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 March 31, 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 April 27, 2022, 62,318,745 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 MARCH 31, 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), Sunosi® (solriamfetol), 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® (recombinant Erwinia asparaginase) and Sativex® (nabiximols) oral solution. This report also includes trademarks, service marks and trade names of other companies. Trademarks, service marks and trade names appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

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

	March 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 490,835	$ 591,448
Accounts receivable, net of allowances	572,392	563,360
Inventories	985,454	1,072,721
Prepaid expenses	117,399	131,413
Other current assets	243,888	252,392
Assets held for sale	90,888	—
Total current assets	2,500,856	2,611,334
Property, plant and equipment, net	257,632	256,837
Operating lease assets	83,412	86,586
Intangible assets, net	6,783,057	7,152,328
Goodwill	1,782,444	1,827,609
Deferred tax assets, net	314,672	311,103
Deferred financing costs	11,336	12,029
Other non-current assets	35,508	40,813
Total assets	$ 11,768,917	$ 12,298,639
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 73,336	$ 100,298
Accrued liabilities	604,710	666,304
Current portion of long-term debt	31,000	31,000
Income taxes payable	26,677	9,608
Deferred revenue	1,686	2,093
Total current liabilities	737,409	809,303
Deferred revenue, non-current	347	463
Long-term debt, less current portion	5,992,868	6,018,943
Operating lease liabilities, less current portion	83,078	87,200
Deferred tax liabilities, net	1,222,084	1,300,541
Other non-current liabilities	124,644	116,998
Commitments and contingencies (Note 9)		
Shareholders' equity:		
Ordinary shares	6	6
Non-voting euro deferred shares	55	55
Capital redemption reserve	472	472
Additional paid-in capital	3,239,327	3,534,792
Accumulated other comprehensive loss	(590,720)	(400,360)
Retained earnings	959,347	830,226
Total shareholders' equity	3,608,487	3,965,191
Total liabilities and shareholders' equity	$ 11,768,917	$ 12,298,639

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

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

	Three Months Ended March 31,	
	2022	2021
Revenues:		
Product sales, net	$ 809,837	$ 603,531
Royalties and contract revenues	3,884	4,050
Total revenues	813,721	607,581
Operating expenses:		
Cost of product sales (excluding amortization of acquired developed technologies)	115,284	40,189
Selling, general and administrative	308,813	260,508
Research and development	129,981	76,573
Intangible asset amortization	172,094	68,192
Total operating expenses	726,172	445,462
Income from operations	87,549	162,119
Interest expense, net	(70,684)	(27,376)
Foreign exchange gain (loss)	(10,540)	943
Income before income tax expense and equity in loss (gain) of investees	6,325	135,686
Income tax expense	536	18,019
Equity in loss (gain) of investees	4,142	(4,165)
Net income	$ 1,647	$ 121,832
Net income per ordinary share:		
Basic	$ 0.03	$ 2.16
Diluted	$ 0.03	$ 2.09
Weighted-average ordinary shares used in per share calculations - basic	61,865	56,468
Weighted-average ordinary shares used in per share calculations - diluted	62,907	58,393

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

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

	Three Months Ended March 31,	
	2022	2021
Net income	$ 1,647	$ 121,832
Other comprehensive income (loss):		
Foreign currency translation adjustments	(190,488)	(46,220)
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 $— and $166, respectively	—	1,160
Unrealized loss on cash flow hedging activities, net of income tax benefit of $— and ($3), respectively	—	(16)
Other comprehensive loss	(190,360)	(45,076)
Total comprehensive income (loss)	$ (188,713)	$ 76,756

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

	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

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)

	Three Months Ended March 31,	
	2022	**2021**
Operating activities		
Net income	$ 1,647	$ 121,832
Adjustments to reconcile net income to net cash provided by operating activities:		
Intangible asset amortization	172,094	68,192
Acquisition accounting inventory fair value step-up adjustment	63,943	—
Share-based compensation	50,070	34,485
Deferred tax benefit	(45,339)	(19,110)
Non-cash interest expense	12,168	15,688
Depreciation	7,617	4,779
Provision for losses on accounts receivable and inventory	2,170	1,083
Other non-cash transactions	(14,701)	7,766
Changes in assets and liabilities:		
Accounts receivable	(9,723)	(18,245)
Inventories	(24,812)	(22,014)
Prepaid expenses and other current assets	23,170	(2,897)
Operating lease assets	3,095	3,690
Other non-current assets	979	157
Accounts payable	(27,617)	51,292
Accrued liabilities	(23,241)	13,719
Income taxes payable	16,767	24,625
Deferred revenue	(523)	(637)
Operating lease liabilities, less current portion	(3,915)	(4,182)
Other non-current liabilities	5,130	4,774
Net cash provided by operating activities	208,979	284,997
Investing activities		
Proceeds from maturity of investments	—	760,000
Purchases of property, plant and equipment	(12,292)	(2,168)
Acquisition of intangible assets	(25,000)	—
Acquisition of investments	—	(20,700)
Net cash (used in) provided by investing activities	(37,292)	737,132
Financing activities		
Proceeds from employee equity incentive and purchase plans	21,729	50,407
Payment of employee withholding taxes related to share-based awards	(33,776)	(23,784)
Repayments of long-term debt	(258,764)	(8,347)
Net cash (used in) provided by financing activities	(270,811)	18,276
Effect of exchange rates on cash and cash equivalents	(1,489)	(641)
Net (decrease) increase in cash and cash equivalents	(100,613)	1,039,764
Cash and cash equivalents, at beginning of period	591,448	1,057,769
Cash and cash equivalents, at end of period	$ 490,835	$ 2,097,533

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 both cataplexy and 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;
- **Sunosi® (solriamfetol)**, a product approved by FDA and marketed in the U.S., Canada, EU and Great Britain to improve wakefulness in adult patients with EDS associated with narcolepsy or obstructive sleep apnea, or OSA; and
- **Sativex® (nabiximols) oral solution**, a product approved and marketed in more than 25 markets 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 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 was approved in September 2021 for the treatment of adults with Stage III or metastatic SCLC, who have progressed on or after platinum-containing therapy;
- **Rylaze® (recombinant Erwinia asparaginase)**, 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 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, and recently in Switzerland (marketed as Vyxeos® liposomal in the EU and Great Britain) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia, or t-AML, or AML with myelodysplasia-related changes (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 report, 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 report, all references to “ordinary shares” refer to Jazz Pharmaceuticals plc’s ordinary shares.

Basis of Presentation

These unaudited condensed consolidated financial statements have been prepared following the requirements of the U.S. Securities and Exchange Commission for interim reporting. As permitted under those rules, certain footnotes and other financial information that are normally required by U.S. generally accepted accounting principles, or U.S. GAAP, can be condensed or omitted. The information included in this Quarterly Report on Form 10-Q should be read in conjunction with our annual consolidated financial statements and accompanying notes included in our Annual Report on Form 10-K for the year ended December 31, 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 months ended March 31, 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 will be lower as a result of adoption of this guidance. During the three months ended March 31, 2022 the effect of adoption reduced interest expense, net and increased net income by approximately $12 million and increased basic and diluted EPS by approximately $0.19 per share. For the three months ended March 31, 2022, the Exchangeable Senior Notes were determined to be anti-dilutive. 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 the Delta and Omicron variants and other variants with increased transmissibility, even in some cases in vaccinated people, 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 idiopathic hypersomnia in adults and adoption in that indication; competition from the introduction of authorized generic and 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 recently 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 addition, the success of the GW 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. 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 March 31, 2022, we had foreign exchange forward contracts with notional amounts totaling $610.1 million. As of March 31, 2022, the outstanding foreign exchange forward contracts had a net liability fair value of $4.7 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 March 31, 2022 and December 31, 2021, allowances on receivables were not material. As of March 31, 2022, three customers accounted for 74% of gross accounts receivable, Express Scripts Specialty Distribution Services, Inc. and its affiliates, or ESSDS, which accounted for 55% of gross accounts receivable, McKesson Corporation and affiliates, or McKesson, which accounted for 10% of gross accounts receivable, and Cardinal Health, Inc., or Cardinal, 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. Cash and Available-for-Sale Securities

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

	March 31, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents
Cash	$ 410,125	$ —	$ —	$ 410,125	$ 410,125
Money market funds	80,710	—	—	80,710	80,710
Totals	$ 490,835	$ —	$ —	$ 490,835	$ 490,835

	December 31, 2021				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents
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 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. Interest income from available-for-sale securities was $0.2 million and $1.2 million in the three months ended March 31, 2022 and 2021, respectively.

