additional debt or equity financing to operate during general economic or business downturns; or
- unable to compete effectively, take advantage of new business opportunities or grow in accordance with our plans.

Our failure to comply with any of the covenants could result in a default under the credit agreement and the indenture governing our senior secured notes, which, if not cured or waived, could result in us having to repay our borrowings before their due dates. Such default may allow the lenders or the note holders to accelerate the related debt and may result in the acceleration of any other debt to which a cross-acceleration or cross-default provision applies. If we are forced to refinance these borrowings on less favorable terms or if we were to experience difficulty in refinancing the debt prior to maturity, our results of operations or financial condition could be materially affected. In addition, an event of default under the credit agreement may permit the lenders to refuse to permit additional borrowings under the revolving credit facility or to terminate all commitments to extend further credit under the revolving credit facility. Furthermore, if we are unable to repay the amounts due and payable under the credit agreement or senior secured notes, the lenders and note holders may be able to proceed against the collateral granted to them to secure that indebtedness. In the event our lenders or note holders accelerate the repayment of such borrowings, we cannot assure you that we will have sufficient assets to repay such indebtedness.

Moreover, our failure to repurchase our senior secured notes or our exchangeable senior notes at a time when the repurchase is required by the indentures governing our senior secured notes and our exchangeable senior notes or to pay any cash payable on future exchanges of our exchangeable senior notes as required by the indenture governing our exchangeable senior notes, would constitute a default under those indentures.

A default under the indentures governing our exchangeable senior notes could also lead to a default under other debt agreements or obligations, including the credit agreement and indenture governing the senior secured notes. Likewise, a default under the credit agreement or senior secured notes could lead to a default under other debt agreements or obligations, including the indentures governing our exchangeable senior notes.

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 and grow our business.

The scope of our business and operations has grown substantially, including through a series of business combinations and acquisitions. 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. 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. Our ability to raise additional capital may be adversely impacted by worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures, the COVID-19 pandemic or otherwise. In addition, under Irish law we must have authority from our shareholders to issue any ordinary shares, including ordinary shares that are part of our authorized but unissued share capital, and we currently have such authorization. Moreover, as a matter of Irish law, when an Irish public limited company issues ordinary shares to new shareholders for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders on a pro-rata basis, unless this statutory pre-emption obligation is dis-applied, or opted-out of, by approval of its shareholders. At our annual general meeting of shareholders in July 2022, our shareholders voted to approve our proposal to dis-apply the statutory pre-emption obligation on terms that are substantially more limited than our general pre-emption opt-out authority that had been in effect prior to August 4, 2021. This current pre-emption opt-out authority is due to expire in December 2023. If we are unable to obtain further pre-emption authorities from our shareholders in the future, or otherwise continue to be limited by the terms of new pre-emption authorities approved by our shareholders in the future, our ability to use our unissued share capital to fund in-licensing, acquisition or other business opportunities, or to otherwise raise capital, could be adversely

affected. In any event, an inability to borrow or raise additional capital in a timely manner and on attractive terms could prevent us from expanding our business or taking advantage of acquisition opportunities and could otherwise have a material adverse effect on our business and growth prospects. 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 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 and are subject to an impairment analysis whenever events or changes in circumstances indicate the carrying amount of the asset may not be recoverable. Additionally, goodwill and indefinite-lived assets are subject to an impairment test at least annually. Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. For example, in the third quarter of 2022, we recorded a $133.6 million asset impairment charge as a result of the decision to discontinue our nabiximols program. 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.

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 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. 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, which could adversely affect our operating results. Although we utilize foreign exchange forward contracts to manage currency risk primarily related to certain intercompany balances denominated in non-functional currencies, our efforts to manage currency risk may not be successful.

Changes in our effective tax rates 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, the U.K. 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 changes to or differences in interpretation of tax laws. For example, our income tax expense for the year ended December 31, 2021 included an expense of $259.9 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory tax rate in the U.K. following enactment of the U.K. Finance Act 2021.

We are subject to reviews and audits by the U.S. Internal Revenue Service, 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 additional taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our products or seek to raise additional funds. Any of these actions could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

Although we are incorporated in Ireland, the IRS may assert that we should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal tax purposes pursuant to Section 7874 of the 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 when the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company were combined in a merger transaction in January 2012, or 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 could 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 affiliates' ability to use their net operating losses and carryforward tax losses to offset potential taxable income is limited under applicable law and could be subject to further limitations if we do not generate taxable income in a timely manner or if certain "ownership change" provisions of applicable law result in further 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 use U.S. tax attributes such as net operating losses, or NOLs, to offset U.S. taxable income resulting from certain transactions. 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 in 2022 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 before they expire, 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 also depends on our ability to generate future income that is taxable in the U.S. before the NOLs expire. 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 limitations under the "ownership change" provisions of Sections 382 and 383 of the Code and similar state provisions. Additionally, U.K. carryforward tax losses may become subject to limitations in the event of certain changes in the ownership interest of significant shareholders where there is also a major change in the nature of conduct of a trade or business within a specified period of time. These limitations may cause us to lose or forfeit additional NOLs or carryforward tax losses before we can use these attributes. Subsequent ownership changes and changes to the U.S. federal or state or U.K. tax rules with respect to the use of NOLs and carryforward tax losses may further affect our ability to use these losses in future years.

Changes to 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," or BEPS. Many countries have implemented or begun to implement legislation and other guidance to align their international tax rules with the OECD's BEPS recommendations. In addition, the OECD has been working on an extension of the BEPS project, referred to as BEPS 2.0, focusing on (1) global profit allocation and (2) a global minimum tax rate. In particular, the OECD has released a framework proposal reflecting the agreement of over 140 jurisdictions, including Ireland, to implement a global minimum tax rate of 15% for large multinational corporations on a jurisdiction-by-jurisdiction basis by 2023. The EU is currently proposing implementation of this global minimum tax rate for its member states by the start of 2024. 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.

Further, on August 16, 2022, President Biden signed the IRA into law, which, among other things, introduced new tax provisions, including a 15 percent corporate alternative minimum tax for certain large corporations, and a one percent excise tax on certain share repurchases by publicly traded corporations, including certain repurchases by specified domestic affiliates of publicly traded foreign corporations. These provisions will be effective for 2023. The IRS has not yet issued guidance on the corporate alternative minimum tax, the excise tax and many of the other provisions in the IRA. We are currently evaluating the effect, if any, of the new law on our financial results. The U.S. and other jurisdictions in which we operate continue to consider other changes in tax laws that apply to multinationals which, if enacted, could adversely impact our tax provision, cash tax liability and effective tax rate.

A substantial portion of our indebtedness bears interest at variable interest rates based on 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, or FCA, 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. FCA also announced that certain of the commonly used USD LIBOR tenors will continue to be published until June 30, 2023; however, the Federal Reserve, Federal Deposit Insurance Corporation and the Office of the Comptroller of Currency in the U.S. as well as the FCA announced that all market participants should stop using LIBOR in new contracts after December 31, 2021, subject to limited exemptions for loans and derivative products. Accordingly, new contracts entered into after December 31, 2021, must utilize an alternative reference rate. Our credit agreement is 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. Furthermore, 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 is likely to continue to be volatile in the future, and the value of your investment could decline significantly.

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, which has resulted in decreased market prices, notwithstanding the lack of a fundamental change in the underlying business models of those companies. Worsening economic conditions and other adverse effects or developments may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. The market price for 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 in this “Risk Factors” section.

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.

In addition, the market price of our ordinary shares may decline if the effects of our acquisition of GW and other strategic transactions 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 our exchangeable senior notes who may view our 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 our 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, mergers, amalgamations and acquisitions, takeovers and shareholder lawsuits. 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, our credit agreement and the indentures governing our senior secured notes and 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. In addition to our articles of association, several mandatory provisions of Irish law could prevent or delay an acquisition of us. 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,

our credit agreement limits our ability to enter into certain fundamental changes, and the indentures governing our senior secured notes and exchangeable senior notes require us to offer to repurchase such notes for cash if we undergo certain fundamental changes. Additionally, in certain circumstances, the indentures governing our exchangeable senior notes require us to increase the exchange rate for a holder of our exchangeable senior notes in connection with a fundamental change. A takeover of us may trigger a default under the credit agreement or the requirement that we offer to purchase our senior secured notes or exchangeable senior notes and/or increase the exchange rate applicable to our exchangeable senior notes, which could make it more costly for a potential acquirer 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.

Future sales and issuances of our ordinary shares, securities convertible into our ordinary shares or rights to purchase ordinary shares or convertible securities could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to decline.

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. To the extent we raise additional capital by issuing equity securities or securities convertible into or exchangeable for ordinary shares, our shareholders may experience substantial dilution. We may sell ordinary shares, and we may sell convertible or exchangeable securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell such ordinary shares, convertible or exchangeable securities or other equity securities in subsequent transactions, existing shareholders may be materially diluted.

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

We do not currently plan to pay cash dividends in the foreseeable future. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, compliance with the terms of the credit agreement and the indenture governing our senior secured notes, 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.

General Risk Factors

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, including our executive management team. In addition, changes we make to our current and future work environments may not meet the needs or expectations of our employees or may be perceived as less favorable compared to other companies' policies, which could negatively impact our ability to hire and retain qualified personnel, whether in a remote or in-office environment. The loss of services and institutional knowledge of one or more additional members of our executive management team or other key personnel could delay or prevent the successful completion of some of our vital activities and may negatively impact our operations and future growth. We do not carry "key person" insurance. In addition, changes in our organization as a result of executive management transition may have a disruptive impact on our ability to implement our strategy. Until we integrate new personnel, and unless they are able to succeed in their positions, we may be unable to successfully manage and grow our business. In any event, if we are unable to attract, retain and motivate quality individuals, or if there are delays, or if we do not successfully manage personnel and executive management transitions, our business, financial condition, results of operations and growth prospects could be adversely affected.

Our business and operations could be negatively affected if we become subject to shareholder activism or hostile bids, 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. Stock price declines may also increase our vulnerability to unsolicited approaches. If we become the subject of certain forms of shareholder activism, such as proxy contests or hostile bids, 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.

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

Issuer Purchases of Equity Securities

In November 2016, our board of directors authorized a share repurchase program and as of September 30, 2022 had authorized the repurchase of ordinary shares having an aggregate purchase price of up to $1.5 billion, exclusive of any brokerage commissions. Under this program, which has no expiration date, we may repurchase ordinary shares from time to time on the open market. During the three months ended September 30, 2022, we did not repurchase any of our ordinary shares. In the nine months ended September 30, 2022, we spent a total of $0.1 million to purchase 338 of our ordinary shares under the share repurchase program at a total purchase price, including commissions, of $160.70 per share. All ordinary shares repurchased were canceled. As of September 30, 2022, the remaining amount authorized under the share repurchase program was $431.2 million.

Under our share repurchase program, we are authorized to repurchase shares from time to time through open market repurchases. Such repurchases may be pursuant to Rule 10b-18 or Rule 10b5-1 agreements as determined by our management and in accordance with the requirements of the Securities and Exchange Commission.

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).
2.10‡	Transaction Agreement, dated as of February 3, 2021, by and among Jazz Pharmaceuticals UK Holdings Limited, Jazz Pharmaceuticals Public Limited Company and GW 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 February 4, 2021).
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 April 29, 2021, among Jazz Securities Designated Activity Company, the guarantors party thereto, U.S. Bank National Association, as trustee and acknowledged by U.S. Bank National Association, as collateral trustee. (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 April 29, 2021).
4.2B	Form of 4.375% Senior Notes due 2029 (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 April 29, 2021).
4.2C	First Supplemental Indenture, dated as of July 21, 2021, among GW Pharmaceuticals Limited, GW Global Services (International) Limited, GW Pharma Limited, GW Research Limited, GW UK Services Limited and Greenwich Biosciences, Inc., Jazz Securities Designated Activity Company, and U.S. Bank National Association, as trustee under the Indenture, dated as of April 29, 2021.
10.1#	Settlement Agreement, dated as of April 5, 2017, by and between Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited, and Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC.

10.2#	Clinical and Commercial Manufacturing and Supply Agreement, dated as of December 22, 2010, between Celator Pharmaceuticals, Inc. and Baxter Oncology GmbH.
10.3#	Amendment No. 1 Clinical and Commercial Manufacturing and Supply Agreement, dated as of January 18, 2018, by and between Jazz Pharmaceuticals Ireland Limited and Baxter Oncology GmbH.
10.4	Amendment No. 6, dated as of August 24, 2022, to Pharmacy Master Services Agreement, dated as of July 1, 2020, by and between Jazz Pharmaceuticals, Inc. and Express Scripts Specialty Distribution Services, Inc.
10.5	Amendment No. 7, dated as of September 28, 2022, to Pharmacy Master Services Agreement, dated as of July 1, 2020, by and between Jazz Pharmaceuticals, Inc. and Express Scripts Specialty Distribution Services, Inc.
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
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

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† Confidential treatment has been granted for portions of this exhibit (indicated by "[*]"). Omitted portions have been filed separately with the SEC.

‡ Certain portions of this exhibit have been omitted pursuant to Item 601(b)(2) of Regulation S-K.

Portions of this document (indicated by "[*]") have been omitted pursuant to Item 601(b)(10) of Regulations S-K because they are both not material and are the type that the Company treats as private and confidential.

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

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: November 9, 2022

JAZZ PHARMACEUTICALS PUBLIC LIMITED COMPANY
(Registrant)

/s/ Bruce C. Cozadd

Bruce C. Cozadd

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

/s/ Renée Galá

Renée Galá

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

/s/ Patricia Carr

Patricia Carr

Senior Vice President, Chief Accounting Officer
(Principal Accounting Officer)

Exhibit 10.1

CERTAIN PORTIONS OF THIS EXHIBIT (INDICATED BY [*]) HAVE BEEN EXCLUDED PURSUANT TO ITEM 601(B)(10) OF REGULATION S-K BECAUSE THEY ARE BOTH NOT MATERIAL AND ARE THE TYPE THAT THE COMPANY TREATS AS PRIVATE AND CONFIDENTIAL.

Execution Copy Confidential

SETTLEMENT AGREEMENT

This Settlement Agreement (collectively with Exhibits A through C, **"Settlement Agreement"**) is made and entered into as of the 5th day of April, 2017 (the **"Execution Date"**) by and between, on the one hand, Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited (collectively, **"Jazz,"** or each separately, a "**Jazz Party**"), and on the other hand, Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC (collectively, **"Roxane,"** or each separately, a "**Roxane Party**") (collectively, the **"Parties,"** or each separately, a **"Party"**).

RECITALS

WHEREAS, Jazz owns the Licensed Patents covering XYREM® brand 500 mg/mL sodium oxybate oral solution, a pharmaceutical product which is sold in the Territory under NDA No. 21-196;

WHEREAS, pursuant to ANDA No. 202090, Roxane has sought and obtained marketing authorization from the FDA to Market a generic sodium oxybate oral solution 500 mg/mL product indicated for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy in the United States;

WHEREAS, actions for patent infringement are pending in the United States District Court for the District of New Jersey (the **"Court"**) in relation to the Roxane ANDA and the proposed generic product set forth therein, captioned *Jazz Pharmaceuticals, Inc. v. Roxane Laboratories, Inc.*, Civil Action No. 10-6108, *Jazz Pharmaceuticals, Inc., et al. v. Roxane Laboratories, Inc.*, Civil Action No. 15-1360, and *Jazz Pharmaceuticals, Inc. v. Roxane Laboratories, Inc., et al.*, Civil Action No. 16-4971 (collectively with any related proceedings, the **"Actions"**); and

WHEREAS, the Parties are willing to settle the Actions on the terms set forth in this Settlement Agreement.

NOW THEREFORE, in consideration of the promises and mutual covenants set forth herein, the sufficiency of which is hereby acknowledged, the Parties hereby agree as follows.

The capitalized terms in this Settlement Agreement are defined in Exhibit C.

1. Dismissal of the Actions.

In consideration of the mutual benefits of entering into this Settlement Agreement, the Parties shall enter into and cause to be filed with the Court, within three (3) business days of the Execution Date, a stipulation and order of dismissal substantially in the form annexed hereto as Exhibit A (**"Stipulation and Order of Dismissal"**). If the Court does not grant the Stipulation and Order of Dismissal substantially in the form filed by the Parties, the Parties agree to confer in good faith and revise that document consistent with the terms of this Settlement Agreement and the requirements of the Court. The date upon which the last of the Actions has been dismissed by the Court shall be the "**Effective Date**".

2. License Agreement and AG Agreement.

Contemporaneously with the execution of this Settlement Agreement, Jazz and certain of the Roxane Parties are entering into a license agreement (the **"License Agreement"**) and an authorized generic agreement (the **"AG Agreement"**). Such agreements are being executed contemporaneously herewith and shall be deemed effective on the Effective Date.

3. Legal Fees.

Within three (3) business days of the Effective Date, Jazz shall make a one-time payment of [*] by wire transfer to an account designated by Roxane, in recognition of the savings inuring to Jazz in terms of the avoidance of costs and expenditure of time and resources associated with prosecuting the Actions.

4. Legal Compliance.

The Parties shall submit this Settlement Agreement to the U.S. Federal Trade Commission (**"FTC"**) and the Antitrust Division of the U.S. Department of Justice (the **"DOJ"**) as soon as practicable after the Effective Date and in no event later than ten (10) business days after the Effective Date pursuant to Section 1112(a), Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066, 2461-62 (2003).

5. Released Claims; Covenants. In addition to the dismissal of the Actions, as set forth in the Stipulation and Order of Dismissal, each Party shall make the following releases, which shall be effective upon the Effective Date.

(a) Each Roxane Party, for itself and its Affiliates, and each of their respective successors, hereby releases and forever discharges each Jazz Party and each of its Affiliates and each of their respective representatives, shareholders, members, trustees, officers, directors, managers, employees, agents, attorneys, partners, divisions, distributors, suppliers, manufacturers, customers, REMS administrators and REMS vendors, or any heirs, administrators, executors, predecessors, successors, or assigns of the foregoing, from any and all past and present (on or before the Execution Date) claims, counterclaims, demands, obligations, actions, causes of action, wrongful death claims, rights, damages, liabilities, costs, losses, losses of services, expenses, obligations, and liabilities of any nature whatsoever, whether based on a tort, contract or other theory of recovery, whether known or unknown, that each Roxane Party or any of its Affiliates asserted or could have asserted from any occurrence on or prior to the Execution Date, including without limitation, claims and counterclaims that each Roxane Party or any of its Affiliates in each case asserted or could have asserted in the Actions, or in any judicial, United States Patent and Trademark Office (**"USPTO"**), or any other legal proceeding relating to any or all of the Licensed Patents, asserting that any or all of the Licensed Patents are unenforceable, unpatentable, invalid or not infringed by the filing of the Roxane ANDA and/or Roxane's manufacture, use, sale, offer for sale or importation of the Roxane Generic Product in the Territory (all of the above, collectively, "**Roxane's Released Claims**"). For clarity, Roxane's Released Claims do not preclude Roxane from asserting any claim arising in connection with this Settlement Agreement, the AG Agreement (including any agreement

contemplated thereby, such as a supply agreement and a services agreement), or the License Agreement.

(b) Each Jazz Party, for itself and its Affiliates, and each of their respective successors, hereby releases and forever discharges each Roxane Party and each of its Affiliates and each of their respective representatives, shareholders, members, trustees, officers, directors, managers, employees, agents, attorneys, partners, divisions, distributors, suppliers, manufacturers, importers, customers, REMS administrators and REMS vendors, or any heirs, administrators, executors, predecessors, successors, or assigns of the foregoing, from any and all past and present (on or before the Execution Date) claims, counterclaims, demands, obligations, actions, causes of action, wrongful death claims, rights, damages, liabilities, costs, losses, losses of services, expenses, obligations, and liabilities of any nature whatsoever, whether based on a tort, contract or other theory of recovery, whether known or unknown, that each Jazz Party or any of its Affiliates asserted or could have asserted from any occurrence on or prior to the Execution Date, including without limitation, claims and counterclaims that each Jazz Party or any of its Affiliates in each case asserted or could have asserted in the Actions, or in any judicial, USPTO, or any other legal proceeding relating to any or all of the Licensed Patents, asserting that any or all of the Licensed Patents are or would be infringed by the filing of the Roxane ANDA and/or Roxane's manufacture, use, sale, offer for sale or importation of the Roxane Generic Product in the Territory (all of the above collectively, **"Jazz's Released Claims"**). Jazz's Released Claims do not preclude Jazz from asserting any or all of the Licensed Patents against: (i) any ANDA or ANDAs other than the Roxane ANDA and/or (ii) any product or products, including a Roxane product, other than the Roxane Generic Product. For clarity, Jazz's Released Claims do not preclude Jazz from asserting any claim arising in connection with this Settlement Agreement, the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement), or the License Agreement.

(c) Subject to the terms of this Settlement Agreement and Roxane's compliance with the terms of the Settlement Agreement, the License Agreement and the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement), each Jazz Party, for itself and its Affiliates, covenants to Roxane that it will not sue, assert any claim or counterclaim against, or otherwise participate in any action or other judicial or legal proceeding against, any Roxane Party or any of its Affiliates or any of their respective representatives, shareholders, members, licensees, sublicensees, trustees, officers, directors, managers, employees, agents, attorneys, partners, divisions, distributors, customers, suppliers, importers, manufacturers, distributors, or insurers, or any patients, physicians, pharmacists, REMS administrators, REMS vendors or other health care providers or entities, or any heirs, administrators, executors, predecessors, successors, or assigns of the foregoing, or cause, assist, or authorize any person or entity to do any of the foregoing, in each case claiming or otherwise asserting that the filing of the Roxane ANDA, the labeling for the Roxane ANDA as of the Execution Date and any Permitted Minor Modifications thereafter, and/or Roxane's manufacture, use, sale, distribution, marketing, offer for sale or importation of the Roxane Generic Product in the Territory infringes the Licensed Patents or any other U.S. patents or patent applications owned, licensed or controlled by a Jazz Party or any of its Affiliates either on the Execution Date or thereafter (the **"Jazz Covenant Not to Sue"**). Jazz shall impose the Jazz Covenant Not to Sue on any Third Party to which any Jazz Party or any of its Affiliates may after the Effective

Date of this Settlement Agreement assign, license or otherwise transfer or grant any rights under any Licensed Patents.

(d) Subject to the terms of this Settlement Agreement and Jazz's compliance with the terms of the Settlement Agreement, the License Agreement and the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement), each Roxane Party, for itself and its Affiliates, covenants to Jazz that it will not sue, assert any claim or counterclaim against, or otherwise participate in any action or in any judicial, USPTO, or other legal proceeding against, any Jazz Party or any of its Affiliates or any of their respective representatives, shareholders, members, licensees, sublicensees, trustees, officers, directors, managers, employees, agents, attorneys, partners, divisions, distributors, customers, suppliers, importers, manufacturers, distributors, or insurers, or any heirs, administrators, executors, predecessors, successors, or assigns of the foregoing, or cause, assist, or authorize any person or entity to do any of the foregoing, in each case claiming or otherwise asserting that any or all of the Licensed Patents are invalid, unpatentable, or unenforceable, or that the filing of the Roxane ANDA and/or Roxane's manufacture, use, sale, offer for sale, or importation of the Roxane Generic Product in the Territory does not or would not infringe valid claims of any or all of the Licensed Patents or any other U.S. patents or patent applications owned, licensed or controlled by a Jazz Party or any of its Affiliates either on the Execution Date or thereafter (the **"Roxane Covenant Not to Sue"**) unless the Licensed Patents or any other U.S. patents or patent applications owned, licensed or controlled by a Jazz Party or any of its Affiliates or assignees or grantees is asserted against a Roxane Party. Each Roxane Party, for itself and each of its Affiliates, further agrees that, except for safety-related reasons or in response to labeling changes effectuated by Jazz after the Execution Date, it will not request labeling for the Roxane Generic Product with "Indications and Usage" and "Dosage and Administration" sections that deviate from the "Indications and Usage" and "Dosage and Administration" labeling sections for the NDA Product as of the Execution Date, unless required to effectuate Permitted Minor Modifications. Each Roxane Party for itself and each of its Affiliates shall impose the Roxane Covenant Not to Sue on any Third Party to which any Roxane Party or any of its Affiliates may after the Effective Date assign, license or otherwise transfer or grant any rights under the Roxane ANDA.

(e) This Settlement Agreement shall constitute a final settlement of the Actions between the Parties, and, except as required by Laws or compelled by legal process, neither any Roxane Party nor any of its respective Affiliates shall assist or cooperate with, or permit any agent or consultant it controls to assist or cooperate with, any Third Party in, or participate in, any litigation before a court, or any Inter Partes review, Covered Business Method review, Post-Grant review, or any other proceeding before the USPTO, or any similar adversarial proceeding against any Jazz Party or any of its Affiliates, or any licensees or sublicensees thereof, involving any product for which Xyrem® is the reference listed drug. Nothing in the foregoing shall be construed as preventing any Roxane Party or any of its Affiliates from assisting or cooperating with any Third Party, or from itself participating in, any action brought by a Jazz Party or any of its Affiliates against the FDA or others (i) pertaining to the safety of the NDA Product or Generic Equivalent, (ii) pertaining to the Xyrem REMS, (iii) with respect to the FDA's issuance of a waiver releasing Roxane and any of its Affiliates from the requirement to participate with any Jazz Party or any of its Affiliates in a single, shared system of Elements to Assure Safe Use

or any subsequent FDA action or step relating thereto, or (iv) pertaining to any REMS program associated with a waiver contemplated by the preceding subclause (iii).

(f) The Parties, and their agents and consultants under their control, shall continue to maintain the confidentiality of any non-public information exchanged between them in the Actions to the extent required by the terms of the Discovery Confidentiality Order in the Actions (if any) or District of New Jersey Local Rule 5.3(b), or any other applicable confidentiality restriction, unless so ordered by the Court or compelled by law or regulation.

(g) Except as provided below in this subsection (g), Roxane agrees that, as of the Effective Date, other than in accordance with all of the terms and conditions of this Settlement Agreement, the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement) and the License Agreement, Roxane will not, directly or indirectly, alone or in cooperation with any other person or entity, make, have made, use, sell, ship or offer to sell, import or distribute, or authorize, permit or solicit others to make, have made, use, sell, ship or offer to sell, import or distribute, or participate in the profits of others arising from, the sale of any Generic Equivalent or any Authorized Generic. Notwithstanding the foregoing, the provisions of this subsection 5(g) shall not be construed as applying to Roxane's ongoing participation in the planning, development, construction, implementation, testing, or any similar activities relating to any separate shared REMS system in accordance with the FDA's approval of Roxane's ANDA and issuance of a waiver from the requirement to participate with any Jazz Party or any of its Affiliates in a single, shared system of Elements to Assure Safe Use; nor shall the provisions of this subsection 5(g) apply to the Roxane Generic Product and/or any Generic Equivalent following the earlier of (A) the date of the expiration of the last to expire of the Licensed Patents, including any extensions and pediatric exclusivities, or (B) the date of a Final Decision that all of the asserted claims of all of the asserted Licensed Patents are invalid and/or unenforceable.

(h) Nothing in this Section 5 (including but not limited to Roxane's Released Claims and/or the Roxane Covenant Not To Sue), or elsewhere in this Settlement Agreement, shall preclude Roxane from: (i) maintaining any Paragraph IV Certification(s) in the Roxane ANDA; (ii) supplementing or amending the Roxane ANDA to include certifications (including Paragraph IV certification(s)) to any patents that may be listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) for Xyrem® after the Effective Date; (iii) challenging the validity, enforceability or infringement of any patent that Jazz or any Jazz Affiliate asserts against Roxane or any Roxane Affiliate in relation to any Roxane product other than the Roxane Generic Product; or (iv) in relation to any Roxane product other than the Roxane Generic Product, making a Paragraph IV certification or otherwise challenging the validity, enforceability or infringement of any patent that Jazz or any Jazz Affiliate lists in the Orange Book in connection with any product other than Xyrem®.

(i) Subject to Roxane's compliance with the terms of this Settlement Agreement, the License Agreement and the AG Agreement, and except as provided below, no Jazz Party or any of its Affiliates shall threaten, commence, pursue, or maintain, or encourage, finance, or otherwise support any Third Party to engage in, any activity (including, but not limited to, the submission of any Citizen Petition(s) or filing of any claim against or involving the FDA) that, if successful, would reasonably be expected to interfere with Roxane's effort or ability to: (1)

obtain or maintain FDA approval for the Roxane ANDA and any associated REMS program; or (2) Market the Roxane Generic Product as provided in the License Agreement. In addition, with respect to Permitted Minor Modifications, Jazz and its Affiliates hereby waive any and all regulatory exclusivities that may inhibit the Marketing of the Roxane Generic Product in the Territory as of the Launch Date, and will, in response to a request from FDA or a commercially reasonable request from Roxane to enable compliance with applicable Laws, submit appropriate and reasonable documentation to FDA to assist Roxane in effectuating the license grants, waivers and covenants contained in the Settlement Agreement, the License Agreement, and the AG Agreement. Nothing in this Settlement Agreement shall be construed as preventing any Jazz Party or any of its Affiliates from assisting or cooperating with any Third Party, or from itself initiating or participating in, any activity (including but not limited to the submission of any Citizen Petition(s) or filing of any claim against or involving the FDA or others), (i) pertaining to the safety of the NDA Product or Generic Equivalent, (ii) pertaining to the Xyrem REMS, (iii) with respect to the FDA's issuance of a waiver releasing Roxane and any of its Affiliates from the requirement to participate with any Jazz Party or any of its Affiliates in a single, shared system of Elements to Assure Safe Use or any subsequent FDA action or step relating thereto, or (iv) pertaining to any REMS program associated with a waiver contemplated by the preceding subclause (iii).

(j) Subject to Roxane's compliance with this Settlement Agreement, the License Agreement and the AG Agreement, and except as provided below, no Jazz Party or any of its Affiliates shall take any action, or have any interaction, with the Drug Enforcement Agency (DEA) that would reasonably be expected to interfere with Roxane's efforts or ability to (1) obtain or maintain FDA approval for the Roxane ANDA and any associated REMS program; or (2) market the Roxane Authorized Generic Product as set forth in the AG Agreement or Roxane Generic Product as set forth in the License Agreement, including but not limited to obtaining DEA quota for sodium oxybate or materials needed for the manufacture of Roxane's ANDA product, provided however that nothing in the foregoing shall be construed as preventing any Jazz Party, or any of its Affiliates, from assisting or cooperating with any Third Party, or from itself initiating or participating in, any action or interaction with the DEA (i) pertaining to the safety of the NDA Product or Generic Equivalent, (ii) pertaining to the Xyrem REMS, (iii) with respect to the FDA's issuance of a waiver releasing Roxane and any of its Affiliates from the requirement to participate with any Jazz Party or any of its Affiliates in a single, shared system of Elements to Assure Safe Use or any subsequent FDA action or step relating thereto, or (iv) pertaining to any REMS program associated with a waiver contemplated by the preceding subclause (iii).

(k) The Parties hereby agree to confer [*] if necessary, for the purpose of discussing in good faith whether there is a reasonable possibility that the AG Launch Date could be accelerated to a date within the three-month period immediately following the Parties' discussion. If the Parties agree there is a reasonable possibility that the AG Launch Date may be so accelerated, Jazz agrees that it will, within [*] of any such discussion, make all necessary filings with the FDA regarding NDA No. 21-196 to amend or modify the Xyrem REMS (as defined in the AG Agreement) for the Roxane Authorized Generic Product to be sold under the Xyrem REMS. If the Parties are not able to reach agreement regarding whether

there is a reasonable possibility that the AG Launch Date may be so accelerated, then either Party shall have the right to submit such matter to the dispute resolution procedures set forth in Exhibit B of this Settlement Agreement. If the Parties do not identify an event that is reasonably likely to accelerate the AG Launch Date by [*], Jazz will make all necessary filings with the FDA regarding NDA No 21-196 to amend or modify the Xyrem REMS (as defined in the AG Agreement) by no later than [*]. Nothing in this subsection (k) should be construed to impede or delay Jazz from making all necessary filings with the FDA regarding NDA No 21-19 to amend or modify the Xyrem REMS (as defined in the AG Agreement) for the Roxane Authorized Generic to be sold under the Xyrem REMS.

6. Acknowledgement and California Civil Code Section 1542 Waiver.

(a) ROXANE ACKNOWLEDGES THAT IT MAY HEREAFTER DISCOVER CLAIMS OR FACTS IN ADDITION TO OR DIFFERENT FROM THOSE WHICH IT NOW KNOWS OR BELIEVES TO EXIST WITH RESPECT TO ROXANE'S RELEASED CLAIMS, THE FACTS AND CIRCUMSTANCES ALLEGED IN THE ACTIONS AND/OR THE SUBJECT MATTER OF THIS SETTLEMENT AGREEMENT, WHICH, IF KNOWN OR SUSPECTED AT THE TIME OF EXECUTING THIS SETTLEMENT AGREEMENT, MAY HAVE MATERIALLY AFFECTED THIS SETTLEMENT AGREEMENT. NEVERTHELESS, UPON THE EFFECTIVENESS OF THE RELEASE OF ROXANE'S RELEASED CLAIMS AS SET FORTH IN SECTION 5 ABOVE, ROXANE HEREBY ACKNOWLEDGES THAT ROXANE'S RELEASED CLAIMS INCLUDE WAIVERS OF ANY RIGHTS, CLAIMS OR CAUSES OF ACTION THAT MIGHT ARISE AS A RESULT OF SUCH DIFFERENT OR ADDITIONAL CLAIMS OR FACTS. ROXANE ACKNOWLEDGES THAT IT UNDERSTANDS THE SIGNIFICANCE AND POTENTIAL CONSEQUENCES OF SUCH A RELEASE OF UNKNOWN UNITED STATES JURISDICTION CLAIMS AND OF SUCH A SPECIFIC WAIVER OF RIGHTS. ROXANE INTENDS THAT THE CLAIMS RELEASED BY IT UNDER THIS RELEASE BE CONSTRUED AS BROADLY AS POSSIBLE TO THE EXTENT THEY RELATE TO UNITED STATES JURISDICTION CLAIMS. ROXANE IS AWARE OF CALIFORNIA CIVIL CODE SECTION 1542, WHICH PROVIDES AS FOLLOWS:

> "A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her, must have materially affected his or her settlement with the debtor."

ROXANE AGREES TO EXPRESSLY WAIVE ANY RIGHTS IT MAY HAVE UNDER THIS CODE SECTION OR UNDER FEDERAL, STATE OR COMMON LAW STATUTES OR JUDICIAL DECISIONS OF A SIMILAR NATURE, AND KNOWINGLY AND VOLUNTARILY WAIVES SUCH UNKNOWN CLAIMS.

(b) JAZZ ACKNOWLEDGES THAT IT MAY HEREAFTER DISCOVER CLAIMS OR FACTS IN ADDITION TO OR DIFFERENT FROM THOSE WHICH IT NOW KNOWS OR BELIEVES TO EXIST WITH RESPECT TO JAZZ'S RELEASED CLAIMS, THE FACTS AND CIRCUMSTANCES ALLEGED IN THE ACTIONS AND/OR THE SUBJECT MATTER OF THIS SETTLEMENT AGREEMENT, WHICH, IF KNOWN OR

SUSPECTED AT THE TIME OF EXECUTING THIS SETTLEMENT AGREEMENT, MAY HAVE MATERIALLY AFFECTED THIS SETTLEMENT AGREEMENT. NEVERTHELESS, UPON THE EFFECTIVENESS OF THE RELEASE OF JAZZ'S RELEASED CLAIMS AS SET FORTH IN SECTION 5 ABOVE, JAZZ HEREBY ACKNOWLEDGES THAT JAZZ'S RELEASED CLAIMS INCLUDE WAIVERS OF ANY RIGHTS, CLAIMS OR CAUSES OF ACTION THAT MIGHT ARISE AS A RESULT OF SUCH DIFFERENT OR ADDITIONAL CLAIMS OR FACTS. JAZZ ACKNOWLEDGES THAT IT UNDERSTANDS THE SIGNIFICANCE AND POTENTIAL CONSEQUENCES OF SUCH A RELEASE OF UNKNOWN UNITED STATES JURISDICTION CLAIMS AND OF SUCH A SPECIFIC WAIVER OF RIGHTS. JAZZ INTENDS THAT THE CLAIMS RELEASED BY IT UNDER THIS RELEASE BE CONSTRUED AS BROADLY AS POSSIBLE TO THE EXTENT THEY RELATE TO UNITED STATES JURISDICTION CLAIMS. JAZZ IS AWARE OF CALIFORNIA CIVIL CODE SECTION 1542, WHICH PROVIDES AS FOLLOWS:

> "A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her, must have materially affected his or her settlement with the debtor."

JAZZ AGREES TO EXPRESSLY WAIVE ANY RIGHTS IT MAY HAVE UNDER THIS CODE SECTION OR UNDER FEDERAL, STATE OR COMMON LAW STATUTES OR JUDICIAL DECISIONS OF A SIMILAR NATURE, AND KNOWINGLY AND VOLUNTARILY WAIVES SUCH UNKNOWN CLAIMS.

7. **Competition-Related Claims**. The Parties shall use reasonable efforts to defend against any investigation, administrative proceeding or litigation brought by a government entity or Third Party related to the Settlement Agreement, the AG Agreement, the License Agreement or other related agreements, including any claim of unfair competition (which may also include claims of untrue, false or misleading advertising), and shall discuss in good faith whether to enter into a joint defense agreement, and whether to share in the costs and/or expenses incurred by either Party arising out of such response or defense (including reasonable attorneys' fees). Regardless of any such agreement, the Parties will be deemed to have a common legal interest for purposes of asserting any applicable privilege (including, but not limited to, the attorney-client privilege) unless such common interest is explicitly repudiated. Nothing in this Settlement Agreement, however, shall prevent the Parties, whether collectively or individually, from entering into settlement negotiations with a Third Party or governmental entity, provided that, to the extent permitted by law, if either Party enters into discussions related to a settlement negotiation or consent agreement, such Party shall provide notice to the other Party of such discussions within five (5) business days after the initiation of such discussions. Subject to the foregoing, each Party shall have the right to defend itself against such investigation, administrative proceeding or litigation, including by settlement or other consensual resolution, as it sees fit in the exercise of its sole discretion; provided however, to the extent permitted by law, that neither Party shall enter into a settlement agreement or consent order with a Third Party or government entity without providing to the extent practicable ten (10) business days' prior written notice thereof to the other Party, or to the extent such settlement agreement or consent

order includes terms or admissions that are reasonably likely to materially adverse to the other Party's interests, other than a general admission of liability of such Party.