3. Fair Value Measurement

The following table summarizes, by major security type, our available-for-sale securities and derivative contracts as of March 31, 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):

	March 31, 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	$ 80,710	$ —	$ 80,710	$ 80,701	$ —	$ 80,701
Foreign exchange forward contracts	—	3,712	3,712	—	580	580
Totals	$ 80,710	$ 3,712	$ 84,422	$ 80,701	$ 580	$ 81,281
Liabilities:						
Cross-currency interest rate contracts	$ —	$ —	$ —	$ —	$ 15,232	$ 15,232
Foreign exchange forward contracts	—	8,418	8,418	—	3,187	3,187
Totals	$ —	$ 8,418	$ 8,418	$ —	$ 18,419	$ 18,419

As of March 31, 2022, our available-for-sale securities included money market funds 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.

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 March 31, 2022 and December 31, 2021, the carrying amount of investments measured using the measurement alternative for equity investments without a readily determinable fair value was $5.0 million. The carrying amount, which is recorded within other non-current assets, is based on the latest observable transaction price.

As of March 31, 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 $594 million, $1.2 billion, $1.5 billion and $3.1 billion respectively. The fair values of each of these debt facilities was estimated using quoted market prices obtained from brokers (Level 2).

As of March 31, 2022, assets measured at fair value on a non-recurring basis subsequent to initial recognition included assets classified as held for sale on the condensed consolidated balance sheet. These assets related to an asset purchase agreement with Axsome Therapeutics, or Axsome, pursuant to which Axsome will purchase certain assets related to Sunosi. Refer to Note 15, Assets Held for Sale, for additional information. The carrying amount of $90.9 million for assets held for sale is equal to estimated fair value, which is based on the sales price agreed less costs to sell, and represents a Level 3 input.

4. 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 Euro Term Loan, we entered into a cross-currency interest rate swap contract in May 2021, which matured on March 31, 2022. 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.

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

Cross-Currency Interest Rate Contract:	Three Months Ended March 31, 2022
Loss reclassified from accumulated other comprehensive income (loss) to foreign exchange gain (loss), net of tax	$ 128
Loss recognized in foreign exchange gain (loss)	(2,646)

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 March 31, 2022 and December 31, 2021, the notional amount of foreign exchange contracts where hedge accounting is not applied was $610.1 million and $347.2 million, respectively.

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

	Three Months Ended March 31,	
Foreign Exchange Forward Contracts:	2022	2021
Loss recognized in foreign exchange gain (loss)	$ (21,025)	$ (13,050)

The cash flow effects of our derivative contracts for the three months ended March 31, 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 months ended March 31, 2021 was as follows (in thousands):

Interest Rate Contracts:	Three Months Ended March 31, 2021
Loss recognized in accumulated other comprehensive income (loss), net of tax	$ (16)
Loss reclassified from accumulated other comprehensive income (loss) to interest expense, net of tax	1,160

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

	Classification	March 31, 2022	December 31, 2021
Assets			
Derivatives not designated as hedging instruments:			
Foreign exchange forward contracts	Other current assets	$ 3,712	$ 580
Liabilities			
Derivatives not designated as hedging instruments:			
Foreign exchange forward contracts	Accrued liabilities	$ 8,418	$ 3,187
Derivatives designated as hedging instruments:			
Cross-currency interest rate contract	Accrued liabilities	—	15,232
Total fair value of derivative liability instruments		$ 8,418	$ 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):

	March 31, 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	$ 3,712	$ —	$ 3,712	$ (3,100)	$ —	$ 612
Derivative liabilities	(8,418)	—	(8,418)	3,100	—	(5,318)

	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)

5. Inventories

Inventories consisted of the following (in thousands):

	March 31, 2022	December 31, 2021
Raw materials	$ 26,335	$ 21,550
Work in process	775,804	886,849
Finished goods	183,315	164,322
Total inventories	$ 985,454	$ 1,072,721

As of March 31, 2022 and December 31, 2021 inventories included $727.4 million and $811.3 million, respectively, related to the purchase accounting inventory fair value step-up on inventory acquired in the GW Acquisition.

6. 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 assets held for sale [(1)]	(12,927)
Foreign exchange	(32,238)
Balance at March 31, 2022	$ 1,782,444

[(1)] In March 2022, we entered into a definitive agreement to divest Sunosi to Axsome. See Note 15 for further information relating to this transaction.

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

		March 31, 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	11.2	$ 7,948,903	$ (1,316,734)	$ 6,632,169	$ 8,195,675	$ (1,198,333)	$ 6,997,342
Manufacturing contracts	—	11,883	(11,883)	—	12,124	(12,124)	—
Trademarks	—	2,887	(2,887)	—	2,893	(2,893)	—
Total finite-lived intangible assets		7,963,673	(1,331,504)	6,632,169	8,210,692	(1,213,350)	6,997,342
Acquired in-process research and development assets		150,888	—	150,888	154,986	—	154,986
Total intangible assets		$ 8,114,561	$ (1,331,504)	$ 6,783,057	$ 8,365,678	$ (1,213,350)	$ 7,152,328

The decrease in the gross carrying amount of intangible assets as of March 31, 2022 compared to December 31, 2021 primarily reflects the reclassification of the Sunosi intangible asset to assets held for sale as a result of the execution of the definitive agreement to divest Sunosi to Axsome in March 2022, partially offset by the negative impact of foreign currency translation adjustments due to the weakening of sterling and euro against the U.S. dollar.

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

Based on finite-lived intangible assets recorded as of March 31, 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)	$ 455,447
2023	607,262
2024	607,262
2025	607,262
2026	607,262
Thereafter	3,747,674
Total	$ 6,632,169

7. Certain Balance Sheet Items

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

	March 31, 2022	December 31, 2021
Construction-in-progress	$ 88,111	$ 86,511
Manufacturing equipment and machinery	72,387	69,079
Leasehold improvements	65,425	66,318
Land and buildings	63,562	64,008
Computer software	29,604	25,646
Computer equipment	20,937	16,234
Furniture and fixtures	10,302	14,412
Subtotal	350,328	342,208
Less accumulated depreciation and amortization	(92,696)	(85,371)
Property, plant and equipment, net	$ 257,632	$ 256,837

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

	March 31, 2022	December 31, 2021
Deferred charge for income taxes on intercompany profit	$ 205,233	$ 203,480
Other	38,655	48,912
Total other current assets	$ 243,888	$ 252,392

Accrued liabilities consisted of the following (in thousands):

	March 31, 2022	December 31, 2021
Rebates and other sales deductions	$ 258,649	$ 215,397
Employee compensation and benefits	126,479	158,870
Clinical trial accruals	27,741	25,612
Accrued interest	21,228	48,640
Accrued royalties	19,441	20,345
Sales return reserve	18,749	15,814
Inventory-related accruals	18,708	16,166
Consulting and professional services	17,527	22,507
Current portion of lease liabilities	16,155	15,763
Selling and marketing accruals	14,666	21,566
Derivative instrument liabilities	8,418	18,419
Accrued construction-in-progress	3,978	2,894
Accrued milestones	—	25,000
Other	52,971	59,311
Total accrued liabilities	$ 604,710	$ 666,304

8. Debt

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

	March 31, 2022	December 31, 2021
2024 Notes	$ 575,000	$ 575,000
Unamortized - debt issuance costs	(4,023)	(4,401)
Unamortized discount - equity component	—	(66,836)
2024 Notes, net	570,977	503,763
2026 Notes	1,000,000	1,000,000
Unamortized - debt issuance costs	(10,879)	(11,407)
Unamortized discount - equity component	—	(139,323)
2026 Notes, net	989,121	849,270
Secured Notes	1,474,346	1,473,810
Term Loan [1]	2,989,424	3,223,100
Total debt	6,023,868	6,049,943
Less current portion	31,000	31,000
Total long-term debt	$ 5,992,868	$ 6,018,943

(1) In May 2021, we entered into a credit agreement that provided for (i) the Dollar Term Loan, (ii) a seven-year $625.0 million term loan B facility, or 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.

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 months ended March 31, 2022, we recognized interest expense of $5.5 million, of which $5.0 million related to the contractual coupon rate and $0.5 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 months ended March 31, 2022, we recognized interest expense of $2.5 million, of which $2.1 million related to the contractual coupon rate and $0.4 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 March 31, 2022 were as follows (in thousands):

Year Ending December 31,	Scheduled Long-Term Debt Maturities
2022 (remainder)	$ 23,250
2023	31,000
2024	606,000
2025	31,000
2026	1,031,000
Thereafter	4,429,500
Total	$ 6,151,750

9. 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 March 31, 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 March 31, 2022, we had $74.4 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 February 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. In January 2021, the United States District Court for the Northern District of California issued a Case Management Order that schedules this case for trial in February 2023.

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.

A hearing on class certification is scheduled for November 2022. 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 FT-218 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.

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 FT-218 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 FT-218 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.

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. 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.

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.

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 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.

10. Shareholders' Equity

Accumulated Other Comprehensive Income (Loss)

The components of accumulated other comprehensive income (loss) as of March 31, 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	—	(190,488)	(190,488)
Amounts reclassified from accumulated other comprehensive income (loss)	128	—	128
Other comprehensive income (loss), net	128	(190,488)	(190,360)
Balance at March 31, 2022	$ —	$ (590,720)	$ (590,720)

During the three months ended March 31, 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.

11. Net Income per Ordinary Share

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

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

	Three Months Ended March 31,	
	2022	2021
Numerator:		
Net income	$ 1,647	$ 121,832
Denominator:		
Weighted-average ordinary shares used in per share calculations - basic	61,865	56,468
Dilutive effect of employee equity incentive and purchase plans	1,042	1,584
Dilutive effect of Exchangeable Senior Notes	—	341
Weighted-average ordinary shares used in per share calculations - diluted	62,907	58,393
Net income per ordinary share:		
Basic	$ 0.03	$ 2.16
Diluted	$ 0.03	$ 2.09

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 per ordinary share for the three months ended March 31, 2022.

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

	Three Months Ended March 31,	
	2022	2021
Exchangeable Senior Notes	9,044	9,798
Employee equity incentive and purchase plans	2,509	1,671

12. Revenues

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

	Three Months Ended March 31,	
	2022	2021
Xyrem	$ 247,497	$ 335,550
Xywav	186,080	75,416
Total Oxybate	433,577	410,966
Epidiolex/Epidyolex	157,893	—
Sunosi	15,878	11,606
Sativex	4,742	—
Total Neuroscience	612,090	422,572
Zepzelca	59,338	54,334
Rylaze	54,220	—
Vyxeos	33,757	33,155
Defitelio/defibrotide	49,489	49,619
Erwinaze/Erwinase	—	41,068
Total Oncology	196,804	178,176
Other	943	2,783
Product sales, net	809,837	603,531
Royalties and contract revenues	3,884	4,050
Total revenues	$ 813,721	$ 607,581

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

	Three Months Ended March 31,	
	2022	2021
United States	$ 740,583	$ 548,292
Europe	61,028	47,233
All other	12,110	12,056
Total revenues	$ 813,721	$ 607,581

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 March 31,	
	2022	2021
ESSDS	55 %	67 %
McKesson	12 %	14 %

Financing and payment

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

Contract Liabilities - Deferred Revenue

The deferred revenue balance as of March 31, 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 during the three months ended March 31, 2022, 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 three months ended March 31, 2022 (in thousands):

	Contract Liabilities
Balance as of December 31, 2021	$ 2,556
Amount recognized within royalties and contract revenues	(523)
Balance as of March 31, 2022	$ 2,033

13. 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 March 31,	
	2022	2021
Selling, general and administrative	$ 34,785	$ 23,846
Research and development	12,436	8,643
Cost of product sales	2,849	1,996
Total share-based compensation expense, pre-tax	50,070	34,485
Income tax benefit from share-based compensation expense	(8,823)	(6,753)
Total share-based compensation expense, net of tax	$ 41,247	$ 27,732

Share Options

There were no share options granted in the three months ended March 31, 2022. 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 three months ended March 31, 2021:

	Three Months Ended March 31, 2021
Shares underlying options granted (in thousands)	95
Grant date fair value	$ 51.33
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	— %

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 March 31,	
	2022	2021
RSUs granted (in thousands)	1,888	1,201
Grant date fair value	$ 152.38	$ 169.87

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

In March 2022, 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, 2024. 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 March 31, 2022
PRSUs granted (in thousands)	281
Grant date fair value	$ 179.19

As the PRSUs granted in March 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. There were no PRSUs granted in the three months ended March 31, 2021.

As of March 31, 2022, compensation cost not yet recognized related to unvested share options, RSUs and PRSUs was $29.7 million, $418.8 million and $56.6 million, respectively, which is expected to be recognized over a weighted-average period of 1.6 years, 3.2 years and 2.3 years, respectively.

14. Income Taxes

Our income tax expense was $0.5 million for the three months ended March 31, 2022, compared to $18.0 million for the same period in 2021. The decrease in the income tax expense resulted primarily from the mix of pre-tax income and losses incurred across tax jurisdictions. 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 Italian subsidiaries are currently under examination by the Italian taxing authorities for the year ended December 31, 2017. 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.

15. Assets Held for Sale

On March 25, 2022, we entered into a definitive agreement to divest Sunosi to Axsome. Under the terms of the agreement, Axsome will acquire the rights to Sunosi in all of the existing territories available to us. We will receive a upfront payment of $53 million, 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 respective obligations of Jazz and Axsome to consummate the transactions contemplated by the definitive agreement are subject to the satisfaction or waiver of a number of customary conditions.

The transaction is structured to be completed in sequential closings for the U.S. and ex-U.S. territories. Subject to the satisfaction or waiver of the closing conditions, the companies expect the U.S. transaction to close in the second quarter of 2022 and the ex-U.S. transaction close to occur within 60 days following the close of the U.S. transaction.

The assets to be divested met the assets held for sale criteria and were reclassified to assets held for sale as of March 31, 2022. We determined this is the disposal of a business and have allocated goodwill to these assets using the relative fair value method.

We have determined that the expected disposition of these assets does not qualify for reporting as a discontinued operation since the expected sale does not represent a strategic shift that has or will have a major effect on our operations and financial results.

The following assets were segregated and classified as assets held for sale in the condensed consolidated balance sheet (in thousands):

	March 31, 2022
Intangible assets, net	$ 56,680
Inventories	21,163
Goodwill	12,927
Other	118
Total assets held for sale	$ 90,888

We will account for the contingent consideration in the form of the future royalty as earned. As a result, we expect to record a loss on disposal of approximately $40.0 million when the transaction closes as the determination of the initial gain or loss will include the upfront consideration only and not include an amount for the contingent consideration.

16. Subsequent Events

In the second quarter of 2022, we acquired development and commercialization rights to two preclinical compounds, 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 (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. Pending approval, Werewolf is eligible to receive a tiered, mid-single-digit percentage royalty on net sales of JZP898. The upfront payment totaling $15.0 million will be expensed to Acquired in-process research and development, or IPR&D, in the second quarter of 2022.

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, which we have designated 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 will make an upfront payment of $50.0 million to Sumitomo, and Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to $1.09 billion. Pending approval, Sumitomo is eligible to receive a tiered, low double-digit royalty on Jazz's net sales of JZP441. The upfront payment totaling $50.0 million will be expensed to Acquired IPR&D in the second 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 I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2021. 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 in adult patients with EDS associated with narcolepsy or obstructive sleep apnea, or OSA.	March 2019	U.S.
	Improve wakefulness and reduce EDS in adult patients with narcolepsy (with or without cataplexy) or adult patients with 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.

Vyxeos® (daunorubicin and cytarabine) liposome for injection	Treatment of newly-diagnosed therapy-related therapy-related acute myeloid leukemia, or t-AML or AML with myelodysplasia-related changes (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 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 pending in certain markets

***In March 2022, we announced that we had entered into a definitive agreement to divest Sunosi to Axsome Therapeutics, or Axsome

Neuroscience

We are the global leader in the development and commercialization of oxybate therapy for patients with sleep disorders. Xyrem was approved by the U.S. Food and Drug Administration, or 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 (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 both existing and new-to-oxybate narcolepsy patients. 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 for approximately 90% of commercial lives.

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. 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 have seen strong adoption of Xywav in narcolepsy since its launch in November 2020. Exiting the first quarter of 2022, there were approximately 7,800 patients taking Xywav, including approximately 7,050 patients with narcolepsy and approximately 750 patients with IH. With respect to Xywav and Xyrem in the aggregate, the average number of active oxybate patients on therapy was approximately 16,650 in the first quarter of 2022.

Sunosi was launched in the U.S. in 2019 as a therapy to improve wakefulness in adult patients with EDS associated with narcolepsy or OSA. Sunosi was approved in Europe in 2020, and the rolling launch is ongoing. Sunosi was approved in Canada in 2021. In March 2022, we announced that we had entered into a definitive agreement to divest Sunosi to Axsome. Under the terms of the agreement, Axsome will receive the rights to Sunosi in all of the existing territories available to us and we will receive an upfront payment of $53 million, 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. The respective obligations of the companies to consummate the transactions contemplated by the definitive agreement are subject to the satisfaction or waiver of a number of customary conditions. The transaction is structured to be completed in sequential closings for the U.S. and ex-U.S. territories. Subject to the satisfaction or waiver of the closing conditions, the companies expect the U.S. transaction to close in the second quarter of 2022 and the ex-U.S. transaction close to occur within 60 days following the close of the U.S. transaction.