8. Confidentiality.

The terms of this Settlement Agreement, the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement) and the License Agreement shall be maintained in strict confidence by the Parties except: (i) as provided by Section 4 of this Settlement Agreement; (ii) that any Party or any of its Affiliates may disclose such terms as may be necessary in connection with any litigation or other legal proceeding relating to any of the Licensed Patents, provided that such disclosure is made subject to a protective order or confidentiality agreement and that such Party first provides the other Party with reasonable notice of the intended disclosure and provides the other Party with a reasonable period of time in which to assert an objection to the intended disclosure, in each case to the extent reasonably obtainable by the disclosing Party; (iii) that any Party or any of its Affiliates may disclose such terms of this Settlement Agreement, the License Agreement, and the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement), including but not limited to the Launch Date, the AG Launch Date and the Royalty, if and as reasonably determined by such Party or any of its Affiliates to be required by law or regulation, including, without limitation, reporting requirements of the U.S. Securities and Exchange Commission, or by the rules or regulations of any stock exchange to which such Party is subject including, with respect to Jazz and its Affiliates, in a filing on Form 8-K with the U.S. Securities and Exchange Commission with substantially the content provided by Jazz to Roxane prior to the execution of this Settlement Agreement; (iv) that any Party or any of its Affiliates may disclose such terms to the extent necessary to allow attorneys, auditors and advisors, who agree, or have a professional responsibility, to keep such terms confidential, to render professional services to the Parties or their Affiliates; (v) that the Parties or any of either of their Affiliates may each (x) issue a press release with respect to the matters contemplated by this Settlement Agreement, the License Agreement, and the AG Agreement (including any agreement contemplated thereby, such as a supply agreement and a services agreement) in substantially the forms agreed between the Parties prior to the execution of this Settlement Agreement, (y) provide other information consistent with talking points provided by Jazz to Roxane prior to the execution of this Settlement Agreement and (z) provide such other information to the extent approved by the other Party, which approval shall not be unreasonably withheld, conditioned, or delayed; (vi) that the Parties or any of their Affiliates may communicate with the FDA on a confidential basis concerning this Settlement Agreement, the License Agreement and the AG Agreement and the licenses, authorizations, and waivers provided for herein and therein; (vii) that either Party or any of its Affiliates may disclose such terms as needed to perform under this Settlement Agreement, the License Agreement, and the AG Agreement (and any agreement contemplated thereby), including any subcontractor of a Party's obligations thereunder; and (viii) that either Party or any of its Affiliates may disclose such terms to actual or potential investors, acquirors and other financial partners solely for the purpose of evaluating or carrying out an actual or potential investment, acquisition or other transaction, provided that in each such case such recipients are bound by appropriate confidentiality and non-use obligations. Notwithstanding the foregoing, each Party or any of its Affiliates may disclose publicly or to a Third Party without the consent of the other Party any

information previously disclosed in any press release made pursuant to clause (v) or filing required of the U.S. Securities and Exchange Commission made pursuant to clause (iii) above, provided that such information remains accurate as of such time. The Parties acknowledge and agree that, upon its filing with the Court, the Stipulation and Order of Dismissal will be a matter of public record and shall not be subject to any confidentiality restrictions. The Parties further agree that, upon the filing of the Stipulation and Order of Dismissal with the Court, the fact that the Parties have settled the Actions will be a matter of public record and shall not be subject to any confidentiality restrictions, but the terms of such settlement shall be maintained in confidence as provided by this Section 7.

9. Term and Termination.

This Settlement Agreement shall continue from the Execution Date until the earlier of: (a) the expiration of the last to expire of the Licensed Patents; or (b) the date of a Final Decision that all of the asserted claims of all of the asserted Licensed Patents are invalid and/or unenforceable. The releases and discharges set forth in Section 5 and Section 6 shall survive the termination of this Settlement Agreement, and the confidentiality obligations set forth in Section 7 shall survive for a period of seven (7) years from the expiration or termination of the Settlement Agreement.

10. No Assignment.

This Settlement Agreement shall not be assignable in whole or in part by any Party to any Third Party without the prior written consent of the other Parties, such consent not to be unreasonably withheld, conditioned or delayed. Notwithstanding the foregoing, either Party may assign this Settlement Agreement to any of its Affiliates or to any successor to all or substantially all of the assets, business or operating business unit or division of such Party through which such Party (i) with respect to Roxane, operates its U.S. generic oral pharmaceuticals business in the ordinary course of business prior to such assignment and (ii) with respect to Jazz, performs its obligations under this Settlement Agreement in the ordinary course of business prior to such assignment, in the case of clause (i) or (ii) above, whether through a merger, consolidation, sale of stock, or otherwise, provided that such successor agrees in writing to assume all of the obligations of such Party hereunder. Any purported assignment, delegation or other transfer in violation of the preceding sentences shall be null and void. Subject to the foregoing, this Settlement Agreement shall be binding upon, and inure to the benefit of, the permitted successors and assigns of each Party.

11. Notice.

All notices, requests, claims, demands and other communications under this Settlement Agreement shall be in writing and shall be given by delivery by hand, by facsimile, by registered or certified mail (postage prepaid, return receipt requested), or by email to the respective Parties at the following addresses (or at such other address for a Party as shall be specified by like notice).

If to Jazz, to:	Jazz Pharmaceuticals, Inc. 3180 Porter Drive Palo Alto, California 94304 Attn: General Counsel Facsimile: (650) 496-3781 Email: jazz_notices@jazzpharma.com
with a copy to:	Nick Cerrito Quinn Emanuel Urquhart & Sullivan, LLP 51 Madison Avenue 22nd Floor New York, New York 10010 Facsimile: (212) 849-7100 Email: nickcerrito@quinnemanuel.com
If to Roxane, to:	West-Ward Pharmaceuticals Corp. 401 Industrial Way West Eatontown, NJ Attn: General Counsel Facsimile: 732-720-2872 Email: dberger@west-ward.com
with a copy to:	Alan Clement Locke Lord LLP 200 Vesey Street New York, NY 10281 Facsimile: 212-812-8378 Email: aclement@lockelord.com

Any such notice shall be deemed to have been received on the date actually received. Either Jazz or Roxane may change its address by giving the other Party written notice delivered in accordance with this Section.

12. Severability.

If any provision of this Settlement Agreement is declared illegal, invalid or unenforceable by a court having competent jurisdiction, it is mutually agreed that this Settlement Agreement shall endure except for the part declared invalid or unenforceable by order of such court; provided, however, that in the event that the terms and conditions of this Settlement Agreement are materially altered, the Parties will, in good faith, renegotiate the terms and conditions of this Settlement Agreement (including Section 5 hereof) to reasonably replace such invalid or

unenforceable provisions in light of the intent of this Settlement Agreement; provided further that if the Parties do not succeed in reaching mutually acceptable modifications to this Settlement Agreement within thirty (30) calendar days of such material alteration, then the Parties agree to comply with the Dispute Resolution Provisions in accordance with the terms set forth in Exhibit B in order to reach agreement on an appropriate modification of this Settlement Agreement.

13. Amendment.

This Settlement Agreement may not be changed, waived, discharged, or terminated except by an instrument in writing signed by the Parties and making specific reference to this Section 12 and signed by a duly authorized officer of each Party.

14. Superiority of Agreements.

The Parties agree that the provisions of this Settlement Agreement, together with the License Agreement and the AG Agreement, and when executed and delivered by all parties thereto, the Supply Agreement and the Master Services Agreement, and any permitted amendments to any such agreement, supersede and shall prevail over any inconsistent statements, understandings, promises, or provisions contained in any prior discussions, arrangements, or communications between the Parties or in any documents passing between the Parties. Notwithstanding anything herein to the contrary, the Settlement Agreement, this License Agreement, and the AG Agreement shall be construed together in a consistent manner as reflecting a single intent and purpose. Except as otherwise set forth herein, nothing in this Settlement Agreement is intended to, and shall not, confer upon any Third Party any rights or remedies.

15. Governing Law.

This Settlement Agreement shall be governed, interpreted, and construed in accordance with the laws of the State of New Jersey, without giving effect to choice of law principles. The Parties expressly exclude application of the United Nations Convention for the International Sale of Goods. If a dispute arises between the Parties concerning this Settlement Agreement, then the Parties will confer, as soon as practicable, in an attempt to resolve the dispute. If the Parties are unable to resolve such dispute amicably, then the Parties irrevocably agree that the federal district court in the State of New Jersey shall have exclusive jurisdiction to deal with any disputes arising out of or in connection with this Settlement Agreement and that, accordingly, any such proceeding arising out of or in connection with this Settlement Agreement shall be brought in the United States District Court for the District of New Jersey. Notwithstanding the foregoing, if there is any dispute for which the federal district court in the State of New Jersey does not have subject matter jurisdiction, the state courts in New Jersey shall have jurisdiction. In connection with any dispute arising out of or in connection with this Settlement Agreement, each Party hereby expressly consents and submits to the personal jurisdiction of the federal and state courts located in the State of New Jersey.

16. Headings.

The article and section headings contained in this Settlement Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of this Settlement

Agreement.

17. Interpretation.

References in this Settlement Agreement to any gender include references to all genders, and references to the singular include references to the plural and vice versa. The words "include", "includes" and "including" when used in this Settlement Agreement shall be deemed to be followed by the phrase "without limitation". Unless the context otherwise requires, references in this Settlement Agreement to Articles, Sections, Exhibits and Schedules shall be deemed references to Articles and Sections of, and Exhibits and Schedules to, this Settlement Agreement. Unless the context otherwise requires, the words "hereof", "hereby" and "herein" and words of similar meaning when used in this Settlement Agreement refer to this Settlement Agreement in its entirety and not to any particular Article, Section or provision of this Settlement Agreement. All references to contracts, agreements, or other arrangements shall refer to oral as well as written matters.

18. Construction.

The Parties expressly agree that any rule of construction to the effect that ambiguities are to be resolved against the drafting Party shall not be applied in the construction or interpretation of this Settlement Agreement.

19. Waiver.

A waiver by either Party of any of the terms and conditions of this Settlement Agreement in any instance shall not be deemed or construed to be a waiver of such term or condition for the future, or of any other term or condition hereof. All rights, remedies, undertakings, obligations and agreements contained in this Settlement Agreement shall be cumulative and none of them shall be in limitation of any other remedy, right, undertaking, obligation or agreement of either Party.

20. Counterparts.

This Settlement Agreement may be executed in one or more counterparts, all of which shall be considered one and the same agreement and shall become effective when one or more counterparts have been signed by each of the Parties and delivered to the other Parties. Delivery of an executed counterpart of a signature page of this Settlement Agreement by facsimile or other electronic image scan transmission shall be effective as delivery of a manually executed counterpart of this Settlement Agreement.

21. Representations and Warranties.

Each Party represents and warrants to the other Parties that the execution and delivery by such Party of this Settlement Agreement and the performance of its obligations hereunder have been duly authorized by all necessary corporate action and will not (i) violate any provision of Laws or any ruling, writ, injunction, order, judgment or decree of any court, administrative agency or other governmental body to which such Party is subject, (ii) conflict with or result in any breach of any of the terms, conditions or provisions of any agreement to which such Party or any of its Affiliates is a party or by which it or any of its Affiliates or any of its or their properties or assets is bound or affected, or (iii) violate or conflict with any provision of the organizational documents of such Party.

* * * * *

IN WITNESS WHEREOF, this Settlement Agreement has been executed by the duly authorized representatives of the Parties.

JAZZ PHARMACEUTICALS, INC.

By: /s/ Suzanne Sawochka Hooper
Name: Suzanne Sawochka Hooper
Title: Executive VP & General Counsel

JAZZ PHARMACEUTICALS IRELAND LIMITED

By: /s/ Hugh Kiely
Name: Hugh Kiely
Title: Director

IN WITNESS WHEREOF, this Settlement Agreement has been executed by the duly authorized representatives of the Parties.

ROXANE LABORATORIES, INC.

By: /s/ Brian Hoffman
Name: Brian Hoffman
Title: President

WEST-WARD PHARMACEUTICALS CORP.

By: /s/ Brian Hoffman
Name: Brian Hoffman
Title: President

EUROHEALTH (USA), INC.

By: /s/ David Berger
Name: David Berger
Title: Secretary

HIKMA PHARMACEUTICALS PLC

By: /s/ Said Darwazah
Name: Said Darwazah
Title: Chairman and Chief Executive

Exhibit A

Stipulation And Order of Dismissal

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

JAZZ PHARMACEUTICALS, INC., Plaintiff, v. ROXANE LABORATORIES, INC., Defendant.	Civil Action No. 10-6108 (ES)(JAD) CONSOLIDATED (Filed Electronically)
JAZZ PHARMACEUTICALS, INC. and JAZZ PHARMACEUTICALS IRELAND LIMITED, Plaintiffs, v. ROXANE LABORATORIES, INC., Defendant.	Civil Action No. 15-1360 (ES)(JAD) CONSOLIDATED (Filed Electronically)
JAZZ PHARMACEUTICALS, INC., Plaintiff, v. ROXANE LABORATORIES, INC., WESTWARD PHARMACEUTICALS CORP., EUROHEALTH (USA), INC., and HIKMA PHARMACEUTICALS PLC, Defendant.	Civil Action No. 16-4971 (ES)(JAD) (Filed Electronically)

STIPULATION AND ORDER OF DISMISSAL

Pursuant to Federal Rules of Civil Procedure 41(a)(1)(A)(ii) and 41(c), and by agreement between Plaintiffs Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited (collectively, "Plaintiffs") and Defendants Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC ("Roxane," and together with Plaintiffs, the "Parties"), the Parties hereby stipulate and agree that all claims, counterclaims and affirmative defenses asserted by the Parties against each other in the above-captioned actions (the "Actions") are hereby dismissed without prejudice and, except as specifically provided by agreement, without costs, disbursements, or attorneys' fees to any party. It is further stipulated that the U.S. District Court for the District of New Jersey retains jurisdiction to enforce and resolve any disputes related to the parties' resolution of the Actions.

SO STIPULATED:

Dated: _____, 2017

SAUL EWING LLP

Charles M. Lizza
William C. Baton
One Riverfront Plaza, Suite 1520
Newark, New Jersey 07102-5426
(973) 286-6700
clizza@saul.com

Attorneys for Plaintiffs
Jazz Pharmaceuticals, Inc. and
Jazz Pharmaceuticals Ireland Limited

SILLS CUMMIS & GROSS P.C.

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The Legal Center
One Riverfront Plaza
Newark, New Jersey 07102
(973) 643-7000

Attorney for Defendants
Roxane Laboratories, Inc.,
West-Ward Pharmaceuticals Corp.,
Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC

SO ORDERED:

This _____day of _____, 2017

Hon. Esther Salas, U.S.D.J.

Exhibit B

Dispute Resolution Provisions

Any dispute arising under the Settlement Agreement that refers to dispute resolution as set forth in this Exhibit B shall be determined by the following dispute resolution procedure, with all references to days being to calendar days. All negotiations and communications pursuant to this process will be confidential and shall be treated as compromise and settlement negotiations for purposes of the applicable rules of evidence, including Federal Rule of Evidence 408.

(a) For purposes of these Dispute Resolution Provisions, **"Agreement"** or **"Agree"** shall mean confirmation in writing by all Parties to the dispute that the dispute has been resolved.

(b) To initiate this dispute resolution procedure, any Party shall give written notice to any other Party of a dispute setting forth the agreement at issue, nature of the dispute, including an identification of the facts and legal claims at issue, and a summary of the arguments supporting the notifying Party's position.

(c) Within fourteen (14) days of receipt of notice, an attorney for a Jazz Party and an attorney for a Roxane Party must confer in good faith either in person or telephonically in order to attempt to reach an Agreement regarding the dispute.

(d) If Agreement is not reached within fourteen (14) days through the process described in Exhibit B, paragraph (c) above then the Parties will have fourteen (14) days during which an in-house attorney for a Jazz Party and an in-house attorney for a Roxane Party must confer in good faith either in person or telephonically in order to attempt to reach an Agreement regarding the dispute.

(e) If Agreement is not reached within fourteen (14) days through the process described in Exhibit B, paragraph (d) above, then the Parties will have fourteen (14) days during which an executive for any Jazz Party having a rank or title not less than that of a vice president (or an equivalent thereof) and an executive for any Roxane Party having a rank or title not less than that of a vice president (or an equivalent thereof) must confer in good faith either in person or telephonically in order to attempt to reach an Agreement regarding the dispute.

(f) If Agreement is not reached within fourteen (14) days through the process described in Exhibit B, paragraph (e) above, then the Parties will have fourteen (14) days during which the chief executive officer for Jazz and chief executive officer for Roxane must confer in good faith either in person or telephonically in order to attempt to reach an Agreement regarding the dispute.

(g) If an Agreement is not reached upon completion of the process set forth in paragraphs (b) through (f) above of the foregoing dispute resolution procedures, either Party may initiate litigation by filing a complaint and avail itself in full of all available legal action and remedies.

(h) A Party may designate the same individual to confer for more than one of the procedures set forth in paragraphs (c) through (f) above so long as the individual otherwise meets the criteria set forth in that paragraph.

(j) The Parties agree that they will not use this dispute resolution process, including either the fact that a Party engaged in the process or the substance of the discussions that take place during this process, for purposes of supporting or otherwise advancing any defense or position in any litigation that may follow.

(k) Any deadline set forth in the foregoing Dispute Resolution Provisions may be shortened or extended by written agreement of all Parties.

Exhibit C
Defined Terms

1. **"Affiliate"** shall mean, with respect to a particular Party, a person, corporation, partnership, or other entity that controls, is controlled by or is under common control with such Party. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of fifty percent (50%) or more of the voting stock or other equity interest of such entity, or by contract or otherwise. For clarity, a person or other entity shall be deemed an Affiliate only for so long as this definition is satisfied with respect to such person or entity.

2. **"AG Agreement"** shall have the meaning set forth in Section 2 of the Settlement Agreement.

3. **"AG Launch Date"** shall mean the date on which Roxane is permitted to Market the Roxane Authorized Generic pursuant to the AG Agreement.

4. **"ANDA"** shall mean an Abbreviated New Drug Application.

5. **"Authorized Generic"** shall mean any generic product that: (a) contains the Compound as the sole active ingredient; (b) is Marketed in the Territory without use of the Trademark; and (c) is authorized by Jazz to be Marketed in the Territory pursuant to NDA No. 21-196.

6. **"Compound"** shall mean 500 mg/mL sodium oxybate oral solution.

7. **"DOJ"** shall have the meaning set forth in Section 4 of the Settlement Agreement.

8. **"Effective Date"** shall have the meaning set forth in Section 1 of the Settlement Agreement.

9. **"FDA"** shall mean the U.S. Food and Drug Administration and any successor agency thereto.

10. **"Final Decision"** shall mean the issuance of a final decision from a district court or from the Patent Trial and Appeal Board of the United States Patent and Trademark Office (in either case from which no appeal can be taken), or a mandate from a court of appeals from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) can be taken.

11. **"FTC"** shall have the meaning set forth in Section 4 of the Settlement Agreement.

12. **"Generic Equivalent"** shall mean a pharmaceutical product that has received FDA approval for sale pursuant to an ANDA or 505(b)(2) filing as an AB-rated equivalent to the NDA Product.

13. **"Jazz Covenant Not to Sue"** shall have the meaning set forth in Section 5(c) of the Settlement Agreement.

14. **"Jazz's Released Claims"** shall have the meaning set forth in Section 5(b) of the Settlement Agreement.

15. **"Launch Date"** shall mean the date on which Roxane is permitted to Market the Roxane Generic Product pursuant to the License Agreement.

16. **"Laws"** shall mean all applicable international, supranational, national, federal, state, provincial, regional and local laws, statutes, ordinances, codes, rules, regulations, orders, decrees or other pronouncements of any governmental, administrative or judicial authority in the Territory.

17. **"License Agreement"** shall have the meaning set forth in Section 2 of the Settlement Agreement.

18. **"Licensed Patents"** shall mean [A] U.S. Patent Nos. 6,472,431, 6,780,889, 7,262,219, 7,851,506, 8,263,650, 8,324,275, 8,461,203, 7,668,730, 7,765,106, 7,765,107, 7,895,059, 8,457,988, 8,589,182, 8,731,963, 8,772,306, 8,859,619, 8,952,062, 9,050,302, 9,486,426, and 9,539,330 including any divisionals, continuations, continuations-in-part, reexaminations, or reissues thereof, and all patent term extensions and any pediatric exclusivities applicable to the corresponding NDA Product, in each case whether granted or allowed prior to or after the Execution Date and [B] any other U.S. patents owned by or licensed to any Jazz Party or any of its Affiliates that become listed in the Orange Book after the Effective Date in connection with the NDA Product, solely to the extent and for the sole purpose of any FDA requirement that Roxane file a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV) with respect to the Roxane ANDA, and subject to Roxane filing such a Paragraph IV certification with respect to such patents that become listed in the Orange Book in connection with the NDA Product after the Effective Date.

19. **"Market"** shall mean to use, advertise, market, offer, sell, offer to sell, or to otherwise commercialize a pharmaceutical product, and "**Marketing**" shall have a corresponding meaning. For the avoidance of doubt, Market and Marketing shall include "commercial marketing" as defined in 21 C.F.R. §314.3(b), as that regulation exists as of the Effective Date.

20. **"NDA Product"** shall mean the branded product that: (a) contains the Compound as the sole active ingredient; (b) is Marketed with use of the Trademark in the Territory; and (c) is approved for Marketing in the Territory pursuant to NDA No. 21-196.

21. **"Permitted Minor Modification"** shall mean any modification to ANDA No. 202090 (as supplemented or amended as of the Execution Date or, solely to incorporate any modifications described in this definition, thereafter) that does not materially change the active ingredient, concentration, dosage form, indication, reference listed drug (unless the reference listed drug is first changed for the NDA Product), or AB rating of any generic product defined by such ANDA and/or does not add one or more additional active ingredients to any generic product defined by such ANDA. For the avoidance of doubt, a modification of such ANDA to add a second active ingredient to any generic product defined by such ANDA, to materially change

any generic product covered by such ANDA to a different dosage form, to materially change any generic product covered by such ANDA to a different salt, or to materially change any generic product covered by such ANDA to add any approved new indication for the NDA Product after the Execution Date for which such ANDA has not sought approval as of the Execution Date are not Permitted Minor Modifications. Any modification of such ANDA for the purpose of modifying any approved indication for the generic product covered by such ANDA as of the Execution Date, or any other labeling-related modification, is not a Permitted Minor Modification unless such modification to such approved indication or other labeling-related modifications are both (i) first made to the NDA Product and (ii) required by the FDA or reasonably necessitated by Laws to maintain approval of the Roxane ANDA.

22. **"Roxane ANDA"** shall mean Roxane's ANDA No. 202090 as supplemented or amended as of the Execution Date, or, solely to incorporate any Permitted Minor Modification, thereafter.

23. **"Roxane Authorized Generic"** shall mean a generic product that: (a) contains the Compound as the sole active ingredient; (b) is Marketed in the Territory without use of the Trademark, except as otherwise provided herein (including in any agreement contemplated hereby, such as the Supply Agreement and the Master Services Agreement), or in the Settlement Agreement; (c) is Marketed by Roxane in the Territory pursuant to NDA No. 21-196; and (d) is supplied by or on behalf of Jazz to Roxane under the terms and conditions of the AG Agreement and the Supply Agreement.

24. **"Roxane Covenant Not to Sue"** shall have the meaning set forth in Section 5(d) of the Settlement Agreement.

25. **"Roxane's Released Claims"** shall have the meaning set forth in Section 5(a) of the Settlement Agreement.

26. **"Royalty"** shall mean the royalty payable under the AG Agreement.

27. **"Stipulation and Order of Dismissal"** shall have the meaning set forth in Section 1 of the Settlement Agreement.

28. **"Territory"** shall mean the United States of America, including its territories, districts, and possessions, including the Commonwealth of Puerto Rico.

29. **"Third Party"** shall mean any person or entity other than the Parties and each of their Affiliates.

30. **"USPTO"** shall have the meaning set forth in Section 5(a) of the Settlement Agreement.

31. **"Xyrem REMS"** means the Risk Evaluation and Mitigation Strategy (**"REMS"**) program approved by the FDA on February 27, 2015 under NDA No. 21-196 (as it may be modified from time to time).

CERTAIN PORTIONS OF THIS EXHIBIT (INDICATED BY [*]) HAVE BEEN EXCLUDED PURSUANT TO ITEM 601(B)(10) OF REGULATION S-K BECAUSE THEY ARE BOTH NOT MATERIAL AND ARE THE TYPE THAT THE COMPANY TREATS AS PRIVATE AND CONFIDENTIAL.

CLINICAL AND COMMERCIAL MANUFACTURING AND SUPPLY AGREEMENT

THIS CLINICAL AND COMMERCIAL MANUFACTURING AND SUPPLY AGREEMENT (this **"Agreement"**) is made effective as of the 22nd day of December, 2010 (**"Effective Date"**) by and between **BAXTER ONCOLOGY GmbH**, with an address at Kantstrasse 2, 33790 Halle / Westphalia, Germany (**"Baxter"**) and **CELATOR PHARMACEUTICALS, INC.**, a Delaware corporation, having offices at 303B College Road East, Princeton, New Jersey 08540 (**"Celator"**).

RECITALS

1. Celator is among other pharmaceutical activities engaged in the development of pharmaceutical products;

2. Baxter is among other pharmaceutical activities engaged in the formulation, filling, inspection, labeling and packaging of pharmaceutical products for various pharmaceutical companies, including competitors of Celator and Baxter;

3. Celator and Baxter desire to have Baxter formulate, fill, inspect, package, label, and test the pharmaceutical product, CPX-351, for Celator for clinical and/or commercial use.

NOW, THEREFORE, in consideration of the mutual covenants and agreements contained herein, Celator and Baxter, hereinafter sometimes referred to as **"Party"** or **"Parties"**, agree as follows:

Article 1, DEFINITIONS

1.1 As used in this Agreement, the following words and phrases shall have the following meanings:

"Active Pharmaceutical Ingredient" or **"API"** shall collectively refer to cytarabine and daunorubicin.

"Affiliate" shall mean any corporation or other business entity directly or indirectly controlled by, controlling, or under common control with a Party or its parent corporation, the term **"control"** (including, with correlative meaning, the terms "controlled by," "controlling" and "under common control with") means: (a) in the case of corporate entities, direct or indirect ownership of at least fifty percent (50%) of shares of capital stock having the right to vote for the election of directors, or (b) the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of such Party, whether through the ownership of voting securities, by contract or otherwise, or such other relationship as, in fact, constitutes actual control.

“Annual Obligation” shall be defined as set forth in Article 4.

“Batch” shall mean a specific quantity of a Product comprising a number of Units mutually agreed upon in writing between the Parties in the Product Master Plan, and that (a) is intended to have uniform character and quality within specified limits, and (b) is Produced according to a single manufacturing order during the same cycle of Production.

“Baxter SOPs” shall mean Baxter’s Standard Operating Procedures relating to the Product, which shall be reviewed and approved by Celator prior to entering into the Product Master Plan. Celator shall have the right to access and inspect SOPs during annual audits and may request and review specific SOPs at any time.

“**Baxter-supplied Components**” shall mean all Components other than Celator-supplied Components.

“**Celator-supplied Components**” shall mean API, DSPC and DSPG supplied by Celator to Baxter.

“Clinical Product” means vials of Product Produced by Baxter for clinical use by Celator as set forth in a Product Master Plan.

“Celator Trademarks” shall mean the proprietary mark(s) for Product owned by Celator.

“Commercial Product” means vials of Product Produced for commercial sale.

“Components” shall mean all components, including the Raw Materials and Packaging Materials, used by Baxter in the Production of Product under this Agreement. Components are listed in the Product Master Plan.

“Component Specifications” shall mean the specifications and testing to be performed for the Components, as set forth in the Product Master Plan.

“Confidential Information” shall be defined as set forth in Article 18.

“**Contract Year**” shall be defined as (i) the calendar year in which Celator obtains Regulatory Approval allowing the commercialization of Product in the United States or Europe and (ii) each successive year of the Term.

“Current Good Manufacturing Practices” or **“cGMP”** shall mean (a) the good manufacturing practices required by the Regulatory Authorities and set forth in the applicable law, policies or guidelines,

in effect at any time during the term of this Agreement, for the Production and testing of pharmaceutical materials as applied solely to Product.

"DSPC" shall mean the excipient, distearoylphosphatidyl choline.

"DSPG" shall mean the excipient, distearoylphosphatidyl glycerol.

"Effective Date" shall mean the date first set forth above.

"FDA" shall mean the United States Food and Drug Administration or any successor entity thereto.

"FD&C Act" shall mean the United States Federal Food and Cosmetic Act, as amended, or any corresponding Act in each jurisdiction.

"Firm Purchase Order" shall be defined as set forth in Section 4.4.

"Intellectual Property" shall mean ideas, concepts, discoveries, inventions, developments, know-how, trade secrets, techniques, methodologies, modifications, innovations, improvements, writings, documentation, data and rights (whether or not protectable under state, federal or foreign patent, trademark, copyright or similar laws) or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which contained and whether or not patentable or copyrightable.

"Inventions" shall mean any inventions, discoveries, innovations, methods, improvements, processes, techniques or other valuable developments, whether patentable or copyrightable or not, relating to a Product, the API or their manufacture, arising out of the performance of services under this Agreement by Baxter and/or any use of either the Celator Intellectual Property and/or the API. For the avoidance of doubt, Inventions include Process Inventions, as defined below.

"Long Range Forecast" shall be defined as set forth in Section 4.2.

"Master Batch Record" or **"MBR"** shall mean, with respect to each Presentation of Clinical Product or Commercial Product to be Produced hereunder, a formal set of instructions for the Production of each Presentation of such Product. The MBR shall be developed and maintained in Baxter's standard format by Baxter, using Celator's master formula and technical support.

"Maximum Supply Obligation" shall mean Baxter's supply obligation as set forth in Article 4.

"NDA" shall mean the FDA-required New Drug Application (applicable for U.S. production only).

“Packaging Materials” as used in this Agreement shall mean material employed in the packaging of the Product, including the Baxter standard packaging material for outer packaging used for transportation or shipment to a distributor. Packaging Materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the Product. All Packaging Materials are listed in the Product Master Plan.

“Pick-Up Date” shall mean the date that Product is Released by Baxter to Celator and made available to Celator or its designated carrier for pick-up at Baxter’s facility.

“Presentation” shall mean the specific formula and Components for the Product.

“Process Inventions” shall mean any Inventions that are new manufacturing technologies, methods, processes or techniques, or are improvements to existing manufacturing technologies, methods, processes or techniques, and that are broadly applicable to pharmaceutical products in general. For purposes of clarity, Process Inventions shall not include such Inventions that (i) are applicable only to Product and/or the API and/or (ii) require the use of Product and/or the API.

“Produce” or **“Production”** shall mean the formulation, filling, packaging, inspecting, labeling, and testing of Product by Baxter.

“Product” shall mean Clinical Product or Commercial Product, as the case may be, and as further specified in the Product Master Plan.

“Product Master Plan” shall mean a written plan executed by the Parties in conjunction with this Agreement relating to Product Produced hereunder, which may include, without limitation, Product, Product Specifications, Components, Component Specifications, Regulatory Authorities, the countries where such Product will be used in clinical trials or sold commercially, Presentations, and pricing for such Product Produced under this Agreement.

“**Production Price**” shall be defined as set forth in Section 5.1.

“Product Specifications” shall mean, with respect to Product, the specifications and testing to be performed for the Raw Materials, the Product, and/or the stability program that are set forth in Baxter’s SOPs and the Master Batch Records. The Product Specifications include all tests that Baxter is required to conduct or cause to be conducted as specified in the Product Master Plan. The Product Specifications may be modified from time to time only by a written agreement of Celator and Baxter.

“Purchase Order” shall mean written orders from Celator to Baxter which shall specify (a) the quantity of Product ordered, (b) shipping instructions (e.g., choice of container, temperature requirements), (c) requested pick-up dates, and (d) delivery destinations.

"**Purchase Price**" shall be defined as set forth in Section 5.1.

"Qualified Person" or "QP" shall mean the person designated by Directive 2001/83/EC Article 48-52.

"Quality Agreement" shall mean a written agreement executed by the Parties in conjunction with this Agreement, under which the Parties allocate the pharmaceutical responsibilities.

"Raw Materials" shall mean all materials used by Baxter in the Production of Product under this Agreement with the exception of Packaging Materials. All Raw Materials are listed in the Product Master Plan.

"Regulatory Approval" shall mean all authorizations by the appropriate Regulatory Authority for use of Product in clinical trials and/or as necessary for commercial sale in a jurisdiction, including without limitation, approval of labeling, price, reimbursement and Production.

"Regulatory Authority" shall mean the FDA, the EMA, the BfArM in Germany and the respective Regulatory Authorities in other European countries, in Japan, in Canada and in such other jurisdictions as are set forth in the Product Master Plan or any successor entity thereto.

"Released" or **"Release"** shall mean Baxter's release to Celator of a Batch of Product by a Baxter Qualified Person.

"Released Executed Batch Record" shall mean the completed batch record and associated deviation reports, investigation reports, certificates of compliance and certificates of analysis created for each Batch of Product as specified in the Product Master Plan.

"Reservation Fees" shall be the fees payable by Celator for modification or cancellation of a Firm Purchase Order as set forth in the Product Master Plan.

"Rolling Forecast" shall mean Celator's projected requirements for Product for each of the upcoming [*].

"Term" shall be defined as set forth in Section 8.1 of this Agreement

"Testing Standards and Procedures" shall mean, with respect to Product Produced hereunder, the written standards and procedures for evaluating compliance with the applicable Product Specifications, as mutually agreed upon in writing by Celator and Baxter, and incorporated in the Product Master Plan.

"Unit" shall mean an individually packaged dose of a Product, including by way of example only, vial, as specified in the Product Master Plan.

Article 2, PRODUCT MASTER PLAN AND QUALITY AGREEMENT

2.1 Product Master Plan. For Clinical Product or Commercial Product to be Produced by Baxter hereunder, the Parties have agreed in writing upon a Product Master Plan. Baxter shall not be required to schedule any Production until a Product Master Plan for such Product has been approved in writing by both Baxter and Celator.

2.2 Quality Agreement. For the Production by Baxter hereunder, the Parties have entered into a Quality Agreement to allocate and coordinate the pharmaceutical responsibilities. The Parties agree that Production will not be scheduled until a Quality Agreement has been signed by both Celator and Baxter.

2.3 Amendment. This Agreement, the Quality Agreement and the Product Master Plan may be amended from time to time upon mutual written agreement of the Parties. The Quality Agreement and the Product Master Plan shall be deemed to be incorporated herein by reference and made an integral part of this Agreement. In case of any inconsistencies between this Agreement and the Quality Agreement or the Product Master Plan, the terms and provisions of the Quality Agreement shall prevail for matters of quality and the terms and provisions of this Agreement shall prevail for all other matters.

2.4 Effect of Failure to Execute Plans or Addendum. Failure to execute a Quality Agreement or Product Master Plan with respect to the Product will not relieve either Party of any obligation accruing with respect to such Product prior to such failure to execute. In the event of such failure, if this Agreement shall therefore be terminated, Celator shall reimburse Baxter for all non-cancelable costs incurred by Baxter for work performed and Baxter-supplied Components ordered with respect to such Product.

Article 3, PURCHASE AND SUPPLY OF PRODUCT

3.1 Agreement to Purchase and Supply. Pursuant to the terms and conditions of this Agreement, Celator will purchase Product from Baxter in accordance with Article 4, and Baxter shall Produce and deliver to Celator the Product in accordance with Article 4 of this Agreement.

3.2 Reproduction, Rework or Reprocessing. If, during the Production of any Batch of Product, any reprocessing, rework, reproduction, or change is required in order to meet the Product Specifications, or if Celator requests any change with respect to any matter set forth in the Product Master Plan, Baxter shall conduct such reprocessing, rework, or reproduction and implement such change in compliance with cGMP's. Any reprocessing, rework, reproduction or change, concerning compounding, aseptic filling, or capping must be approved in writing by Celator prior to implementation unless immediate action is required. Celator shall promptly reimburse Baxter for all costs and expenses incurred in connection with such reprocessing, rework, reproduction, or change, except that in the event that any

such reprocessing, rework, reproduction, or change results solely from Baxter's failure to Produce Products according to Product Requirements or Baxter's negligence or willful misconduct, Baxter shall be responsible for, and promptly reimburse Celator for, [*] in connection with such reprocessing, rework, reproduction, or change.

3.3 Components. As set forth in the Product Master Plan, Celator shall purchase and supply Celator-supplied Components which Celator, at its sole cost and expense (including, without limitation, shipping costs), shall supply to Baxter, in a timely manner, required to satisfy the terms of this Agreement. Baxter shall procure, in a timely manner, and have available for Production of Product Baxter-supplied Components, at its sole cost and expense (including, without limitation, shipping costs), required to satisfy the terms of this Agreement. On receipt of the Components, Baxter shall test such materials as set forth in the Product Master Plan. If, notwithstanding such testing, Celator determines to assert a claim against a supplier of a Baxter-supplied Component because Celator discovers a defect in or adulteration of such Baxter-supplied Component that was not discovered by Baxter, Baxter agrees to provide Celator with all information regarding such Baxter-supplied Component and the supplier thereof as Celator shall reasonably request and to cooperate with Celator in the assertion of each such claim.

3.3.1 Vendor/Supplier Qualification. The responsibility for vendor/supplier qualification is set forth in the Quality Agreement.

3.4 Importer of Record. In the event any material or equipment to be supplied by Celator in accordance with the Product Master Plan is imported into Germany for delivery to Baxter (**"Imported Goods"**), such Imported Goods shall be imported DDP Halle/K✔nsebeck (Incoterms 2000). Celator shall be the **"Importer of Record"** of such Imported Goods. As the Importer of Record, Celator shall be responsible for all aspects of the Imported Goods including, without limitation (a) customs and other regulatory clearance of Imported Goods, (b) payment of all tariffs, duties, customs, fees, expenses and charges payable in connection with the importation and delivery of the Imported Goods, and (c) keeping all records, documents, correspondence and tracking information required by applicable laws, rules and regulations arising out of or in connection with the importation or delivery of the Imported Goods.

3.5 Storage

3.5.1 Product Storage. Baxter will store Product at its facility after Product has been Released for up to thirty (30) calendar days free of charge. After thirty (30) calendar days from the Product Release, Baxter may charge storage fees as set forth in the Product Master Plan.

3.5.2 Third Party Storage. After the time frame set forth in Section 3.5.1, Baxter shall be permitted to store Product in third party storage facilities qualified by Baxter; such qualified facilities shall be at the discretion of Baxter; provided however that, prior to storing any Product at a third party storage facility, Baxter shall notify

Celator in writing of Baxter's intent to do so and shall provide the name of the third party and the location of the storage facility.

Article 4, FORECASTS, ORDERS AND CAPACITY

4.1 Forecasts for Clinical Product. Commencing on the Effective Date of this Agreement and prior to the tenth (10^{th}) calendar day of each month thereafter, Celator will provide Baxter in writing with a Rolling Forecast. The first [*] months of the Rolling Forecast for Clinical Product shall be binding for the Parties. It is understood by the Parties that forecasting of Clinical Product requirements is difficult and unforeseen issues can occur; therefore, it is understood that Baxter will use reasonable efforts to accommodate changes to the first [*] months of the Rolling Forecast if able to do so. In the event that Celator requests cancellation or rescheduling of a Firm Order for Production of Clinical Product, Baxter shall use good faith efforts to fill the open capacity resulting from the cancellation or rescheduling. In the event Baxter is unable to fill such open capacity, Baxter may charge Celator a Reservation Fee as set forth in the Product Master Plan.

4.2 Forecasts for Commercial Product. Commencing no less than [*] months prior to the date of the Production of the first Batch of Commercial Product, and prior to the first day of July of each year thereafter during the Term, Celator will provide to Baxter in writing a forecast of Celator's estimated requirements for Commercial Product for each of the upcoming [*] years (the **"Long Range Forecast"**). Commencing with the first regulatory filing for marketing approval of the Product in any major market, and prior to the tenth (10^{th}) calendar day of each month thereafter, Celator will provide Baxter in writing a Rolling Forecast of Celator's estimated contract requirements for Commercial Product. Baxter specifically agrees that such Long Range Forecasts and Rolling Forecasts submitted by Celator will be for general planning purposes only, and shall not be binding on either Party, except as provided below in Section 4.3.