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 expands 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. The clobazam restriction is limited to EU and Great Britain. Outside the U.S. and Europe, Epidiolex/Epidyolex is approved in Israel and Australia.

Sativex (nabiximols) is approved in more than 25 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 market Sativex directly in the U.K. and through licensing agreements with partners across other countries. We are working toward potential approval of nabiximols in the U.S. with multiple Phase 3 clinical trials in progress.

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 (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 (IM) dosing regimen of 25 mg/m^2 every 48 hours. We submitted a supplemental Biologics License Application (sBLA) with additional data in support of a Monday/Wednesday/Friday (M/W/F) IM dosing schedule in January 2022 and submitted a separate sBLA for intravenous administration in April 2022, both which have been granted review under the RTOR program. We anticipate that data from the current development program will support regulatory filings in Europe in mid-2022, with potential for approval in 2023. The Company is also working with a partner 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 therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes 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 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 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 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 planned initiation of a pivotal Phase 3 clinical trial of Epidiolex for the treatment of Epilepsy with Myoclonic-Atonic Seizures, or EMAS, also known as Doose syndrome, in the first half of 2022. This trial is expected to evaluate 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.

For nabiximols, we have three ongoing Phase 3 clinical trials in MS-related spasticity. Spasticity occurs in up to 84% of MS patients, and approximately one-third of those who experience spasticity live with uncontrolled symptoms. The first trial is a smaller, shorter trial relative to the other two. If results from this first trial are supportive, there is the potential for a New Drug Application, or NDA, submission in the U.S. by the end of 2022.

Additionally, in December 2021 we initiated Phase 2 clinical trials for suvecaltamide (JZP385) for essential tremor, or ET, and for JZP150 for post-traumatic stress disorder, or PTSD. These are both patient populations that suffer significant impacts to their quality of life and for whom 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 will include advanced urothelial cancer, large cell neuroendocrine tumor of the lung, and homologous recombination deficient (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 are planning regulatory submissions in Europe in mid-2022.

In the second quarter of 2022, we acquired development and commercialization rights to two preclinical compounds, 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 (IFNα) INDUKINE™ molecule. Under the terms of the agreement, we made an upfront payment of $15 million to Werewolf, and Werewolf is eligible to receive development, regulatory and commercial milestone payments of up to $1.26 billion. Pending approval, 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, which we have designated 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 will make 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. Pending approval, 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 (planned study)
Nabiximols	MS Spasticity (multiple studies ongoing) Spinal cord injury spasticity (planned study)
Phase 2b	
Suvecaltamide (JZP385)	ET (ongoing study)
Phase 2	
JZP150	PTSD (ongoing study)
Additional cannabinoids	Autism spectrum disorders (ongoing study)
Phase 1	
JZP324	Oxybate extended-release formulation (planned study)
Additional cannabinoids	Neonatal hypoxic-ischemic encephalopathy (ongoing study) Neuropsychiatry targets (ongoing study)
Preclinical	
JZP441 (DSP-0187)	Potent, highly selective oral orexin-2 receptor agonist
Undisclosed targets	Neuroscience Cannabinoids
ONCOLOGY	
Regulatory Review	
Rylaze	ALL/LBL FDA approval in June 2021; submitted sBLA in January 2022 seeking approval for Monday/Wednesday/Friday intramuscular dosing schedule; submitted separate sBLA seeking approval for intravenous administration; regulatory submission planned for Europe in mid-2022
Phase 3	
Zepzelca	First-line extensive stage SCLC in combination with Tecentriq (collaboration with Roche) (ongoing study) Confirmatory Study (PharmaMar study) (ongoing study)
Vyxeos	AML or high-risk Myelodysplastic Syndrome, or MDS (AML18) (cooperative group studies) (ongoing study) Newly diagnosed adults with standard- and high-risk AML (AML Study Group cooperative group study) (ongoing study) Newly diagnosed pediatric patients with AML (Children’s Oncology Group cooperative group study) (ongoing study)

Product Candidates	Description
Phase 2	
Zepzelca	Basket trial including urothelial cancer, large cell neuroendocrine tumor of the lung, and HRD (homologous recombination deficient) cancers (ongoing study)
Vyxeos	High-risk MDS (European Myelodysplastic Syndromes (cooperative group study) (ongoing study) Newly diagnosed older adults with high-risk AML (cooperative group study) (planned study)
Vyxeos + venetoclax	De novo or relapsed/refractory, or R/R, AML (MD Anderson collaboration study) (ongoing study)
Phase 1	
Vyxeos	Low intensity dosing for higher risk MDS (MD Anderson collaboration study) (ongoing study)
Vyxeos + other approved therapies	R/R AML or hypomethylating agent failure MDS (MD Anderson collaboration study) (ongoing study) First-line, fit AML (Phase 1b study) (ongoing study) Low intensity therapy for first-line, unfit AML (Phase 1b study) (ongoing study)
Preclinical	
CombiPlex®	Hematology/oncology exploratory activities
JZP341 (long-acting *Erwinia* asparaginase)	ALL and other hematological malignancies (collaboration with Ligand)
JZP815/Pan-Raf inhibitor program	Raf and Ras mutant tumors (acquired from Redx, which is continuing development)
JZP898	Conditionally-activated interferon alpha (IFNα) INDUKINE™ molecule
Undisclosed targets	Ras/Raf/MAP kinase pathway (collaboration with Redx) Oncology
Exosome targets (up to 4)	Hematological malignancies/solid tumors (collaboration with Codiak BioSciences, Inc., or Codiak)
Undisclosed targets	Oncology

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 virtual scientific congresses designed to ensure we can continue to provide promotional and non-promotional interactions and have supported 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. We anticipate that our teams will increase 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 the Delta and Omicron variants and other variants with increased transmissibility, even in some cases 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 remote work and in-person initiatives. 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 begun reopening some of our sites to enable our employees to return to our global offices, which take into account applicable public health authority and local government guidelines and which are designed to ensure community and employee safety. We are moving to a more flexible mix of virtual and in-person working to advance our culture, drive innovation and agility and enable greater balance and well-being for our workforce. This will 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 essential staff onsite and office-based staff working onsite and remotely 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 limited COVID-19-related impact to our mid- and late-stage clinical trial activity, despite delays in initiating trial sites. 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. Similarly, 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. Supply chain disruptions related to the pandemic may also impact our ability to initiate clinical trials in a timely manner.

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 idiopathic hypersomnia 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, in the future, we expect our oxybate products to face competition from generic and authorized 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 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 after launch, 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 successfully combining our and GW's businesses and we plan to continue to devote substantial management attention and resources to integrating our business practices and operations with GW's in an effort to fully realize the anticipated benefits of the GW Acquisition. 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. Conversely, the liabilities assumed in the GW Acquisition may be greater than originally anticipated. In addition, difficulties may arise during the process of combining the operations of our companies that could result in the failure to achieve the synergies or free cash flow that we anticipate, the failure to integrate operations and internal systems, programs and controls, the loss of key employees that may be difficult to replace in the very competitive pharmaceutical field, the failure to harmonize both companies' corporate cultures, and the disruption of each company's ongoing businesses or inconsistencies in standards, controls, procedures and policies that adversely affect our ability to maintain relationships with customers, suppliers, distributors, collaboration partners, clinical trial investigators or managers of our clinical trials. 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 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 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 U.S. Drug Enforcement Administration, or DEA, will make a scheduling determination. If any foreign regulatory authority determines that Epidyolex may have potential for abuse, or if DEA makes a similar determination for nabiximols, it 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 and, if approved by FDA, nabiximols. 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 expense and could be distracted from operation of our business and execution of our strategy. From June 2020 to February 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 9, 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 or government action; 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. 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 I, Item 1A of the annual report on Form 10-K for the year ended December 31, 2021.

Results of Operations

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

	Three Months Ended March 31,		Increase/ (Decrease)
	2022	2021[1]	
Product sales, net	$ 809,837	$ 603,531	34 %
Royalties and contract revenues	3,884	4,050	(4)%
Cost of product sales (excluding amortization of acquired developed technologies)	115,284	40,189	N/A(2)
Selling, general and administrative	308,813	260,508	19 %
Research and development	129,981	76,573	70 %
Intangible asset amortization	172,094	68,192	N/A(2)
Interest expense, net	70,684	27,376	N/A(2)
Foreign exchange loss (gain)	10,540	(943)	N/A(2)
Income tax expense	536	18,019	N/A(2)
Equity in loss (gain) of investees	4,142	(4,165)	N/A(2)

(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.

Revenues

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

	Three Months Ended March 31,		Increase/ (Decrease)
	2022	2021[1]	
Xyrem	$ 247,497	$ 335,550	(26)%
Xywav	186,080	75,416	147 %
Total Oxybate	433,577	410,966	6 %
Epidiolex/Epidyolex	157,893	—	N/A(2)
Sunosi	15,878	11,606	37 %
Sativex	4,742	—	N/A(2)
Total Neuroscience	612,090	422,572	45 %
Zepzelca	59,338	54,334	9 %
Rylaze	54,220	—	N/A(2)
Vyxeos	33,757	33,155	2 %
Defitelio/defibrotide	49,489	49,619	— %
Erwinaze/Erwinase	—	41,068	N/A(2)
Total Oncology	196,804	178,176	10 %
Other	943	2,783	(66)%
Product sales, net	809,837	603,531	34 %
Royalties and contract revenues	3,884	4,050	(4)%
Total revenues	$ 813,721	$ 607,581	34 %

(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.

Product Sales, Net

Total oxybate product sales increased by $22.6 million in the three months ended March 31, 2022 compared to the same period in 2021. Total oxybate revenue bottle volume increased by 3% in the three months ended March 31, 2022 compared to

the same period in 2021 reflecting our continued investment in patient access programs during the launch of Xywav. Average active oxybate patients on therapy were approximately 16,650 in the first quarter of 2022, an increase of approximately 6% compared to the same period in 2021. Xyrem product sales decreased in the three months ended March 31, 2022 compared to the same period in 2021 primarily due to a decrease in sales volume, reflecting the continued adoption of Xywav by existing Xyrem patients, and higher gross to net deductions, 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 months ended March 31, 2022 compared to the same period in 2021 primarily due to higher sales volumes, with bottle volume increasing by 148%. Epidiolex/Epidyolex product sales in the three months ended March 31, 2022 were $157.9 million. On a pro forma basis, Epidiolex/Epidyolex product sales increased by 6% in the three months ended March 31, 2022 compared to the same period in 2021, primarily due to an increase in commercial sales volumes and higher average net selling price. Price increases were instituted in January 2021 and January 2022. Sunosi product sales increased in the three months ended March 31, 2022, compared to the same period in 2021 primarily due to an increase in sales volume.

Zepzelca product sales increased in the three months ended March 31, 2022 compared to the same period in 2021 primarily due to a higher average net selling price. Price increases were instituted in July 2021 and January 2022. Rylaze product sales were $54.2 million in the three months ended March 31, 2022, following its U.S. launch in July 2021. Vyxeos and Defitelio/defibrotide product sales for the three months ended March 31, 2022 were in line with the same period in 2021. 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 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 an expected reduction in Sunosi upon completion of the sale to Axsome.

Cost of Product Sales

Cost of product sales increased in the three months ended March 31, 2022 compared to the same period in 2021 primarily due to the cost of product sales acquired in the acquisition of GW, including the acquisition accounting inventory fair value step-up expense, or fair value step-up expense of $63.9 million. Gross margin as a percentage of net product sales was 85.8% for the three months ended March 31, 2022 compared to 93.3% for the same period in 2021. The decrease in our gross margin percentage was primarily due to the impact of the fair value step-up expense. 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 increased in the three months ended March 31, 2022 compared to the same period in 2021, primarily due to an increase in compensation-related expenses driven by higher headcount due to the acquisition of GW. We expect selling, general and administrative expenses in 2022 to decrease compared to 2021, primarily due to a reduction in transaction and integration-related expenses and a reduction in costs associated with Sunosi upon completion of the sale to Axsome, 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.

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 March 31,	
	2022	2021
Clinical studies and outside services	$ 56,429	$ 31,046
Personnel expenses	55,301	36,226
Other	18,251	9,301
Total	$ 129,981	$ 76,573

Research and development expenses increased by $53.4 million in the three months ended March 31, 2022, compared to the same period in 2021. Clinical studies and outside services costs increased in the three months ended March 31, 2022 compared to the same period in 2021 primarily due to the addition of costs related to clinical programs for Epidiolex, nabiximols, cannabinoids and an increase in costs related to JZP150 and suvecaltamide (JZP385). Personnel expenses increased by $19.1 million in the three months ended March 31, 2022, compared to the same period in 2021 due to increased headcount primarily driven by the acquisition of GW.

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 as we prepare for anticipated data read-outs from clinical trials, initiate and undertake additional clinical trials and related development work and potentially acquire rights to additional product candidates.

Intangible Asset Amortization

Intangible asset amortization increased by $103.9 million in the three months ended March 31, 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. 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.

Interest Expense, Net

Interest expense, net increased by $43.3 million in the three months ended March 31, 2022, compared to the same period in 2021, primarily due to higher interest expense from (i) a seven-year $3.1 billion term loan B facility, or the Dollar Term Loan and (ii) a seven-year $625.0 million term loan B facility, or the Euro Term Loan, together with the Dollar Term Loan, collectively known as the Term Loan and 4.375% senior secured notes, due 2029, or the Secured 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

Our income tax expense was $0.5 million for the three months ended March 31, 2022, compared to $18.0 million for the same period in 2021. The decrease in the income tax expense resulted primarily from the mix of pre-tax income and losses incurred across tax jurisdictions. 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 March 31, 2022, we had cash and cash equivalents of $490.8 million, borrowing availability under our revolving credit facility of $500.0 million and long-term debt principal balance of $6.2 billion. Our long-term debt included $3.1 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 2.00% exchangeable senior notes due 2026, or the 2026 Notes and $575.0 million principal amount of the 1.50% exchangeable senior notes due 2024, or the 2024 Notes. We generated cash flows from operations of $209.0 million during the three months ended March 31, 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 the first quarter of 2022, we repaid €208.3 million, or $251.0 million which represents the remaining principal amount of the Euro Term Loan. We have made voluntary repayments of €625.0 million, or $753.0 million, relating to Euro Term Loan and mandatory repayments of $23.3 million 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 8, 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” in Part I, Item 1A in our Annual Report on Form 10-K for the year ended December 31, 2021 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 and cash equivalents, cash we expect to generate from operations and funds available under our Revolving Credit Facility will be sufficient to fund our operations and to meet our existing obligations for the foreseeable future. The adequacy of our cash resources depends on many assumptions, including primarily our assumptions with respect to product sales and expenses, as well as the other factors set forth in “Risk Factors” in Part I, Item 1A in our Annual Report on Form 10-K for the year ended December 31, 2021 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, as a result of the COVID-19 pandemic the global financial markets have experienced significant volatility. 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, 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 extraordinary general meeting of shareholders in September 2021, 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 preemption opt-out authority that had been in effect prior to August 4, 2021, which could adversely affect our ability to effectively use our unissued share capital to fund in-licensing or acquisition opportunities, or to otherwise raise additional capital for our business. 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):

	Three Months Ended March 31,	
	2022	2021
Net cash provided by operating activities	$ 208,979	$ 284,997
Net cash (used in) provided by investing activities	(37,292)	737,132
Net cash (used in) provided by financing activities	(270,811)	18,276
Effect of exchange rates on cash and cash equivalents	(1,489)	(641)
Net (decrease) increase in cash and cash equivalents	$ (100,613)	$ 1,039,764

Operating activities

Net cash provided by operating activities decreased by $76.0 million in the three months ended March 31, 2022 compared to the same period in 2021, primarily due to a decrease in net cash inflow related to changes in operating assets and liabilities.

Investing activities

Net cash (used in) provided by investing activities decreased by $774.4 million in the three months ended March 31, 2022 compared to the same period in 2021, primarily due to the following:

- $739.3 million in net proceeds from maturity of investments, primarily time deposits, in the three months ended March 31, 2021; and
- $25.0 million milestone payment to PharmaMar in relation to our first sales-based milestone for Zepzelca in the three months ended March 31, 2022.

Financing activities

Net cash (used in) provided by financing activities decreased by $289.1 million in the three months ended March 31, 2022 compared to the same period in 2021, primarily due to:

- Repayment of long-term debt of $258.8 million in the three months ended March 31, 2022, compared to $8.3 million in the three months ended March 31, 2021;
- A decrease of $28.7 million in proceeds from employee equity incentive and purchase plans; and
- An increase of $10.0 million in payment of employee withholding taxes related to share-based awards.