4.3 Annual Obligation for Commercial Product and Maximum Supply Obligation. Celator shall be obligated, upon receiving Regulatory Approval of the Product in the United States or Europe, to purchase from Baxter a minimum number of Batches of Commercial Product in each calendar year during the Term of this Agreement (the **"Annual Obligation"**) as set forth in Exhibit A, which Annual Obligation shall be prorated for any partial calendar year. For any volume shortfall under and below the contractual Annual Obligation, Celator will pay an indemnity per Batch as set forth in the Product Master Plan. In any calendar year during the Term of this Agreement, in no event shall Baxter be obligated to Produce more than the number of Batches set forth in Exhibit B (**"Maximum Supply Obligation"**). If changes (increase/decrease) in the annual order volume require changes in equipment and/or process, Celator will cover the costs of such changes.

4.3.1 For any Contract Year following the last Contract Year identified in Exhibits A and B or as further set forth in a Product Master Plan, no less than [*] prior to the end of the last Contract Year, the Parties shall mutually agree on Celator's Annual Obligation and Baxter's Maximum Supply Obligation for any upcoming Contract Year(s) and such Annual Obligation and Maximum Supply Obligation will be set forth in the Product Master Plan signed by both Parties. In the event the Parties are unable to reach mutual agreement on an Annual Obligation and/or Maximum Supply Obligation [*] prior to the end of the last Contract Year, this Agreement shall terminate in accordance with Section 8.1 and shall be subject to Section 8.4.

4.4 Purchase Orders. Celator shall submit Purchase Orders to Baxter covering Celator's purchases of Product pursuant to this Agreement. Celator shall not, without the written consent of Baxter, designate a requested pick-up date in a Purchase Order earlier than [*] months from the date Celator submits the Purchase Order.

Baxter shall provide a confirmation of receipt of each Purchase Order setting forth the Pick-Up Date that Baxter will meet and setting forth Baxter's filling date for such order within ten (10) business days of receiving Celator's Purchase Order. Upon sending of the confirmation, such Purchase Order shall become a **"Firm Purchase Order"**.

If Baxter is unable to meet the requested pick-up date specified by Celator, Baxter shall so notify Celator within ten (10) business days of receiving Celator's Purchase Order and provide to Celator an alternative Pick-Up date, which shall not be more than [*] later than the initial requested pick-up date designated by Celator in its Purchase Order.

In the event that Celator modifies or cancels a Firm Purchase Order without Baxter's written consent, Celator shall pay the Reservation Fees as set forth in the Product Master Plan. To the extent of any conflict between Purchase Orders submitted by Celator and this Agreement, this Agreement shall control.

Celator shall order full batches of Product on a single Purchase Order.

4.5 Component Delivery Delays. Timely delivery of Celator-supplied Components shall mean that the respective Component and the documents required under the Product Master Plan arrive at Baxter at least thirty (30) business days prior to the scheduled manufacturing date of such Product, as determined by the date set forth in the Firm Purchase Order. Notwithstanding anything in this Agreement to the contrary, in the event that Baxter receives such Celator-supplied Components and associated cGMP documents for the Production of Product from Celator less than thirty (30) business days prior to the scheduled manufacturing date of such Product, Baxter shall use commercially reasonable efforts to reschedule Batch within [*] days after receipt. Baxter shall use good faith efforts to fill the open capacity resulting from the rescheduling. In the

event Baxter is unable to fill such open capacity, Baxter may charge Celator a Reservation Fee as set forth in the Product Master Plan.

Article 5, PRICE

5.1 Purchase Price. The Purchase Price of Product is the sum of the price to be paid by Celator for the Production of Product (the **"Production Price"**) set forth in the Product Master Plan and Baxter's actual cost of Baxter-supplied Components.

5.2 Production Price Adjustment for Commercial Product. Upon the first anniversary of the Effective Date of this Agreement and on each anniversary thereafter, Baxter shall adjust the Production Price of such Commercial Product to reflect changes in Baxter's actual costs since the date on which the Production Price was last established, but in no event shall the Production Price be increased by a percentage that exceeds the percentage change in the Index of Producer Prices of Industrial Products during the previous twelve (12)-month period, as published by the Federal Statistical Office of Germany (www.destatis.de).

Article 6, SHIPMENT AND INVOICING

6.1 Delivery Terms. Product shall be delivered to Celator or to a location designated by Celator in the Purchase Order EXW (Incoterms, 2000) Baxter's facility in Halle/K✔nsebeck, Westphalia, Germany freight collect, by a common carrier designated by Celator in a Purchase Order. Celator shall procure, at its cost, insurance covering damage or loss to the Product during shipping from Baxter's facility.

6.2 Subsequent Export. Celator agrees and represents that Celator is the owner of the goods that are consigned to Baxter for contract manufacturing services and warrants that Celator is responsible for any subsequent export or re-export and will comply with all applicable laws and regulations relating to the export or re-export, including the prohibition against unlawful transshipments. Further, where such goods are destined for export or re-export, Celator agrees and accepts that it shall act as the exporter of record, and warrants that as the exporter of record, it will assume all attendant responsibilities associated with the export or re-export, including obtaining any necessary export licenses. Celator further agrees to defend Baxter against any civil action, civil or criminal, private or public, in connection with the subsequent export or re-export by Celator of the goods.

6.3 Foreign Corrupt Practices Act. Celator acknowledges it is not the agent of Baxter and represents and warrants that it has not, and covenants that it will not pay anything of value to any government employee in connection with the sale of the Product.

6.4 Payment Terms. For Commercial and Clinical Product, Baxter will issue an invoice for payment upon the date of Baxter's disposition of the Batch. Payments shall be made by wire transfer to a bank account specified by Baxter within [*] days of the date of Baxter's invoice by wire transfer to a bank account specified by Baxter. Each invoice shall be payable by Celator in accordance with the terms noted above. Celator is obliged to confirm to Baxter in writing the receipt of the invoice without any delay. All prices quoted by Baxter, e.g., in the Product Master Plan, shall be ex value added taxes and denominated in Euros. Any payment due under this Agreement not received within the time noted above shall bear interest of [*] per month on the outstanding balance compounded monthly.

6.5 Default in Undisputed Payment Obligations. In addition to all other remedies available to Baxter in the event of a Celator default, if Celator fails to make any undisputed payment when due and payable hereunder, Baxter may refuse all further Purchase Orders, refuse to Produce any Product until Celator's account is paid in full, modify the foregoing terms of payment, place the account on a letter of credit basis, require full or partial payment in advance, suspend deliveries of Product until Celator provides assurance of performance reasonably satisfactory to Baxter, and/or take other reasonable means as Baxter may determine. In the event Celator has a good faith dispute of an invoice amount, Celator shall promptly notify Baxter within fifteen (15) days from the date of invoice. Each Party agrees to use good faith efforts to resolve any disputes of an invoice amount within thirty (30) days of notification of such dispute.

Article 7, ACCEPTANCE OF PRODUCT

7.1 Product Conformity. Within fifteen (15) business days from the date of shipment of Product to Celator or the receipt of the Released Executed Batch Record, as defined in Product Master Plan, whichever is later, Celator shall determine whether such Product and related documentation conforms to the Product Specifications, Master Batch Record, and Baxter SOPs (collectively, the **"Product Requirements"**); provided, however, that Celator shall have the right to revoke acceptance if, within thirty (30) business days of receipt of the Batch, Celator discovers a latent defect or adulteration not reasonably discoverable at time of delivery.

7.1.1 If (a) any Product conforms to the Product Requirements, or (b) Celator fails to notify Baxter in accordance with the procedures set forth in Section 7.1 that any Product does not conform to the Product Requirements, then Celator shall be deemed to have accepted the Product and waived its right to revoke acceptance.

7.1.2 If Celator believes Product does not conform to the Product Requirements, it shall notify Baxter by telephone including a detailed explanation of the non-conformity and shall confirm such notice in writing via international courier service. Upon receipt of such notice, Baxter will investigate such alleged non-conformity, and (i) if Baxter agrees such Product is non-

conforming, Baxter and Celator will mutually determine a corrective action plan within sixty (60) calendar days after receipt of Celator's written notice of non-conformity, or such additional time as is reasonably required if such investigation or plan requires data from sources other than Celator or Baxter, or (ii) if Baxter disagrees with Celator's determination that the shipment of Product is non-conforming, Baxter shall so notify Celator by telephone within a ten (10) calendar day period and confirm such notice in writing by overnight delivery to Celator.

7.1.3 If the Parties dispute whether Product is conforming or non-conforming to the Product Requirements, the Product will be submitted to a mutually acceptable laboratory or consultant for resolution, whose determination of conformity or non-conformity, and the cause thereof of non-conformity, shall be binding upon the Parties. Notwithstanding the foregoing, Celator may not release a Batch of Product that Baxter has reasonably rejected in good faith. The costs of such laboratory or consultant are to be borne by the Party whose determination was incorrect.

7.2A Remedies for Non-Conforming Clinical Product.

7.2.1A Celator shall pay for all Clinical Product, including replacement Clinical Product and the cost of the API therefor, except as specifically set forth in Section 7.2.2A.

7.2.2A In the event Baxter agrees that Clinical Product is non-conforming to the Product Requirements, or the laboratory or consultant determines that such Clinical Product is non-conforming, solely as a result of the negligence or willful misconduct of Baxter, Baxter shall replace such non-conforming Clinical Product within thirty (30) days assuming sufficient API is available or will be provided by Celator at no charge to Baxter in due time to carry out the Production. Baxter is not responsible for defects in Celator-supplied Components including without limitation API.

7.2.3A Notwithstanding anything to the contrary in the foregoing, Baxter shall have no obligation to replace the non-conforming Clinical Product if the process provided by Celator is not sufficient to Produce conforming Clinical Product. Baxter agrees that a conclusion that the Celator-provided process is not sufficient to Produce conforming Clinical Product cannot reasonably be made if such process has previously resulted in conforming Clinical Product at Baxter.

7.2B Remedies for Non-Conforming Commercial Product.

7.2.1B Celator shall pay for all Commercial Product, including replacement Commercial Product and the cost of the API therefor, except as specifically set forth in Sections 7.2.2B and 7.2.3B.

7.2.2B In the event Baxter agrees that Commercial Product is non-conforming to the Product Requirements, or the laboratory or consultant determines that such Commercial Product is non-conforming, Celator shall provide replacement API to Baxter and Baxter shall replace such non-conforming Commercial Product as soon as possible assuming sufficient API is available or will be provided by Celator in due time to carry out the Production. Baxter is not responsible for non-conforming Commercial Product that is caused by Celator-supplied Components including without limitation API.

7.2.3B In the event Baxter agrees that Commercial Product is non-conforming to Product Requirements, or the laboratory or consultant determines that Commercial Product is non-conforming to the Product Requirements solely as a result of the negligence or willful misconduct of Baxter, Baxter shall (i) incur the cost of Production of the replacement Commercial Product, and (ii) reimburse Celator for its actual cost of Celator-supplied Components including without limitation the API for the replacement Commercial Product, which cost shall not exceed [*].

7.2C Disposal of Non-Conforming Product. All non-conforming Products shall be returned to Baxter for disposal. If the non-conforming Product was solely due to Baxter's negligence or willful misconduct or solely due to Baxter's breach of its representations and warranties under this Agreement, Baxter shall be responsible for the costs of disposal.

7.3 Exceptions. Production deviations and investigations which occur during Production of Product and which do not cause the Production to be non-compliant with cGMP or with Specifications shall not, in and of themselves, be deemed to cause such Product to be non-conforming. Should the Parties disagree that a Production deviation should be cause for rejection of Product, the Parties shall agree to a mutually acceptable third party Qualified Person to make the determination regarding disposition of the Batch.

Article 8, TERM AND TERMINATION

8.1 Term. Unless terminated pursuant to Section 8.2 herein, this Agreement shall commence on the Effective Date and will continue until the development and clinical Production have been completed, as described in the Product Master Plan for clinical Production, (the **"Clinical Term"**) and shall continue in effect thereafter for commercial Production until such time as one Party provides at least twenty-four (24) months' prior written notice to the other Party of the notifying Party's determination to terminate this Agreement, which notice shall specify the termination date (the **"Commercial Term"**). The Clinical Term and the Commercial Term are collectively referred to as the **"Term"**.

8.1.1 Expiration of Term. In the event that first Regulatory Approval for commercialization of Product in the United States or Europe is not obtained within thirty-six (36) months from the date of last regulatory submission of Product in the United States or Europe, then either Party shall have the right to terminate this Agreement upon ninety (90) days notice if such notice is sent no later than forty-eight months from the last date of regulatory submission.

8.2 Termination for Breach. Either Party may terminate this Agreement upon the breach of any provision of this Agreement by the other Party if such breach is not cured by the breaching Party within thirty (30) calendar days for monetary defaults, and sixty (60) calendar days for non-monetary defaults, after receipt by the breaching Party of written notice from the other Party of such default. A monetary default shall be deemed to occur if an undisputed payment is not made by the date such payment is due and payable under the terms of this Agreement or the Product Master Plan. In the event of any termination for breach, upon Celator's request, **a**ny and all Celator-supplied Components held by Baxter shall be made available for pick-up by Celator at Baxter's facility.

8.3 Termination for Financial Matters. This Agreement may be terminated immediately by either Party by giving the other Party written notice thereof in the event such other Party makes a general assignment for the benefit of its creditors, or proceedings of a case are commenced in any court of competent jurisdiction by or against such Party seeking (a) such Party's reorganization, liquidation, dissolution, arrangement or winding up, or the composition or readjustment of its debts, (b) the appointment of a receiver or trustee for or over such Party's property, or (c) similar relief in respect of such Party under any law relating to bankruptcy, insolvency, reorganization, winding up or composition or adjustment of debt, and such proceedings shall continue undismissed, or an order with respect to the foregoing shall be entered and continue unstated, for a period of more than ninety (90) days.

8.4 Non-cancelable Costs and Expenses. In the event of the termination of this Agreement, except by Celator as a result of a breach by Baxter under Section 8.2, Celator shall (a) reimburse Baxter for all Baxter-supplied Components ordered prior to termination and not cancelable without cost to Baxter or, if less, at Celator's option shall

reimburse Baxter for the costs of cancellation, and (b) pay Baxter for any open Firm Purchase Orders. Moreover, Celator agrees to purchase from Baxter at cost all semi-finished and finished Products in stock. Baxter shall promptly deliver to Celator, at Celator's cost, all Components, semi-finished and finished Products for which Celator reimburses Baxter pursuant to this Section 8.4. Baxter shall use commercially reasonable efforts to mitigate the costs and expenses of Celator under this Section 8.4. Celator shall make payment for all expenses described in this Section 8.4 thirty (30) days after the invoice date, which date shall not be earlier than the date of delivery of any related materials to Celator.

8.5 Payment on Termination of Commercial Production. In addition to the costs and expenses payable in Section 8.4, in the event of termination of this Agreement, except by Celator as a result of a breach by Baxter under Section 8.2 or expiry of the Term of this Agreement, Celator shall pay Baxter (a) the difference, if any, between the Production Price of Product actually ordered and purchased by Celator in the calendar year in which termination occurs and, the greater of the (i) Production Price of the Annual Obligation and (ii) Production Price of the Annual Obligation, as defined in Section 4.3, in such calendar year, (b) as liquidated damages and not as a penalty, [*] of the Production Price of the Annual Obligation for the next succeeding calendar year after the calendar year in which termination occurs.

8.6 Procedure in case of Expiry of Agreement. In the event the Agreement expires pursuant to Section 8.1, Celator is obliged to buy from Baxter all Baxter-supplied Components reasonably ordered by Baxter during the normal course of business unless Baxter can reasonably use these materials otherwise.

8.7 Transfer of Technology.

8.7.1 On termination or expiration of this Agreement through any means and for any reason, the right of Baxter to make Product hereunder shall terminate, and except for termination by Baxter due to a breach by Celator under Section 8.2, Baxter shall reasonably cooperate with Celator by providing to Celator, at Celator's cost, copies or drafts of the following items, to the extent they exist, within sixty (60) days of termination or expiration:

8.7.1.1 Baxter's Manufacturing Batch Records for the Product;

8.7.1.2 Pertinent analytical reports, and manufacturing development and validation reports of studies used to determine and justify the final manufacturing process related to the Product; and

8.7.1.3 Any and all Celator-supplied Components in storage at Baxter which shall be made available for pick-up by Celator at Baxter's facility; and

[*]

8.8 Survival. Termination, expiration, cancellation or abandonment of this Agreement through any means or for any reason, except as set forth in Section 13.1, shall be without prejudice to the rights and remedies of either Party with respect to any antecedent breach of any of the provisions of this Agreement. The provisions of Articles 12, 13, 14, 15, 16, 17 and 18 hereof, and such other provisions of this Agreement that, by their terms, are intended to continue beyond the Term of this Agreement, shall survive expiration or termination of this Agreement.

Article 9, PRODUCTION OF PRODUCT

9.1 Production. Baxter shall Produce Product in accordance with cGMP and all other applicable laws or regulations as set forth in the Product Master Plan. At no additional cost and at times mutually agreed to by the Parties, Celator shall have the right to have a representative of Celator in the facility to observe Production.

9.2 Audits. Celator shall have the right to audit Baxter's facilities to determine compliance with (i) cGMP and (ii) applicable laws and regulations. Such audits shall be scheduled at mutually agreeable times upon reasonable advance written notice to Baxter. Except for the first audit under this Agreement, audits shall be at Celator's expense at one (1) audit every [*] with the exception of any audits arising from a reasonable basis for concern (such as Baxter's compliance status) shall be at Baxter's expense as detailed in Product Master Plan. If Celator requests additional audits which are not due to Baxter's compliance status and Baxter agrees to such audits, Celator will incur fees as reasonably determined by Baxter. Such fees shall be paid promptly upon completion of such audits. In connection with performing such audits, Celator shall comply with all reasonable rules and regulations promulgated by Baxter; provided, however, that such rules and regulations shall not hinder Celator's ability to conduct the audits. All information disclosed or reviewed in such inspections shall be deemed to be the property of Baxter and Baxter Confidential Information.

9.3 Testing. Baxter shall test, or cause to be tested by third party testing facilities qualified by Baxter, in accordance with the Product Specifications, each Batch

of Product Produced pursuant to this Agreement before delivery to Celator. A certificate of analysis for each Batch of Product delivered to Celator shall set forth the items tested by Baxter, specifications and test results. Celator shall assume full responsibility for final release of each Batch of the Product.

9.4 Stability Testing. At Celator's expense, Baxter shall perform all stability testing in compliance with the International Conference on Harmonization for Registration of Pharmaceuticals for Human Use (ICH) requirements performed on clinical, development, conformance and/or commercial Production Batches of Product. Such testing shall be performed in accordance with the procedures set out in the Product specific Baxter SOPs for the stability protocol and Product Master Plan. Prior to any stability testing, Celator shall have the right to review and approve the stability testing protocol and Celator shall receive a summary report of the data generated from the stability tests. All stability data shall be forwarded to Celator within thirty (30) days of the scheduled test date.

9.5 Permits and Licenses. Celator shall have sole responsibility at its expense for obtaining all permits and licenses necessary and required for use, sale and / or distribution of Product Produced by Baxter hereunder. Baxter shall be responsible at its expense to obtain and maintain all generally required licenses required for it to carry out its development, regulatory and production obligations hereunder.

9.6 Regulatory Requirements. Each Party promptly shall notify the other of new regulatory requirements of which it becomes aware which are relevant to the Production of a Product under this Agreement and which are required by an applicable Regulatory Authority or other applicable laws or governmental regulations, and the Parties shall confer with each other with respect to the best means to comply with such requirements. Baxter shall have no obligation to Produce Product in compliance with the explicit requirements of a Regulatory Authority not specified in the Product Master Plan; provided that, if Celator shall request Baxter to do so, the Parties shall confer with each other with respect to such request.

9.7 Equipment Expenses. If Baxter is required by Celator to obtain specialized equipment for use solely to Produce Product for Celator, the costs of such equipment shall be paid by Celator, i.e., [*], including shipping and insurance costs, plus VAT and reasonable installation costs. Baxter shall advise Celator of the specialized equipment required for use solely to Produce Product for Celator and the estimated costs associated with the purchase and installation of such equipment. Such costs shall be agreed upon by the Parties prior to Baxter ordering such equipment. Celator shall be invoiced for all approved costs regarding the specialized equipment purchased by Baxter in accordance with this Section 9.7, and Celator shall make payment therefor promptly thereafter.

9.8 Ownership of Equipment. All specialized equipment supplied by or paid for by Celator shall be Celator's property and shall be used by Baxter only for the Production of Product. This equipment is listed in the Product Master Plan. Upon any

termination or expiration of this Agreement, Celator shall have the option of either (i) taking custody of the specialized equipment supplied by or paid for by it, or (ii) allowing Baxter to purchase such equipment by paying Celator the then current fair market value of such equipment.

9.9 Records. Baxter shall, in accordance with applicable laws and as reasonably requested by Celator, maintain complete cGMP production records and reports relating to its activities performed in providing the services under this Agreement (including, without limitation, keeping accurate records of the manufacture, testing and packaging of the Products). Baxter shall provide Celator with access to all such records at mutually agreeable times; provided, however, that such access shall be required only during normal business hours and with reasonable advance written notice. The Parties agree that Baxter shall have no obligation to provide or disclose its financial records to Celator.

9.10 Celator Property. In accord with Baxter SOPs, Baxter shall properly use, store, handle and maintain all Celator property, including but not limited to Celator-supplied Components, equipment and Product, in Baxter's custody or control.

Article 10, REGULATORY

10.1 Regulatory Approvals. Celator will use commercially reasonable efforts to pursue Regulatory Approval of marketing licenses for Clinical Product Produced by Baxter hereunder. Celator will advise Baxter of document requirements in support of filings and similar applications required of foreign governments and agencies including amendments, license applications, supplements and maintenance of such. Baxter will provide documents and assist Celator in preparation of submissions to Regulatory Authorities designated by Celator in support of Celator's applications required of governments and licenses. All regulatory submission preparation and maintenance performed by Baxter for Celator shall be specified in the Product Master Plan. Prior to submission to the Regulatory Authority, Celator will provide Baxter with a copy of the CMC section for review and comment. A final copy of the CMC section will be provided by Celator to Baxter upon submission to the Regulatory Authority. Upon Regulatory Approval, Celator will notify Baxter within two (2) business days of such approval and the anticipated date of Product launch to the market.

10.2 Regulatory Authority Inspections. At Celator's request, Baxter will authorize Regulatory Authorities to review related applications on Celator's behalf as set forth in the Quality Agreement. Celator shall bear the costs of non-routine Regulatory Authority Inspection or inspections directly relating to the Product as set forth in the Product Master Plan.

Article 11, TRADEMARKS

11.1 Celator grants to Baxter a non-exclusive, royalty free license to use Celator Trademarks for the sole purpose of allowing Baxter to fulfill its responsibilities under this Agreement. Such license shall not be transferable in whole or in part.

11.2 Celator shall be solely responsible for selecting, registering and enforcing Celator Trademarks used to identify the Product and, except as set forth in Section 11.1, shall have sole and exclusive rights in such Celator Trademarks.

Article 12, REPRESENTATIONS AND WARRANTIES

12.1 Mutual Representations. Each Party hereby represents and warrants to the other Party that (a) the person executing this Agreement on behalf of such Party is legally authorized to execute this Agreement; (b) this Agreement is legal and valid and the obligations binding upon such Party enforceable by its terms; and (c) the execution, delivery and performance of this Agreement does not conflict with any agreement, instrument or understanding, oral or written, to which such Party may be bound, nor violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

12.2 Baxter Warranty. Baxter represents and warrants that it shall Produce all Product in accordance with cGMP and, that all Commercial Product shall meet Product Specifications. Baxter represents and warrants that it has obtained (or will obtain prior to Producing Product), and will remain in compliance with during the Term of this Agreement, all permits, licenses and other authorizations (the **"Permits"**) which are required under laws and regulations applicable to the Production only of Product as specified in the Product Master Plan; provided, however, Baxter shall have no obligation to obtain Permits relating to the sale, marketing, distribution or use of Product or with respect to the labeling of Product. Baxter makes no representation or warranty with respect to the sale, marketing, distribution or use of API, Product or to printed materials specified by Celator or its consignee.

12.3 Disclaimer of Warranties. Except for those warranties set forth in Sections 12.1 and 12.2 of this Agreement, Baxter makes no warranties, written, oral, express or implied, with respect to Product or the Production of Product. ALL OTHER WARRANTIES, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT HEREBY ARE DISCLAIMED BY BAXTER. NO WARRANTIES OF BAXTER MAY BE CHANGED EXCEPT IN WRITING AND SIGNED BY A DULY AUTHORIZED REPRESENTATIVE OF BAXTER. Celator accepts Product subject to the terms hereof.

12.4 Celator Warranties. Celator warrants that (a) it has the right to give Baxter any information provided by Celator hereunder, and that Baxter has the right to use such information for the Production of Product, and (b) Celator has no knowledge of any (i) patents or other intellectual property rights that would be infringed by Baxter's Production of Product under this Agreement, or (ii) proprietary rights of third parties which would be violated by Baxter's performance hereunder, and (c) Celator has obtained (or will obtain prior to producing the Product), and will maintain, update and remain in compliance with all permits, licenses and other authorizations during the Term of this Agreement, which are required under federal, state and local law, rules and regulations applicable to the Production, use and sale of the Product. Celator warrants that the API provided to Baxter hereunder will (1) conform to the API specifications and (2) not be adulterated or misbranded within the meaning of the FD&C Act. Celator will use and promote the Product in a manner not inconsistent with its regulatory filings and approvals.

12.5 FD&C Act Matters. Baxter represents and covenants as of the date of this Agreement and continuously during the term of this Agreement that it is not debarred pursuant to Section 335(a) or 335(b) of the FD&C Act. Baxter represents that it has not been debarred under the Act in the past five (5) years. Baxter will not employ or use the services of any person or entity to perform the Production of Product who is debarred under the Act or to Baxter's knowledge has engaged in activities that could lead to being debarred under the Act.

Article 13, LIABILITY AND WAIVER OF SUBROGATION

13.1 Limitation of Liability. Celator's sole and exclusive remedies for breach of this Agreement are limited to those remedies set forth in Article 7, 8, 13.2.1, 14, and 16. Except as expressly provided in this Agreement, under no circumstances shall either Party be liable for loss of use or profits or other collateral, special, consequential or other damages, losses, or expenses, including but not limited to the cost of cover, in connection with or by reason of the Production and delivery of Product under this Agreement whether such claims are founded in tort or contract. The foregoing constitutes the sole and exclusive remedy of Celator and the sole and exclusive liability of Baxter. As permitted by the applicable laws, under no circumstances shall Baxter's aggregate liability to Celator, including but not limited to third party claims, exceed the following: [*]. All claims for breach or default under this Agreement shall be brought within two (2) years after the cause of action incurred or shall be deemed waived.

13.2 Waiver of Subrogation. Except to the extent expressly set forth herein, all Baxter-supplied Components and equipment owned and used by Baxter in the Production of Product (collectively, the **"**Baxter Property**"**) shall at all times remain the property of Baxter until delivery of Product as specified under Section 6.1 and Baxter assumes risk of loss for such Baxter Property. Baxter hereby waives any and all rights of recovery against Celator and its Affiliates, and against any of their respective directors,

officers, employees, agents or representatives, for any loss or damage to Baxter Property to the extent the loss or damage is covered or could be covered by insurance on the Baxter Property (whether or not such insurance is described in this Agreement). Celator assumes all risk of loss for all Celator equipment used in Production, Celator-supplied Components and all Product (collectively, the **"**Celator Property**"**) except as provided in Section 13.2.1. Celator hereby waives any and all rights of recovery against Baxter and its Affiliates, and against any of their respective directors, officers, employees, agents or representatives, for any loss or damage to the Celator Property to the extent the loss or damage is covered or could be covered by insurance on the Celator Property (whether or not such insurance is described in this Agreement).

13.2.1 Reimbursement for Lost or Damaged Celator Property In the event of loss or damage of a Celator-supplied Component or Product that does not occur during Production, if such loss or damage is solely due to Baxter's negligence or willful misconduct, Baxter shall reimburse Celator for its actual out-of-pocket costs for the lost or damaged Celator-supplied Components or Product, at the amount(s) set forth in the Product Master Plan, provided, however, that such reimbursement for any Celator-supplied Components will not exceed [*]. In the event of loss or damage of Celator equipment used by Baxter, which damage or loss is solely due to Baxter's negligence or willful misconduct, Baxter shall promptly replace or repair such equipment [*].

Article 14, INDEMNIFICATION

14.1 Celator Indemnification. Celator shall indemnify, defend and hold harmless Baxter and its Affiliates and any of their respective directors, officers, employees, subcontractors and agents (collectively "Indemnified Baxter Parties") from and against any and all liabilities, obligations, penalties, claims, judgments, demands, actions, disbursements of any kind and nature, suits, losses damages, costs and expenses (including, without limitation, reasonable attorney's fees) arising out of or in connection with property damage or personal injury (including without limitation death) of third parties (collectively "Claims") in connection with (a) Celator's transport, storage, promotion, labeling, marketing, distribution, use or sale of Product, (b) Celator's negligence or willful misconduct, (c) Celator's breach of this Agreement, or (d) any claim that the use, sale, Production, marketing or distribution of Product by Baxter or Celator violates the patent, trademark, copyright or other proprietary rights of any third party, except if any of the foregoing (a) or (d) is caused solely by the negligence or willful misconduct of any of the Indemnified Baxter Parties or [*].

14.2 Baxter Indemnification. Baxter shall indemnify, defend and hold harmless Celator and its Affiliates and any of their respective directors, officers, employees, subcontractors and agents (collectively the "Indemnified Celator Parties")

from and against any and all liabilities, obligations, penalties, claims, judgments, demands, actions, disbursements of any kind and nature, suits, losses, damages, costs and expenses (including, without limitation, reasonable attorney's fees) arising out of or in connection with property damage or personal injury (including without limitation death) of third parties (collectively, the "Claims") resulting solely from Baxter's negligence or willful misconduct [*].

14.3 Indemnitee Obligations. A Party which intends to claim indemnification under this Article 14 (the **"Indemnitee"**) shall promptly notify the other Party (the **"Indemnitor"**) in writing of any action, claim or other matter in respect of which the Indemnitee or any of its Affiliates, or any of their respective directors, officers, employees, subcontractors, or agents, intend to claim such indemnification; provided, however, that failure to provide such notice within a reasonable period of time shall not relieve the Indemnitor of any of its obligations hereunder except to the extent the Indemnitor is prejudiced by such failure. The Indemnitee shall permit, and shall cause its Affiliates, and their respective directors, officers, employees, subcontractors and agents to permit, the Indemnitor, at its discretion, to settle any such action, claim or other matter, and the Indemnitee agrees to the complete control of such defense or settlement by the Indemnitor. Notwithstanding the foregoing, the Indemnitor shall not enter into any settlement that would adversely affect the Indemnitee's rights hereunder, or impose any obligations on the Indemnitee in addition to those set forth herein, in order for it to exercise such rights, without Indemnitee's prior written consent, which shall not be unreasonably withheld or delayed. No such action, claim or other matter shall be settled by the Indemnitor without the prior written consent of the Indemnitee, which shall not be unreasonably withheld or delayed. The Indemnitee, its Affiliates, and their respective directors, officers, employees, subcontractors and agents shall fully cooperate with the Indemnitor and its legal representatives in the investigation and defense of any action, claim or other matter covered by the indemnification obligations of this Article 14. The Indemnitee shall have the right, but not the obligation, to be represented in such defense by counsel of its own selection and at its own expense.

Article 15, INSURANCE

15.1 Celator Insurance. Celator shall procure and maintain, during the Term of this Agreement and for a period one (1) year beyond the expiration date of Product, Commercial General Liability Insurance, including without limitation, Product Liability and Contractual Liability coverage (the **"Celator Insurance"**). Celator Insurance shall cover amounts not less than 10,000,000 € (ten million EURO) combined single limit and shall be with an insurance carrier reasonably acceptable to Baxter. Baxter shall be named as an additional insured on Celator Insurance and Celator promptly shall deliver a certificate of Celator Insurance and endorsement of additional insured to Baxter evidencing such coverage. If Celator fails to furnish such certificates or endorsements, or if at any time during the Term of this Agreement Baxter is notified of the cancellation or lapse of Celator Insurance, and Celator fails to rectify the same within fifteen (15) calendar days after notice from Baxter, in addition to all other remedies available to

Baxter hereunder, Baxter, at its option, may terminate this Agreement. Any deductible and/or self insurance retention shall be the sole responsibility of Celator.

15.2 Baxter Insurance. Baxter acknowledges and agrees that during the Term of this Agreement it shall maintain adequate insurance and/or a self-insurance program for liability insurance, including products liability and contractual liability insurance, to cover Baxter's obligations under this Agreement, including but not limited to those set forth in Section 14.2 of this Agreement. Baxter shall provide Celator with evidence of such insurance and/or self-insurance program, upon Celator's request.

15.3 No Limitation. In no event will the liability of either Party be limited to that which is recoverable by insurance.

Article 16, COMPLAINTS, RECALL OF PRODUCT

16.1 Complaints. In case Celator or Baxter receives complaints regarding Products which require Baxter to perform any investigations or conduct tests, Celator agrees to reimburse Baxter for any costs incurred in connection with such complaints. Notwithstanding the foregoing, in the event of a complaint regarding Commercial Product, if the Product is non-conforming solely due to the negligence or willful misconduct of Baxter, such investigations or tests to be performed by Baxter shall be at Baxter's expense.

16.2 Recalls. In the event Celator shall be required to recall any Product because such Product may violate local, state or federal laws or regulations, the laws or regulations of any applicable foreign government or agency or the Product Specifications, or in the event that Celator elects to institute a voluntary recall, Product withdrawal or field correction, Celator shall be responsible for coordinating such recall. Celator promptly shall notify Baxter if any Product is the subject of a recall and provide Baxter with a copy of all documents relating to such recall. Baxter shall cooperate with Celator in connection with any recall, at Celator's expense. Celator shall be responsible for all of the costs and expenses of such recall, withdrawal or field correction. With respect to Commercial Product, if the recall, withdrawal or field correction arises solely from the negligence or willful misconduct of Baxter [*]. Furthermore, in the event of any Product recall where the recall is necessitated solely due to the negligence or willful misconduct of Baxter [*].

Article 17, INTELLECTUAL PROPERTY

17.1 Existing Intellectual Property. Except as the Parties may otherwise expressly agree in writing, each Party shall continue to own its existing patents, trademarks, copyrights, trade secrets and other intellectual property, without conferring any interests therein on the other Party. Without limiting the generality of the preceding sentence, Celator shall retain all right, title and interest arising under the applicable laws, rules and regulations in and to all Drug Products, labeling and trademarks associated therewith (collectively, **"Celator's Intellectual Property"**). Neither Baxter nor any third party shall acquire any right, title or interest in Celator Intellectual Property by virtue of this Agreement or otherwise, except to the extent expressly provided herein.

17.2 Individually Owned Inventions. Except as the Parties may otherwise agree in writing, all Inventions (as defined herein) which are conceived, reduced to practice, or created by a Party in the course of performing its obligations under this Agreement shall be solely owned and subject to use and exploitation by the inventing Party without a duty to account to the other Party.

17.3 Product-Related Inventions. Celator and Baxter each acknowledge and agree that all rights, title and interest in and to any Inventions, as between the Parties, shall be owned by Celator, except for Process Inventions, which shall be owned by Baxter and subject to the restrictions, licenses and conditions set forth in Section 17.4 below.

17.4 Process Inventions. The Parties agree that such Process Inventions shall be owned by Baxter and subject to the restrictions and conditions set forth in this Section 17.4. Specifically, Baxter grants to Celator a non-exclusive, paid-up, royalty-free, irrevocable worldwide license to Process Inventions, with the right of Celator or any of its sub-licensees to sublicense such Process Inventions, for the manufacturing of the Product.

17.5 Disclaimer. Except as otherwise expressly provided herein, nothing contained in this Agreement shall be construed or interpreted, either expressly or by implication, or otherwise, as: (i) a grant, transfer or other conveyance by either Party to the other of any right, title, license or other interest of any kind in any of its Inventions or other intellectual property, (ii) creating an obligation on the part of either Party to make any such grant, transfer or other conveyance or (iii) requiring either Party to participate with the other Party in any cooperative development program or project of any kind or to continue with any such program or project.

17.6 Rights in Intellectual Property. The Party owning any Intellectual Property shall have the worldwide right to control the drafting, filing, prosecution and maintenance of patents covering the Inventions relating to such Intellectual Property, including decisions about the countries in which to file patent applications. Patent costs associated with the patent activities described in this Section shall be borne by the sole

owner. Each Party will cooperate with the other Party in the filing and prosecution of patent applications. Such cooperation will include, but not be limited to, furnishing supporting data and affidavits for the prosecution of patent applications and completing and signing forms needed for the prosecution, assignment and maintenance of patent applications.

17.7 Confidentiality of Intellectual Property. Intellectual Property shall be deemed to be the Confidential Information of the Party owning such Intellectual Property. The protection of each Party's Confidential Information is described in Article 18. Any disclosure of information by one Party to the other under the provisions of this Article 18 shall be treated as the disclosing Party's Confidential Information under this Agreement. It shall be the responsibility of the Party preparing a patent application to obtain the written permission of the other Party to use or disclose the other Party's Confidential Information in the patent application before the application is filed and for other disclosures made during the prosecution of the patent application.

Article 18, CONFIDENTIAL INFORMATION, NONDISCLOSURE AND PUBLICITY

18.1 Definition. "Confidential Information**"** means: (a) all information related to the Product, CPX-351, including, without limitation, documentation, drawings, designs and specifications; (b) all information related to Baxter's contract manufacturing services, technologies and operations; (c) any non-public information of a party, including, without limitation, any information relating to a party's technology, techniques, know-how, research, designs, finances, accounts, procurement requirements, manufacturing, customer lists, business forecasts and marketing plans disclosed in connection with this Agreement; provided, however, that such information of a Party that is disclosed in writing or electronically is designated as "Confidential" or "Proprietary" at the time of disclosure, in the covering letter or transmission or otherwise, or that if disclosed orally, is identified as "Confidential" or "Proprietary" at the time of disclosure and confirmed as such in a writing sent by the disclosing party to the receiving party within thirty (30) days of any such disclosure; and (d) the specific terms and pricing of this Agreement (including any Product transfer prices). Notwithstanding the foregoing, any Confidential Information disclosed by visual observation during a tour, site visit or audit of either Party's or any of its Affiliates laboratories, manufacturing plants or other facilities shall automatically be deemed Confidential Information for purposes of this Agreement.

18.2 Exclusions. The obligations in Section 18.3 will not apply to the extent that it can be demonstrated that any Confidential Information: (a) is or becomes generally known to the public through no fault of or breach of this Agreement by the receiving party; (b) was rightfully in the receiving party's possession at the time of disclosure, without an obligation of confidentiality; (c) is independently developed by the receiving party without use of the disclosing party's Confidential Information; or (d) is rightfully obtained by the receiving party from a third party without restriction on use or disclosure.