Debt

The summary of our outstanding indebtedness under our financing arrangements is included in Note 8, 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 three months ended March 31, 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 three months ended March 31, 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 in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2021. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our plans, objectives, estimates, expectations and intentions only as of the date of this filing. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results and the timing of events may be materially different from what we expect. We hereby qualify our forward-looking statements by our cautionary statements. Except as required by law, we undertake no obligation to update or supplement any forward-looking statements publicly, or to update or supplement the reasons that actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

During the three months ended March 31, 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 March 31, 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 March 31, 2022, other than continuing changes to our internal control process resulting from the acquisition 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 9, 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

There have been no material changes to the risk factors as previously disclosed in Part I, Item 1A in our Annual Report on Form 10-K for the year ended December 31, 2021.

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 March 31, 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 March 31, 2022, we did not repurchase any of our ordinary shares. As of March 31, 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#	Amendment No. 4, dated as of April 18, 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)

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

Portions of this document (indicated by "[***]") have been omitted because they are not material and are the type that the Company treats as private and confidential.

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

* 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: May 4, 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)

[***] = CERTAIN PORTIONS OF THIS AGREEMENT HAVE BEEN OMITTED BECAUSE THE OMITTED PORTIONS ARE BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

Exhibit 10.1

AMENDMENT NO. 4 TO PHARMACY MASTER SERVICES AGREEMENT

THIS AMENDMENT NO. 4 (this "**Amendment**") to the Agreement (as defined below) is entered into as of April 18, 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 Xyrem and Xywav; and

WHEREAS, the Parties desire to amend the Agreement in order to allow ESSDS to perform dispensing, distribution and other services for Jazz Pharmaceuticals for Authorized Generic Product (as defined below).

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. Amendment to Definition of Average Daily Sales. Section 1.4 of the Agreement is hereby amended and restated in its entirety as follows:

   " "Average Daily Sales" shall mean the average number of commercial bottles of Xyrem and Xywav sold per day over the previous six (6) months, excluding all sales of Product (i) for dispensing to VA, and (ii) to Puerto Rico."

2. Amendment to Definition of Bridge Benefit. Section 1.5 of the Agreement is hereby amended and restated in its entirety as follows:

   " "Bridge Benefit" shall mean the Jazz Pharmaceuticals' or Authorized Generic Partner sponsored program that provides Product at no cost to eligible patients who are at risk of an interruption in therapy due to a change in their insurance circumstances."

3. Amendment to Definition of Patient Assistance Program. Section 1.19 of the Agreement is hereby amended and restated in its entirety as follows:

   " "Patient Assistance Program" or "PAP" shall mean the Jazz Pharmaceuticals' sponsored program that provides Xyrem or Xywav at no cost to eligible patients. Jazz Pharmaceuticals has sole discretion over the eligibility criteria and operation

of the PAP. “PAP Patient” shall mean a Patient who has been approved as eligible to participate in the PAP.”

4. Amendment to Definition of PAP Order. Section 1.20 of the Agreement is hereby amended and restated in its entirety as follows:

> **“ “**PAP Order” shall mean each shipment of Xyrem or Xywav by ESSDS to any PAP Patient in accordance with this Agreement.”

5. Amendment to Definition of Product. Section 1.25 of the Agreement is hereby amended and restated in its entirety as follows:

> “ “Product” shall mean (a) Xyrem® (sodium oxybate) oral solution (“Xyrem”) and dosing kit, (b) Xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution (“Xywav”) and dosing kit, and/or (c) for all purposes of this Agreement an Authorized Generic Product. However, references to Xyrem, Xywav, or Authorized Generic Product shall mean the specific product or products referenced.”

6. Amendment to Definition of REMS Documents. Section 1.28 of the Agreement is hereby amended and restated in its entirety as follows:

> “ “REMS Documents” shall mean the approved XYWAV and XYREM REMS Documents, including both the XYWAV and XYREM REMS Document and the XYWAV and XYREM REMS Supporting Document, as well as any modifications or successors documents thereto as approved by the FDA.”

7. Amendment to Definition of REMS Program. Section 1.30 of the Agreement is hereby amended and restated in its entirety as follows:

> “ “REMS Program” shall mean the XYWAV and XYREM REMS Program, as approved by the FDA, or any successor entity thereto as approved by the FDA, including successor entities including additional oxybate formulations, as described in the REMS Documents.”

8. Amendment to Definition of WAC. Section 1.40 of the Agreement is hereby amended and restated in its entirety as follows:

> “ “WAC” shall mean the current wholesale acquisition cost of Xyrem or Xywav as provided by Jazz Pharmaceuticals. WAC does not include discounts, rebates or chargebacks. WAC may not be the actual acquisition cost.”

9. Amendment to Definition of Work Instructions. Section 1.42 of the Agreement is hereby amended and restated in its entirety as follows:

" "Work Instructions" or "WIs" shall mean written work instructions of ESSDS, as of the Effective Date, or any others mutually agreed to by the Parties after the Effective Date, which provide detailed descriptions of the performance of certain tasks and Services that ESSDS will perform with respect to specific Product(s) (i.e., Xyrem, Xywav and/or Authorized Generic Product(s))."

10. Addition of New Definitions. Article I of this Agreement is hereby amended by adding the following definitions as new Sections 1.43 and 1.44 of the Agreement, respectively:

1.43 " "Authorized Generic Partner" shall mean a third party pharmaceutical company that Jazz Pharmaceuticals has appointed as a distributor of Authorized Generic Product in the Territory, and to whom Jazz Pharmaceuticals will supply Authorized Generic Product, in each case, pursuant to certain written agreements between Jazz Pharmaceuticals and such third party pharmaceutical company."

1.44 " "Authorized Generic Product" shall mean a generic product that: (a) contains 500 mg/mL sodium oxybate oral solution as the sole active ingredient; (b) is marketed in the Territory without use of the Trademarks (with the limited exception of REMS Program Items and syringes that bear the Trademarks); (c) is marketed by an Authorized Generic Partner in the Territory pursuant to the NDA 021196; and (d) is supplied by or on behalf of Jazz Pharmaceuticals to the Authorized Generic Partner."

11. Amendment to Section 2.1. Section 2.1 of the Agreement is hereby amended and restated in its entirety as follows:

"Services. During the term of the Agreement, all commercial, non-clinical trial Product sold by Jazz Pharmaceuticals or an Authorized Generic Partner, or made available by Jazz Pharmaceuticals through the PAP, in the Territory will be dispensed exclusively through ESSDS pursuant to the terms of this Agreement. ESSDS agrees to provide those pharmacy and REMS services described in this Agreement and written Work Orders hereunder (the "Pharmacy Services"), including but not limited to pharmacy dispensing services, safety and support services, ancillary supply services, certain education services, and data reporting.

During the term of the Agreement, ESSDS agrees to provide other REMS services described in this Agreement and written Work Orders hereunder (the "REMS Pharmacy Services"), including but not limited to activities directed towards ensuring Jazz Pharmaceuticals' and each Authorized Generic Partner's compliance with the requirements of the REMS Program.

The Pharmacy and REMS Pharmacy Services (collectively, the "Services") to be provided as of the Effective Date are described in written

Work Orders hereunder. These Services may be amended from time to time through the addition of a Work Order. Each Work Order will be numbered in consecutive order. Each Work Order will be deemed incorporated into this Agreement. In the event of a conflict between the terms of this Agreement and the terms of the Work Order, the
terms of this Agreement will govern, unless the Parties have expressly agreed in the Work Order that the Work Order shall amend a specified section of this Agreement, in which case such amendment will only apply to such Work Order.

In addition to the Services set forth in the following, fully executed Work Orders to the Prior Master Services Agreement between the Parties, and for which services are ongoing, shall henceforth be considered Work Orders under this Agreement. Each of these Work Orders shall be subject to the terms and conditions set forth in this Agreement as if they were originally executed hereunder, except that the fees associated with these Work Orders are subject to the annual adjustment specified in Section 3.1, meaning that the fees charged at execution will be those fees agreed upon for calendar year 2020, [***].

For the avoidance of doubt, Jazz Pharmaceuticals' commercial function shall have responsibility for Jazz' Pharmaceuticals oversight of Pharmacy Services, and decisions related to changes to Pharmacy Services shall be directed by personnel in that function. For the avoidance of doubt, Jazz Pharmaceuticals' non-commercial function of Pharmacovigilance, Quality and Safety shall have responsibility for Jazz Pharmaceuticals' oversight of the REMS Pharmacy Services, and decisions related to changes to REMS Pharmacy Services shall be directed by personnel in that function. The Services provided by ESSDS pursuant to this Agreement and the Work Orders entered into by the Parties shall include the provision of Services by ESSDS on behalf of Authorized Generic Partners solely with respect to Authorized Generic Product(s)."