18.3 Obligations. Each Party agrees not to use the other Party's Confidential Information, except as necessary for the performance of this Agreement, and shall not disclose such Confidential Information to any third party, except to those of its directors, officers, employees, consultants, contractors, agents, lawyers, accountants or other professional advisors and subcontractors and those of its Affiliates ("Representatives") who need to know such Confidential Information for the performance of this Agreement or as otherwise expressly permitted in this Agreement, provided that each such Representative is subject to a written agreement that includes binding use and disclosure restrictions that are at least as protective as those set forth herein. Each Party will use all reasonable efforts to maintain the confidentiality of the other Party's Confidential Information in its possession or control, but in no event less than the efforts that it ordinarily uses with respect to its own confidential information of similar nature and importance. The foregoing obligations will not restrict either Party from: (i) disclosing Confidential Information pursuant to the order or requirement of a court, administrative agency, or other governmental body, provided that the Party required to make such disclosure gives reasonable notice to the other party to enable it to contest such order or requirement; (ii) disclosing the terms of this Agreement, in confidence, to its business and legal advisors or to investors or lenders that are engaged in active due diligence regarding a financing of such Party; or (iii) disclosing the terms of this Agreement, in confidence, to potential partners or acquirers that are engaged in active due diligence regarding a transaction involving, among other things, the Product, except for those parties competitive to Baxter identified in Exhibit C, which disclosure will require the approval of Baxter, which approval shall not be unreasonably withheld.

18.4 Limitation of Disclosure. The Parties agree that, except as otherwise may be required by applicable laws, regulations, rules or orders, including without limitation the rules and regulations, and except as may be authorized in Section 18.4 and unless otherwise agreed in the Agreement, no information concerning this Agreement and the transactions contemplated herein shall be made public by either Party without the prior written consent of the other.

18.5 Publicity and SEC Filings. The Parties agree that the public announcement of the execution of this Agreement shall be by only one or more press releases mutually agreed to by the Parties. The failure of a Party to return a draft of a press release with its proposed amendments or modifications to such press release to the other Party within five (5) days of such Party's receipt of such press release shall be deemed as such Party's approval of such press release as received by such Party. Each Party agrees that it shall cooperate fully and in a timely manner with the other with respect to all disclosures to the Securities and Exchange Commission or any other governmental or regulatory agencies, including requests for confidential treatment of Confidential Information of either Party included in any such disclosure.

18.6 Duration of Confidentiality. All obligations of confidentiality and non-use imposed upon the Parties under this Agreement shall expire five (5) years after the expiration or earlier termination of this Agreement.

18.7 Other Initiatives. It is understood that Baxter may have present or future initiatives, including initiatives with third parties, involving products or processes that compete with or are similar to the Product Produced under this Agreement. Accordingly, Celator acknowledges that nothing in this Agreement shall be construed as a representation or inference by either Party that it will not develop for itself, or produce for others products or implement processes that compete with the Product or are similar, provided that Confidential Information is not used in breach of this Agreement.

18.8 Prior Mutual Confidentiality Agreement. The Parties acknowledge the existence of a Mutual Confidentiality Agreement, as further amended, entered into by and between Celator and Baxter effective May 14, 2008 (collectively, the **"CDA"**). The Parties agree that any Confidential Information exchanged prior to the Effective Date of this Agreement shall be governed by the CDA, and any Confidential Information exchanged on or after the Effective Date of this Agreement, shall be governed by this Article 18.

Article 19, FORCE MAJEURE

19.1 Subject to the provisions of Section 16.2 of this Agreement, any delay in the performance of any of the duties or obligations of either Party hereto (except with respect to the payment of monies due) caused by an event outside the affected Party's reasonable control shall not be deemed a breach of this Agreement, and unless provided to the contrary herein, the time required for performance shall be extended for a period equal to the period of such delay. Such events shall include without limitation, acts of God; acts of public enemies; insurrections; riots; terrorist actions; injunctions; embargoes; labor disputes, including strikes, lockouts, job actions, or boycotts; fires; explosions; floods; shortages of material, Components or energy; delays in the delivery of Components; Product recalls or withdrawals; acts or orders of any government or agency thereof or of Regulatory Authority; and other unforeseeable causes beyond the reasonable control and without the fault or negligence of the Party so affected. The Party so affected shall give prompt notice to the other Party of such cause and a good faith estimate of the continuing effect of the force majeure condition and duration of the affected Party's nonperformance, and shall take whatever reasonable steps are necessary or appropriate to relieve the effect of such causes as rapidly as possible. If the period of nonperformance by Baxter because of Baxter force majeure conditions exceeds one hundred eighty (180) calendar days, Celator may terminate this Agreement by written notice to Baxter. If the period of nonperformance by Celator because of Celator force majeure conditions exceeds one hundred eighty (180) calendar days, Baxter may terminate this Agreement by written notice to Celator.

Article 20, NOTICES

20.1 All notices hereunder shall be delivered by facsimile (confirmed by international courier service), to the following address of the respective Parties:

If to Celator: Celator Pharmaceuticals, Inc.
303B College Road East
Princeton, NJ 08540
Attn: Donna Cabral-Lilly, Ph.D.,
Head of Pharmaceutical Development
Fax No. (609) 243-0202
Telephone No. (609) 243-6216

With a copy to: Duane Morris LLP
30 South 17th Street
Philadelphia, PA 19103-4196
Attn: Kathleen M. Shay
Fax No. (215) 689-4382
Telephone No. (215) 979-1210

If to Baxter: Baxter Oncology GmbH
Kantstr. 2
33790 Halle / Westfalen
Germany
Attn: Associate Director, Contract Manufacturing
and Business Development
Fax No. +49 5201 711 1880
Telephone No. +49 5201 711 1864

With a copy to: Baxter Germany
Edisonstr. 4
85719 Unterschleißheim
Germany
Attn: Legal Counsel
Fax No. +49 89 31701 547
Telephone No. +49 89 31701 285

Notices shall be effective on the day following the date of transmission if sent by facsimile, and on the second business day following the date of delivery to the overnight delivery service if sent by overnight delivery. A Party may change its address listed above by notice to the other Party given in accordance with this Section.

Article 21, APPLICABLE LAW

21.1 This Agreement is being delivered and executed in Germany. In any action brought regarding the validity, construction and enforcement of this Agreement, it shall be governed in all respects by the substantive and procedural laws of Germany, without regard to the principles of conflict of laws. The courts of New York, U.S.A., shall have personal jurisdiction over the Parties hereto in all matters arising hereunder.

Article 22, ASSIGNMENT

22.1 Neither Party shall assign this Agreement or any part hereof or any interest herein to any third party (or use any subcontractor) without the prior written approval of the other Party, which shall not be unreasonably withheld. Either Party may assign this Agreement to one of its Affiliates without approval of the other Party; provided, however, that such assignment shall not relieve the assigning Party of responsibility for the performance of its obligations hereunder. Notwithstanding anything to the contrary set forth above: (a) no consent shall be required in the case of a transfer by Baxter in a transaction involving the merger, consolidation, or sale of all or substantially all of the assets of Baxter, and (b) in the case of a transfer by Celator in transaction involving the merger, consolidation, or sale of all or substantially all of the assets of Celator and such transaction relates to the line of business to which the product relates; provided, however, in each case the permitted assignee(s) shall assume all obligations of its assignor under this Agreement and such assignment shall not relieve the assigning Party of responsibility for the performance of its obligations hereunder, unless the Parties agree to such relief.

Article 23, SUCCESSORS AND ASSIGNS

23.1 This Agreement shall be binding upon and shall inure to the benefit of the Parties hereto, their successors and permitted assigns.

Article 24, ENTIRE AGREEMENT

24.1 This Agreement including the Agreements listed in Sections 2.1 and 2.2 and the Mutual Confidentiality Agreement signed by Celator and Baxter Healthcare Corporation (an Affiliate of Baxter Oncology GmbH) and effective on May 14, 2008 constitutes the entire agreement between the Parties concerning the subject matter hereof and supersedes all written or oral prior agreements or understandings with respect thereto.

Article 25, SEVERABILITY

25.1 If any term or provision of this Agreement shall for any reason be deemed to be invalid or unenforceable, such term or provision shall be construed in such a way as to make it valid and enforceable to the maximum extent possible. Any invalidity or unenforceability of any term or provision of this Agreement shall attach only to such term or provision and shall not affect or render invalid or unenforceable any other term or provision of this Agreement.

Article 26, WAIVER AND MODIFICATION OF AGREEMENT

26.1 No waiver or modification of any of the terms of this Agreement shall be valid unless in writing and signed by both Parties hereto. Failure by either Party to enforce any rights under this Agreement shall not be construed as a waiver of such rights nor shall a waiver by either Party in one or more instances be construed as constituting a continuing waiver or as a waiver in other instances.

Article 27, INDEPENDENT CONTRACTOR

27.1 Both Parties shall act as an independent contractor for the other Party in providing the services required hereunder and shall not be considered an agent of, or joint venturer with, the other Party.

Article 28, COUNTERPARTS; METHOD OF TRANSMISSION

28.1 This Agreement may be executed by the Parties on separate counterparts and exchanged by facsimile or other electronic transmission, which counterparts, when so delivered shall each be deemed to be an original and both counterparts, taken together, shall constitute one and the same agreement.

(**Signature page to follow**)

IN WITNESS WHEREOF, the Parties have caused this Clinical and Commercial Manufacturing and Supply Agreement to be signed by their duly authorized representatives as of the Effective Date.

BAXTER ONCOLOGY GmbH		**CELATOR PHARMACEUTICALS, INC.**	
By:	/s/ Brik V. Eyre	By:	/s/ Scott T. Jackson
Name:	Brik Eyre	Name:	Scott T. Jackson
Title:	General Manager BioPharma Solutions	Title:	Chief Executive Officer

EXHIBIT A

CELATOR'S ANNUAL OBLIGATION

Contract Year	One Market Approval (U.S. or Europe)	Two Market Approvals (U.S. and Europe)
Contract Year One	[*]	[*]
Contract Year Two	[*]	[*]
Contract Year Three	[*]	[*]
Contract Year Four	[*]	[*]

Note: For any Contract Year(s) after Contract Year Four, the parties will mutually agree upon an Annual Obligation for any such additional Contract Years as set forth in Section 4.3.1.

EXHIBIT B

BAXTER'S MAXIMUM SUPPLY OBLIGATION

Contract Year(s)	One Market Approval (U.S. or Europe)	Two Market Approvals (U.S. and Europe)
Contract Year One	[*]	[*]
Contract Year Two	[*]	[*]
Contract Year Three	[*]	[*]
Contract Year Four	[*]	[*]

Note: For any Contract Year after Contract Year Four, the parties will mutually agree upon Baxter's Maximum Supply Obligation for any such additional Contract Years as set forth in Section 4.3.1.

EXHIBIT C
PARTIES COMPETITIVE TO BAXTER

Hospira One 2 One
Vetter Pharma International GmbH
Ben Venue Laboratories
Patheon Inc.
Catalent Pharma Solutions Inc.
DSM Pharmaceuticals, Inc.
HollisterStier Contract Manufacturing
Oso BioPharmaceutical Manufacturing LLC
Althea Technologies Inc.
Fresenius Kabi AG
Cook Incorporated
Teva-PharmaChemie
Pierre Fabre Medicament Production
BSP Pharmaceuticals srl
NextPharma Technologies
GP Pharm.

CERTAIN PORTIONS OF THIS EXHIBIT (INDICATED BY [*]) HAVE BEEN EXCLUDED PURSUANT TO ITEM 601(B)(10) OF REGULATION S-K BECAUSE THEY ARE BOTH NOT MATERIAL AND ARE THE TYPE THAT THE COMPANY TREATS AS PRIVATE AND CONFIDENTIAL.

AMENDMENT NO. 1 CLINICAL AND COMMERCIAL MANUFACTURING AND SUPPLY AGREEMENT

This Amendment No. 1 (**"Amendment No. 1"**) is entered into by JAZZ PHARMACEUTICALS IRELAND LIMITED (**"JAZZ"**) and BAXTER ONCOLOGY GmbH (**"Baxter"**) as of January 18, 2018 (**"Amend No. 1 Effective Date"**).

WHEREAS, Celator Pharmaceuticals, Inc. (**"Celator**") and Baxter entered into that certain Clinical and Commercial Manufacturing and Supply Agreement dated as of December 22, 2010 (the **"Agreement"**);

AND WHEREAS, JAZZ acquired Celator effective July 12, 2016 and the Agreement was assigned to JAZZ effective July 13, 2016;

AND WHEREAS, JAZZ and Baxter wish to amend certain provision(s) of the Agreement to change (i) the purchasing of certain JAZZ-supplied Components, (ii) the forecasting and (iii) the obligations to purchase/supply Product, among other things;

NOW, THEREFORE, in consideration of the foregoing recitals and the mutual promises hereinafter set forth JAZZ and Baxter agree that the following amendments shall be made to the Agreement as of the Amend No. 1 Effective Date:

1. All references to "Celator" under the Agreement are hereby amended to read "JAZZ".

2. Article 1 **"DEFINITIONS"**, the definitions for "Baxter-supplied Components", "Contract Year", "JAZZ-supplied Components" and "Reservation Fees" are hereby deleted and replaced with the following definitions:

"Baxter-supplied Components" shall mean those Components to be supplied by Baxter as specified in the Product Master Plan."

"Contract Year" shall mean the twelve (12) month period commencing on 3 August 2017 and each subsequent twelve (12) month period during the Commercial Term."

"**JAZZ-supplied Components**" shall mean those Components to be supplied by JAZZ as specified in the Product Master Plan."

"Reservation Fees" shall be the fees payable by JAZZ for modification or cancellation of a Firm Purchase Order as set forth in Section 4.4

3. Article 1 **“DEFINITIONS”**, the definitions for “DSPC”, “DSPG” and “Production Price” are hereby deleted in their entirety.

4. Article 1 **“DEFINTIONS”**, the following will be added as a new definition “Campaign”:

“Campaign” shall mean the running of at least [*] of Commercial Product in sequence without interruption by a different product manufactured in the same room which Campaign must result in at least the reduction of [*] of set up, [*] of functional testing and [*] of cleaning post functional testing as compared to the Production of a single Batch of Commercial Product.

5. Section 3.3 including subsection 3.3.1 **“Components”** are hereby deleted and replaced with the following:

“3.3 Components. As set forth in the Product Master Plan, Jazz shall purchase and supply Jazz-supplied Components which Jazz, at its sole cost and expense (including, without limitation, shipping costs), shall supply to Baxter, in a timely manner as set forth in Section 4.5 **Component Delivery Delays**. Baxter shall procure, in a timely manner, and have available for Production of Product Baxter-supplied Components, at its sole cost and expense (including, without limitation, shipping costs), required to satisfy the terms of this Agreement. On receipt of the Components, Baxter shall test such materials as set forth in the Product Master Plan. If, notwithstanding such testing, Jazz determines to assert a claim against a supplier of a Baxter-supplied Component because Jazz discovers a defect in or adulteration of such Baxter-supplied Component that was not discovered by Baxter, Baxter agrees to provide Jazz with all information regarding such Baxter-supplied Component and the supplier thereof as Jazz shall reasonably request and to cooperate with Jazz in the assertion of each such claim.

3.3.1 Vendor/Supplier Qualification. The responsibility for vendor/supplier qualification is set forth in the Quality Agreement.

3.3.2 Baxter-supplied Components. Unless otherwise set forth in a Product Master Plan, Baxter will purchase the Baxter-supplied Components in sufficient quantities and with a shelf life of more than [*] at the time of Baxter’s purchase of such Baxter-supplied Components as is required to meet the greater of (a) JAZZ’s forecasted demand for Product as set forth in the [*] JAZZ’s Rolling Forecast, or (b) the minimum order quantity requirements as defined by the third-party supplier.

3.3.2.1 Unused Baxter-supplied Components. Except in the event JAZZ previously pays for unused Baxter-supplied Components as part of the Reservation Fees paid to Baxter resulting from the cancellation or modification of a Firm Purchase Order (as set out in Section 4.4), if any Baxter-supplied Component ordered in accordance with Section 3.3.2 is not used within [*] of Baxter’s receipt of such Component, JAZZ agrees to

pay Baxter [*] within [*] of the date of Baxter's invoice. If the Baxter-supplied Components paid for by JAZZ have not expired, such Components can be booked on a JAZZ specific material number and used in the future for the Production of Product, and in this case, Baxter will rebate the corresponding cost of the Baxter-supplied Component previously paid for by JAZZ from the Batch price.

3.3.2.2 Expired Baxter-supplied Components. Provided Baxter has met its obligations regarding shelf-life under Section 3.3.2, if any quantities of a Baxter-supplied Component ordered in accordance with Section 3.3.2 expire prior to Baxter's use of such Component in Production of Product, [*] the expired Baxter-supplied Component and [*] the expired Component and [*].

3.3.2.3 Additional Baxter-supplied Components. The Parties agree it is the intention of the Parties that Baxter provide additional Components for the Production of JAZZ's Commercial Product Vyxeos, which Components are currently provided by JAZZ. Such additional Components include [*] (**"Additional Baxter-supplied Components"**). Baxter must confirm, at JAZZ's expense, the cGMP compliance status of the suppliers of the Additional Baxter-supplied Components, pursuant to Baxter's requirements with respect new supplier qualification, prior to Baxter providing any such Component. If Baxter begins to provide and use any of these Additional Baxter-supplied Components in the Production of JAZZ's Commercial Product Vyxeos, the Purchase Price of such Commercial Product will increase to include the cost of such Additional Baxter-supplied Components plus [*] of the cost of the Additional Baxter-supplied Components (as a 'service fee'), which service fee will cover those activities as set forth in the Product Master Plan. This Agreement will be amended to reflect such increased Purchase Price in a revised Exhibit C. For the avoidance of doubt, once Baxter begins to procure and use the Additional Baxter-supplied Components, such Components will be considered Baxter-supplied Components and subject to this Section 3.3.2, including subsections 3.3.2.1 and 3.3.2.2."

6. Section 4.1 **"Forecasts for Clinical Product"**, the last sentence beginning with "In the event Baster is unable to fill such open capacity…" is hereby deleted and replaced with the following:

"In the event Baxter is unable to fill such open capacity, Baxter may charge JAZZ a Reservation Fee as set forth in Section 4.4."

7. Section 4.2 **"Forecasts for Commercial Product"** is hereby deleted and replaced with the following:

“4.2 Forecasts for Commercial Product. Commencing no less than [*] prior to the date of the Production of the first Batch of Commercial Product, and prior to April 1 of each year thereafter, JAZZ will provide to Baxter in writing a forecast for each calendar year during the remainder of the Term of JAZZ’s estimated contract requirements for each Product (the **“Long Range Forecast”**). The Long Range Forecast submitted by JAZZ will be for general planning purposes only, and shall not be binding on JAZZ or Baxter. Commencing on 3 August 2017, and prior to the tenth (10^{th}) day of each month thereafter, JAZZ will provide to Baxter in writing [*] rolling forecast, broken down by month, of JAZZ’s estimated requirements for the Product (the **“Rolling Forecast”**). The first [*] of each Rolling Forecast shall be [*] binding on JAZZ and Baxter, subject to Section 4.2.1 (the **“[*] Period”**). JAZZ shall not decrease or increase quantities of Product forecasted within the [*] Period without Baxter’s consent. The remaining [*] months of the Rolling Forecast, i.e. months [*] through [*], shall be non-binding.

4.2.1 Upon Baxter’s receipt of each Rolling Forecast, Baxter will compare the quantities forecasted in the [*] Period to Baxter’s pro-rated Maximum Supply Obligation for such period and to the previous Rolling Forecast submitted by JAZZ. If: (i) the quantities forecasted in the [*] Period are equal to or less than Baxter’s pro-rated Maximum Supply Obligation for such period, and provided that JAZZ has not increased its forecasted quantities in comparison to month [*] of the previous Rolling Forecast when it becomes month [*] of the [*] Period, the quantities forecasted in the [*] Period shall be [*] binding on Baxter and JAZZ; or (ii) such quantities forecasted in the [*] Period are greater than Baxter’s pro-rated Maximum Supply Obligation for such period, Baxter will confirm to JAZZ within [*] what quantities in excess of such pro-rated Maximum Supply Obligation it is able to Produce, and such confirmed additional quantities will also be [*] binding on Baxter and JAZZ (the **“Binding [*] Period”**). If Baxter does not confirm its ability to Produce additional quantities within such [*] period, Baxter shall be deemed to have so confirmed and such additional quantities will be [*] binding on both Parties.”