12. Amendment to Section 2.3. Section 2.3 of the Agreement is hereby amended and restated in its entirety as follows:

"Exclusive Pharmacy. During the term of this Agreement, all commercial, non- clinical trial Product sold by Jazz Pharmaceuticals or an Authorized Generic Partner, or made available by Jazz Pharmaceuticals through the PAP, in the Territory will be dispensed exclusively through ESSDS pursuant to this Agreement. [***] Notwithstanding the foregoing, Jazz Pharmaceuticals may establish a third party pharmacy to make available commercial, non-clinical trial Product in the Territory if ESSDS does not,
or cannot, meet Jazz Pharmaceuticals requirements for dispensing the Product in the Territory in accordance with the terms and conditions of the Agreement."

13. Amendment to Section 2.4.1. Section 2.4.1 of the Agreement is hereby amended and restated in its entirety as follows:

[***]

14. Amendment to Section 4.1(b). Section 4.1(b) of the Agreement is hereby amended and restated in its entirety as follows:

"Transfer of Title. Upon removal of the consigned Xyrem or Xywav by ESSDS from the product storage area to fulfill a Non-PAP Order, title to such Xyrem or Xywav shall pass to ESSDS and ESSDS shall be deemed to have purchased from Jazz Pharmaceuticals such Xyrem or Xywav. ESSDS shall confirm all such purchases and shipments of Xyrem and Xywav in writing to Jazz Pharmaceuticals on a weekly basis via purchase order, which will document all purchases of Xyrem and Xywav by ESSDS during the previous week. If a month ends in the beginning or middle of a week, ESSDS shall send an additional purchase order to Jazz Pharmaceuticals to confirm purchases of Xyrem and Xywav made as of the last day of each month. This transfer of title process applies only to Xyrem and Xywav that has not already been purchased as part of a Buy In option, as described in Section 4.2, where title transfers upon submission of a relevant purchase order."

Upon removal of the consigned Authorized Generic Product by ESSDS from the product storage area to fulfill a Non-PAP Order, title to such Authorized Generic Product shall pass to the applicable Authorized Generic Partner, and then to ESSDS and ESSDS shall be deemed to have purchased from the applicable Authorized Generic Partner such Authorized Generic Product. ESSDS shall confirm all purchases and shipments of each Authorized Generic Product in writing to Jazz Pharmaceuticals on a weekly basis via written confirmation in a format substantially similar to Exhibit E, which will document all purchases of Authorized Generic Product by ESSDS during the previous week. For clarity, there shall be a separate written confirmation for purchases and shipments of each specific Authorized Generic Product. If a month ends in the beginning or middle of a week, ESSDS shall send an additional written confirmation to Jazz Pharmaceuticals to confirm purchases of each Authorized Generic Product made as of the last day of each month. This transfer of title process applies only to Authorized Generic Product that has not already been purchased as part of an agreement reached between an Authorized Generic Partner and ESSDS, where title transfers upon submission of a relevant purchase order."

15. Amendment to Section 4.1(c). Section 4.1(c) of the Agreement is hereby amended and restated in its entirety as follows:

"Pricing of Non-PAP Orders. Subject to the restrictions set forth in Section 6.2 of this Agreement and any FDA requirement or other Applicable Law, ESSDS shall have the sole authority to determine pricing to Patients for Xyrem and

Xywav for Non-PAP Orders. Pricing to Patients for each Authorized Generic Product shall be subject to negotiation between ESSDS and each Authorized Generic Partner."

16. Amendment to Section 4.1(d). A new Section 4.1(d) is hereby added to the Agreement as follows:

"Ordered Quantities. In order to ensure that ESSDS is able to properly fulfill Non- PAP orders with any Authorized Generic Product, during the term of this Agreement, Jazz shall provide ESSDS periodic updates setting forth the number of units of Product that each Authorized Generic Partner has agreed to purchase from Jazz Pharmaceuticals for the period of time covered by the particular update (the "AG Quantities"). In the event there are changes to the AG Quantities, Jazz Pharmaceuticals shall provide additional updates to ESSDS. ESSDS will not fulfill Non-PAP Orders with Authorized Generic Product in excess of the identified AG Quantities, except to the extent that ESSDS has received written permission from Jazz Pharmaceuticals to do so; and to avoid disruptions in patient care Jazz Pharmaceuticals will not unreasonably withhold consent. The process for Jazz Pharmaceuticals to provide the AG Quantities to ESSDS will be mutually agreed upon and captured in Work Instructions.

17. Amendment to Section 4.2. Section 4.2 of the Agreement is hereby amended and restated in its entirety as follows:

"Buy In. ESSDS shall be offered an [***].

18. Amendment to Section 4.3. Section 4.3 of the Agreement is hereby amended and restated in its entirety as follows:

"PAP Orders. Subject to available space as determined by ESSDS, Jazz Pharmaceuticals will deliver to ESSDS at the Certified Pharmacy, at Jazz Pharmaceuticals' own expense, sufficient quantities of Xyrem and Xywav to fulfill PAP orders. ESSDS will maintain a reasonable quantity of components on-site or nearby to allow product disbursements to occur in a timely and efficient manner. The Xyrem or Xywav shipped pursuant to PAP Orders shall be for the account of Jazz Pharmaceuticals, and title to such Xyrem or Xywav shall remain with Jazz Pharmaceuticals until confirmation of the PAP Order in ESSDS' internal order processing system, at which time title will pass to the PAP Patient. ESSDS will fulfill PAP Orders as set forth in the applicable SOP and Business Rules."

19. Amendment to Section 4.4. Section 4.4 of the Agreement is hereby amended and restated in its entirety as follows:

"Risk of Loss. All risk of Product loss or damage during the time that such Product is at the Certified Pharmacy prior to the transfer of title to ESSDS pursuant to Section 4.1(b) shall be borne by Jazz Pharmaceuticals, except to the extent caused by the negligence or willful misconduct of ESSDS or its Affiliates. Payment to Jazz Pharmaceuticals by ESSDS (i) for Xyrem or Xywav lost or damaged while at the Certified Pharmacy after title to such Xyrem or Xywav has transferred to ESSDS pursuant to Section 4.1(b); or (ii) for Product that is lost or damaged as the result of ESSDS' or its Affiliates' negligence or willful misconduct shall be based on Jazz Pharmaceuticals' actual replacement costs, as reasonably determined and documented by Jazz Pharmaceuticals."

20. Amendment to Section 4.5. Section 4.5 of the Agreement is hereby amended and restated in its entirety as follows:

"Returns and Replacement. In the event that (a) Xyrem or Xywav is damaged or destroyed after the product was dispensed and shipped to the Patient pursuant to Section 4.1(b) and (b) such damage or destruction [***], ESSDS shall replace the Xyrem or Xywav to the Patient free of charge once the damaged Xyrem or Xywav is returned to ESSDS. ESSDS shall monitor all reports of lost Product for the potential for abuse or diversion in compliance with relevant SOPs and WIs. ESSDS will cooperate with state and federal authorities fully in any investigations of lost Product, and will promptly provide reports of such loss to Jazz Pharmaceuticals within one (1) week from ESSDS' conclusion of its investigation. Where abuse or diversion is not suspected and the damage or destruction is the direct result of a defect [***], ESSDS will promptly replace the Xyrem or Xywav at no charge to the Patient once approved by the pharmacy. Such replacement of Xyrem or Xywav shall be considered a Non-PAP order and title to such product

shall pass to ESSDS and ESSDS shall be deemed to have purchased such product from Jazz Pharmaceuticals upon removal of the consigned product to fulfill the product replacement Jazz Pharmaceuticals shall reimburse ESSDS for [***].

All Return or Replacement activities will be conducted in accordance with applicable SOPs, Work Instructions, and the REMS Documents. Applicable fees will apply to the processing and shipping of replacement Xyrem and Xywav and WAC price will be applied to the replacement Xyrem or Xywav, and record of the shipment will be kept in the Patient file. Upon receipt of damaged Product, ESSDS will keep damaged Product in a secure locked area in compliance with applicable SOPs, and will dispose of it using Jazz Pharmaceuticals' reverse distributor vendor in compliance with applicable SOPs and Applicable Law. ESSDS will be responsible for covering any shipping costs associated with getting such Product to the reverse distributor for

destruction. All other costs associated with the utilization of Jazz Pharmaceuticals' reverse distributor vendor will be covered by Jazz Pharmaceuticals."