8. Section 4.3 including Subsection 4.3.1 **“Annual Obligation for Commercial Product and Maximum Supply Obligation”**, are hereby deleted and replaced with the following:

“4.3 Annual Obligation for Commercial Product and Maximum Supply Obligation. Jazz shall be obligated, upon receiving Regulatory Approval of the Product in the United States or Europe, to purchase from Baxter a minimum number of Batches of Commercial Product in each Contract Year during the Term of this Agreement (the **"Annual Obligation")** as set forth in Exhibit A, which Annual Obligation shall be prorated for any partial Contract Year. For the avoidance of doubt, in each Contract Year JAZZ must order for delivery in such Contract Year the greater of (i) the Annual Obligation or (ii) the binding portion of the Rolling Forecasts for such Contract Year as set forth above in Section 4.2.1. Within [*] after the end of each Contract Year, JAZZ shall pay Baxter for the difference between the aggregate

Purchase Price of Product actually ordered by JAZZ for delivery pursuant to Section 4.2 in the Contract Year and the aggregate Purchase Price of the greater of (i) the Annual Obligation or (ii) the binding portion of the Rolling Forecasts. In any Contract Year during the Term of this Agreement, in no event shall Baxter be obligated to Produce more than the number of Batches set forth in Exhibit B **("Maximum Supply Obligation")**; provided, however, Baxter will use commercially reasonable efforts to provide additional Batches of Product if requested by JAZZ**.** If changes (increase/decrease) in the annual order volume require changes in equipment and/or process, Jazz will cover the costs of such changes."

4.3.1 At least [*] prior to the expiration of (i) the Commercial Initial Term and (ii) each Commercial Renewal Term, the Parties, acting reasonably, shall mutually agree upon JAZZ's Annual Obligation and Baxter's Supply Obligation for the upcoming Commercial Renewal Term and such obligations shall be set forth in an amended Exhibit A and Exhibit B to the Agreement. In the event the Parties are unable to reach agreement on JAZZ's Annual Obligation Commitment and Baxter's Supply Obligation for any Commercial Renewal Term, JAZZ's Annual Obligation and Baxter's Supply Obligation for such Commercial Renewal Term shall [*] or [*], as the case may be.

4.3.2 Notwithstanding the foregoing, with at least [*] prior notice, JAZZ may request an increase in its Annual Obligation for a Contract Year; which, when agreed to and confirmed in writing by Baxter with Baxter's agreement and confirmation not to be unreasonably withheld, will result in corresponding increases in both JAZZ's Annual Obligation and Baxter's Maximum Supply Obligation for such Contract Year. Exhibits A and B will be amended at that time to reflect such increases.

9. Exhibit A **"JAZZ's ANNUAL OBLIGATION"** and Exhibit B **"BAXTER's MAXIMUM SUPPLY OBLIGATION**" are hereby deleted in their entirety and replaced with the Exhibits A and B attached to this Amendment No. 1.

10. Section 4.4 **"Purchase Orders"**, the second sentence only of the first paragraph beginning "JAZZ shall not, without the written consent of Baxter,…" is hereby deleted and replaced with the following sentence:

"JAZZ shall not, without the written consent of Baxter, designate a requested pick-up date in a Purchase Order earlier than [*] from the date JAZZ submits the Purchase Order."

11. Section 4.4 **"Purchase Orders"**, the final two paragraphs beginning with "In the event that JAZZ modifies or cancels a Firm Purchase Order…" are hereby deleted and replaced with the following two paragraphs:

"In the event that JAZZ modifies or cancels a Firm Purchase Order through no fault of Baxter, without Baxter's written consent (which shall not be unreasonable withheld or

delayed), Baxter may charge JAZZ [*] for each modified or cancelled Batch (a "**Reservation Fee")** [*]. The term "modifies" and "modified" herein shall mean modification which prevents Baxter's Production of a Batch within the scheduled Production slot; provided, however, if the modification is insignificant and Baxter is able to Produce the Batch according to such modification without any material impact to its manufacturing schedule (e.g. Baxter left with open capacity in its manufacturing schedule) and without preventing Baxter's manufacturing of any third party's product, then Baxter will not charge JAZZ a Reservation Fee.

JAZZ shall order full batches of Product on a single Purchase Order, either as single batches or as part of a Campaign(s)."

12. Section 4.5 **"Component Delivery Delay"** is hereby deleted and replaced with the following:

"4.5 Component Delivery Delays. Timely delivery of JAZZ-supplied Components shall mean that the respective Component and the documents required under the Product Master Plan arrive at Baxter at least [*] business days prior to the scheduled manufacturing date of such Product, as determined by the date set forth in the Firm Purchase Order. Notwithstanding anything in this Agreement to the contrary, in the event that Baxter receives such JAZZ-supplied Components and associated cGMP documents for the Production of Product from JAZZ less than [*] business days prior to the scheduled manufacturing date of such Product, Baxter shall use commercially reasonable efforts to reschedule Batch within [*] days after receipt. [*], Baxter may charge JAZZ a Reservation Fee as defined in Section 4.4."

13. Section 5.1 **"Purchase Price"** is hereby deleted and replaced with the following:

"**5.1 "Purchase Price**. The price to be paid by JAZZ for the Production of Product (the **"Purchase Price"**) shall be set forth in the Exhibit C. The Purchase Price includes the cost of the Baxter-supplied Components. For each Batch of Commercial Product Produced in a Campaign, the Purchase Price of each such Batch will be reduced by the amount as set forth in Exhibit C."

14. Section 5.2 **"Production Price Adjustment for Commercial Product"**, is hereby deleted and replaced with the following:

"5.2 Purchase Price Adjustment for Commercial Product. On January 1, 2019, Baxter shall adjust the Purchase Price of Commercial Product to reflect changes in Baxter's actual costs since the date on which the Production Price was last established, but in an amount not to exceed [*] (i) the percentage increase in the Index of Producer Prices of Industrial Products during the previous twelve (12) month period as published by the Federal Statistical Office of Germany (www.destatis.de) and (ii) [*]. Commencing on January 1, 2020 and on each January 1 thereafter during the Term, Baxter shall adjust the Purchase Price of Commercial Product in an amount not to exceed the percentage increase in the Index of Producer Prices of Industrial Products

during the previously twelve (12) month period as published by the Federal Statistical Office of Germany (www.destatis.de). In addition to the foregoing increases, increases by third party suppliers in the price of Baxter-supplied Components used in the Production of Product may also result in increases in the Purchase Price. Written notification of all increases to the Purchase Price will be sent by Baxter to JAZZ. In the event Baxter provides written notification to JAZZ of a price increase due to third party supplier price increases, Baxter will support this by providing supporting supplier verification, prior to implementation of such increases**.**

15. Section 7.2.2B is hereby deleted and replaced with the following;

"7.2.2B In the event Baxter agrees that Commercial Product is non-conforming to the Product Requirements, or the laboratory or consultant determines that such Commercial Product is non-conforming, JAZZ shall provide replacement JAZZ-supplied Components, including API, and any other JAZZ supplied materials to Baxter, at JAZZ's expense, and Baxter shall replace such non-conforming Commercial Product as soon as possible assuming sufficient JAZZ-supplied Components, including API, and any other JAZZ supplied materials are available or will be provided by JAZZ in due time to carry out the Production. Baxter is not responsible to replace non-conforming Commercial Product in accordance with this Section 7.2.2B, if such non-conformance arises out of, is caused by or relates to any of the following:

[*]

In the event a Batch of Commercial Product is non-conforming, provided Baxter has not already done so in accordance with Section 7.1.2 above, Baxter shall duly investigate such non-conformity and the parties will mutually determine a corrective action plan within [*] calendar days after the Parties determine or agree that the Batch is non-conforming or such additional time as is reasonably required if such investigation or plan requires data from sources other than JAZZ or Baxter. If after such investigation, a root cause for such nonconformance cannot be determined, the Parties shall refer the matter to a mutually acceptable laboratory or consultant for investigation, whose determination of root cause shall be binding upon the Parties and the costs of such laboratory or consultant are to be borne by the Party who caused such nonconformance. If such laboratory or consultant cannot determine a root cause for such nonconformance [*].

16. Section 8.1 "Term" is hereby deleted and replaced with the following:

"8.1 Term. Unless terminated pursuant to Section 8.2 herein, this Agreement shall commence on the Effective Date and will continue until the development and clinical Production have been completed, as described in the Product Master Plan for clinical Production (the **"Clinical Term"**) and shall continue in effect thereafter for commercial Production until the expiration of the fifth (5th) Contract Year (the **"Commercial Initial Term"**). This Agreement will be thereafter renewed automatically for further successive periods of three (3) years each (each a **"Commercial Renewal Term"**) unless either JAZZ or Baxter terminates the Agreement by giving the other Party

written notice of intent to terminate at least twenty-four months prior to the expiration of the Commercial Initial Term or prior to the expiration of the Commercial Renewal Term, as applicable. The Commercial Initial Term and the Commercial Renewal Term(s) are collectively referred to herein as the **"Commercial Term"**. The Clinical Term and the Commercial Term are collectively referred to as the **"Term"**.

17. Section 8.5 **"Payment on Termination of Commercial Production"**, all references to "Production Price" in Section 8.5 are hereby changed to "Purchase Price".

18. The following is hereby added to the Agreement as a new Section 8.7.2:

"8.7.2 If at any time during the Term JAZZ requests Baxter's assistance to help JAZZ set up a secondary supplier to manufacture Product, the Parties will in good faith and acting reasonably, mutually agree at that time, in writing, if and to what extent Baxter will assist.

19. Section 12.2 **"Baxter Warranty",** the first sentence is hereby deleted and replaced with the following:

"Baxter represents and warrants that (i) it shall Produce all Product in accordance with cGMP and (ii) subject to Section 7.2.2B(i), all Commercial Product shall meet Product Specifications."

20. Capitalized terms used herein that are not defined herein shall have the defined meaning set forth in the Agreement.

21. Except as modified by this Amendment No. 1, the terms of the Agreement shall continue in full force and effect.

22. This Amendment No. 1 may be executed in counterparts and all of such counterparts taken together shall be deemed one and the same instrument. Any photocopy, facsimile, or pdf of the executed Amendment No. 1 shall constitute an original.

{Signatures on Next Page}

IN WITNESS WHEREOF, the parties have caused this Amendment No. 1 to be duly authorized, executed, and delivered as of the Amendment No. 1 Effective Date.

BAXTER ONCOLOGY GmbH

By: /s/ Dr Sven Remmerbach
Title: Director BDCM

And

By: /s/ Jurgen Fleischer
Title: Director Human Resources & EHS

JAZZ PHARMACEUTICALS IRELAND LIMITED

By: /s/ Aoife Campbell
Title: VP, Strategy & Corporate Development

EXHIBIT A

JAZZ's ANNUAL OBLIGATION

Contract Years	**Annual Obligation**
Contract Year One	[*]
Contract Year Two	[*]
Contract Year Three	[*]
Contract Year Four	[*]
Contract Year Five	[*]

Note: For any Commercial Renewal Term, the parties will mutually agree upon an Annual Obligation as set forth in Section 4.3.1.

EXHIBIT B

BAXTER'S MAXIMUM SUPPLY OBLIGATION

Contract Year	**Maximum Supply Obligation**
Contract Year One	[*]
Contract Year Two	[*]
Contract Year Three	[*]
Contract Year Four	[*]
Contract Year Five	[*]

Note: For any Commercial Renewal Term, the parties will mutually agree upon Baxter's Maximum Supply Obligation as set forth in Section 4.3.1.

EXHIBIT C

PURCHASE PRICE

BAXTER shall charge JAZZ for Product as set forth in the table below plus any occurring Value-Added Taxes (if applicable) (ready for shipment).

Clinical / Commercial Batches		
Batch size	**Number of batches**	**Purchase Price per Batch (includes the cost of the Baxter-supplied Components**
Up to [*]	See Exhibit A of the Agreement for the manufacturing of commercial batches	[*]
Campaign Manufacturing	At least [*] in sequence as defined in the Agreement*	[*]

[*]

The Purchase Price includes Baxter costs for keeping the suppliers of Baxter-supplied Components in an adequate state of qualification.

Associated Batch specific costs: Batch specific selection of sterile filters and bioburden filters and the costs of such filters, including without limitation the testing of such filters, will be set forth in the Product Master Plan.

Exhibit 10.4

AMENDMENT NO. 6 TO PHARMACY MASTER SERVICES AGREEMENT

THIS AMENDMENT NO. 6 (this "**Amendment**") to the Agreement (as defined below) is entered into as of August 24, 2022 (the "**Amendment Effective Date**") by and between Jazz Pharmaceuticals, Inc. with a principal place of business at 3170 Porter Drive, Palo Alto, CA 94304 ("**Jazz Pharmaceuticals**") and Express Scripts Specialty Distribution Services, Inc. with a principal place of business at One Express Way, St. Louis, MO 63121 ("**ESSDS**") (collectively, the "**Parties**," or each separately, a "**Party**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

RECITALS

WHEREAS, Jazz Pharmaceuticals and ESSDS entered into that certain Pharmacy Master Services Agreement (the "**Agreement**"), dated July 1, 2020, pursuant to which ESSDS provides dispensing, distribution and other services for Products; and

NOW THEREFORE, in consideration of the above recitals, each of which is incorporated by this reference, the mutual promises and covenants set forth below, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. Section 11.1 Term; Renewal is deleted in its entirety and replaced with the following: Term; Renewal. Unless otherwise terminated in accordance with the terms hereof, this Agreement will remain in effect until September 30, 2022.

2. General. This Amendment constitutes an amendment in writing to the Agreement in accordance with Section 14.1 of the Agreement.

3. Governing Law. This Amendment, and any dispute related hereto, will be governed and construed in accordance with the laws of the State of Delaware, excluding any choice of law rules which may direct the application of the laws of another jurisdiction. In the event of any dispute between the Parties, prior to any Party commencing an action for damages, each Party will designate a representative and the representatives will meet in person or telephonically in a good-faith attempt to resolve their differences. Prior to such meeting, the complaining Party will provide a written explanation of the dispute.

4. Full Force and Effect. In the event of any conflict or inconsistency between the terms and provisions of the Agreement and the terms and provisions of this Amendment, the terms and provisions of this Amendment will govern and prevail. Except as expressly provided in this Amendment, this Amendment does not in any way change, modify or delete the provisions of the Agreement (or the Parties' rights, remedies or obligations thereunder), and all such provisions shall remain in full force and effect. On and after the Amendment Effective Date, each reference in the Agreement to "this Agreement," "hereunder," "hereof," "herein," or words of like import, and each reference to the Agreement in any other agreements, documents or instruments executed and delivered pursuant to the Agreement, shall mean and be a reference to the Agreement, as amended by this Amendment.

5. Counterparts. This Amendment may be executed in counterparts, each of which will be deemed an original but all of which together will constitute one and the same instrument. Facsimile and pdf signatures will be considered original signatures.

[*Signature Page Follows*]

IN WITNESS WHEREOF, the undersigned have caused this Amendment to be executed, effective as of the Amendment Effective Date.

JAZZ PHARMACEUTICALS, INC.

By: /s/ Ernie Ross
Name: Ernie Ross
Title: Senior VP, U.S. Market Access
26 August 2022

By: _____
Name:
Title:

EXPRESS SCRIPTS SPECIALTY DISTRIBUTION SERVICES, INC.

By: /s/ Joshua Parker
Name: Joshua Parker
Title: VP
08/26/2022 | 11:29 AM CDT

RPM for KC 8.26.22

AMENDMENT NO. 7 TO PHARMACY MASTER SERVICES AGREEMENT

THIS AMENDMENT NO. 7 (this "**Amendment**") to the Agreement (as defined below) is entered into as of September 28, 2022 (the "**Amendment Effective Date**") by and between Jazz Pharmaceuticals, Inc. with a principal place of business at 3170 Porter Drive, Palo Alto, CA 94304 ("**Jazz Pharmaceuticals**") and Express Scripts Specialty Distribution Services, Inc. with a principal place of business at One Express Way, St. Louis, MO 63121 ("**ESSDS**") (collectively, the "**Parties**," or each separately, a "**Party**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

RECITALS

WHEREAS, Jazz Pharmaceuticals and ESSDS entered into that certain Pharmacy Master Services Agreement (the "**Agreement**"), dated July 1, 2020, pursuant to which ESSDS provides dispensing, distribution and other services for Products; and

NOW THEREFORE, in consideration of the above recitals, each of which is incorporated by this reference, the mutual promises and covenants set forth below, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. Section 11.1 Term; Renewal is deleted in its entirety and replaced with the following: Term; Renewal. Unless otherwise terminated in accordance with the terms hereof, this Agreement will remain in effect until November 30, 2022. If no such notice of termination is given, this Agreement can be renewed for one (1) additional one (1) year term at the discretion of Jazz Pharmaceuticals by a written amendment hereto.

2. General. This Amendment constitutes an amendment in writing to the Agreement in accordance with Section 14.1 of the Agreement.

3. Governing Law. This Amendment, and any dispute related hereto, will be governed and construed in accordance with the laws of the State of Delaware, excluding any choice of law rules which may direct the application of the laws of another jurisdiction. In the event of any dispute between the Parties, prior to any Party commencing an action for damages, each Party will designate a representative and the representatives will meet in person or telephonically in a good-faith attempt to resolve their differences. Prior to such meeting, the complaining Party will provide a written explanation of the dispute.

4. Full Force and Effect. In the event of any conflict or inconsistency between the terms and provisions of the Agreement and the terms and provisions of this Amendment, the terms and provisions of this Amendment will govern and prevail. Except as expressly provided in this Amendment, this Amendment does not in any way change, modify or delete the provisions of the Agreement (or the Parties' rights, remedies or obligations thereunder), and all such provisions shall remain in full force and effect. On and after the Amendment Effective Date, each reference in the Agreement to "this Agreement," "hereunder," "hereof," "herein," or words of like import, and each reference to the Agreement in any other agreements, documents or instruments executed and delivered pursuant to the

Agreement, shall mean and be a reference to the Agreement, as amended by this Amendment.

5. Counterparts. This Amendment may be executed in counterparts, each of which will be deemed an original but all of which together will constitute one and the same instrument. Facsimile and pdf signatures will be considered original signatures.

[*Signature Page Follows*]

IN WITNESS WHEREOF, the undersigned have caused this Amendment to be executed, effective as of the Amendment Effective Date.

JAZZ PHARMACEUTICALS, INC.

By: /s/ Ernie Ross
Name: Ernie Ross
Title: Senior VP, U.S. Market Access
29 September 2022

By:
Name:
Title:

EXPRESS SCRIPTS SPECIALTY DISTRIBUTION SERVICES, INC.

By: /s/ Joshua B. Parker
Name: Joshua B. Parker
Title: VP
09/28/2022 | 2:30 PM CDT

RPM for GPM 9.28.22

Exhibit 31.1

CERTIFICATION

I, Bruce C. Cozadd, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: November 9, 2022

By: /s/ Bruce C. Cozadd

Bruce C. Cozadd
Chairman and Chief Executive Officer and Director

Exhibit 31.2

CERTIFICATION

I, Renée Galá, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: November 9, 2022

By: /s/ Renée Galá

Renée Galá
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 Renée Galá, Executive Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2022, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Date: November 9, 2022

/s/ Bruce C. Cozadd

Bruce C. Cozadd
Chairman and Chief Executive Officer and Director

/s/ Renée Galá

Renée Galá
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.