21. Amendment to Section 4.6. Section 4.6 of the Agreement is hereby amended and restated in its entirety as follows:

"Expired Product. Jazz Pharmaceuticals will, at its cost, replace Product that expires prior to the purchase thereof by ESSDS. Jazz Pharmaceuticals will not replace expired Xyrem or Xywav once it has been purchased by ESSDS. ESSDS will dispose of or return expired Product as reasonably directed by Jazz Pharmaceuticals, in accordance with Applicable Law and applicable SOPs and WIs, and Jazz Pharmaceuticals shall promptly reimburse ESSDS for all reasonable out-of-pocket expenses incurred in complying with this Section."

22. Amendment to Section 6.1. Section 6.1 of the Agreement is hereby amended and restated in its entirety as follows:

"6.1 Purchase Price of Products.

(a) Price of Product Purchased from Jazz Pharmaceuticals. With respect to all Xyrem or Xywav purchased by ESSDS from Jazz Pharmaceuticals pursuant to Section 4.1, ESSDS shall pay a purchase price to Jazz Pharmaceuticals [***]. Notwithstanding, ESSDS shall pay Jazz Pharmaceuticals [***].

(b) Price of Product Purchased from Authorized Generic Partners. The Parties understand and agree that ESSDS will enter into separate agreements with each

Authorized Generic Partner for the supply and pricing of each such Authorized Generic Partner's Authorized Generic Product."

23. Amendment to Section 6.2. Section 6.2 of the Agreement is hereby amended and restated in its entirety as follows:

"Payment Terms. ESSDS shall have the right to establish the price at which it resells Xyrem and Xywav to Non-PAP Patients, and shall have all right title and interest in and to any amounts that ESSDS receives from third parties in connection with Xyrem and Xywav dispensed or distributed pursuant to Non-PAP Orders; provided, however, that the price at which ESSDS sells Xyrem and Xywav shall not exceed [***]. This limitation is intended solely to create an upper limit, and is not intended by either Party to indicate a desire, intent, or belief that the practice of pricing at, or near, this upper limit is sufficient to meet current marketplace demands. The Parties acknowledge the vast complexities of pricing within the pharmaceutical marketplace, and ESSDS represents that

typical pricing conventions will apply (example: larger customers may receive better pricing). ESSDS shall make best efforts in all cases to negotiate in good faith with any third party payer in connection with the purchase of Xyrem or Xywav on terms that are commercially reasonable. The Parties have a shared desire to ensure Patients receive drug in a timely manner. From time to time Jazz Pharmaceuticals may become aware of specific third party payer issues that could impact Patients. In the event that Jazz Pharmaceuticals becomes aware of such issues, Jazz Pharmaceuticals may escalate those concerns through the Jazz Pharmaceuticals' Head of US Market Access, directly to the ESSDS VP of Commercial Activity. ESSDS agrees to use best efforts to ensure such issues are quickly resolved. Nothing in this section shall be interpreted as Jazz Pharmaceuticals setting pharmacy pricing or taking any action inconsistent with provisions contained in Article 4.1(c), titled "Pricing of Non-PAP Orders"."

24. Amendment to Section 8.6. Section 8.6 of the Agreement is hereby amended and restated in its entirety as follows:

"Data. ESSDS agrees to maintain the security and confidentiality of all Data, including any Personal Data, in accordance with all Applicable Laws, applicable agreements, patient release forms, consents, the provisions of this Agreement, the SOPs and all Work Orders. For the purposes of this Section, "Personal Data" shall mean computerized or electronic records as well as paper-based files in any medium or format collected by ESSDS in connection with the performance of Services, including but not limited to information received from any patient, health care professional, and other business-to-business customers or vendors that specifically identifies, or when used together with other available information identifies, a particular individual. Personal Data includes name, address, telephone number, fax number, Social Security number, DEA number, other government issued identifier, credit card information, insurance identification number, IP address, email address and information relating to the past, present or future health

or condition (physical or mental) of an individual, but does not include information that is deidentified, encoded or made anonymous. The parties agree that Jazz Pharmaceuticals will not have any ownership in Personal Data created, collected or recorded by ESSDS in connection with the Services. ESSDS agrees that it will not utilize Personal Data outside the scope of this Agreement, provided however, that ESSDS and/or its Affiliates may use Personal Data in the aggregate or on a deidentified basis with other drug-use data, to the extent permitted by Applicable Law, without charge, for research, cost analysis and other internal purposes of ESSDS; provided that said use does not in any way compete with the business of Jazz Pharmaceuticals.

ESSDS will establish commercially reasonable controls to ensure the confidentiality of Confidential Information, Personal Data and Data, and to

ensure that Confidential Information, Personal Data and Data is not disclosed to any Authorized Generic Partner contrary to the provisions of this Agreement; provided, further, without limiting the foregoing, that ESSDS shall implement and/or maintain a comprehensive written information privacy and security program that includes appropriate administrative, technical and physical safeguards and other security measures appropriate to the size and complexity of ESSDS' operations and the nature and scope of its activities that are designed to (a) ensure the security and confidentiality of Data; (b) protect against any anticipated threats or hazards to the security, confidentiality and integrity of Data; and (c) protect against unauthorized access to or use of Data that could result in the destruction, use, modification or unauthorized disclosure of Data.

25. Amendment to Section 9.3.4. Section 9.3.4 of the Agreement is hereby amended and restated in its entirety as follows:

"Jazz Pharmaceuticals represents and warrants that: (i) all programs initiated by Jazz Pharmaceuticals (and not on behalf of an Authorized Generic Partner) and included as part of the Services, including any eligibility criteria for participation in any such programs, shall be structured in accordance with Applicable Law; and
(ii) Jazz Pharmaceuticals is responsible for the content of all materials provided by Jazz Pharmaceuticals for use or distribution in connection with the Services, including REMS Program Items, and Jazz Pharmaceuticals shall ensure that all such materials have received any required regulatory approvals, are educational and not promotional with respect to Xyrem or Xywav or providing Xyrem or Xywav- related or REMS Program-related information."

26. Amendment to Section 10.1. Section 10.1 of the Agreement is hereby amended to add "(including Services relating to Authorized Generic Product)" in clause (a) immediately after "Jazz Pharmaceuticals."

27. Amendment to Section 12.1. Section 12.1 of the Agreement is hereby amended and restated in its entirety as follows:

"Indemnification by Jazz Pharmaceuticals. Subject to the terms hereof, Jazz Pharmaceuticals shall indemnify and defend ESSDS, its Affiliates, and their respective directors, officers, employees, agents, successors and permitted assigns, from and against any liabilities, damages, loss, judgments, settlements or expense (including reasonable attorney's fees) (collectively, "Losses") as a result of any third-party claim, demand or action (collectively, "Claims") to the extent arising from (a) the manufacture, sale or use of a Product; (b) the negligence, recklessness, or willful misconduct of Jazz Pharmaceuticals or any of its employees; (c) Jazz Pharmaceuticals' failure to comply with its obligations under this Agreement; or

(d) Claims by an Authorized Generic Partner relating to the receipt by Jazz Pharmaceuticals of Data related to an Authorized Generic Product that is required to be transmitted by ESSDS to Jazz Pharmaceuticals under this Agreement (for clarity, this indemnification obligation does not apply to ESSDS's transmission of any data or information that ESSDS should not disclose to Jazz Pharmaceuticals under this Agreement, such as confidential information or data, including the price at which an Authorized Generic Partner sells any Product to ESSDS, received by ESSDS pursuant to a separate agreement with an Authorized Generic Partner). Such obligation to indemnify, defend, and hold harmless shall not apply to the extent Losses or Claims are caused by ESSDS' breach hereof, negligence, recklessness or willful misconduct.

28. Amendment to Section 13.4. Section 13.4 of the Agreement is hereby amended and restated in its entirety as follows:

"Exclusivity and Non-Competition. Except for Services performed by ESSDS in connection with an Authorized Generic Product as set forth in a Work Order, from the Effective Date until twelve (12) months after the termination or expiration of this Agreement, ESSDS will not accept or participate in Services related to products related to products related to oxybate and oxybate salts and their derivatives with any other Party without the prior written consent of Jazz Pharmaceuticals. Except for Services performed by ESSDS in connection with an Authorized Generic Product as set forth in a Work Order, from the Effective Date until the termination or expiration of this Agreement, ESSDS will not accept or participate in Services related to products indicated for the treatment of cataplexy or excessive daytime sleepiness in narcolepsy or idiopathic hypersomnia.

29. Amendment to Exhibit A. Exhibit A is deleted in its entirety and replaced with the attached Exhibit A.

30. General. This Amendment constitutes an amendment in writing to the Agreement in accordance with Section 14.1 of the Agreement.

31. 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.

32. 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.

33. 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

05-Apr-2022

By: ___

Name:

Title:

EXPRESS SCRIPTS SPECIALTY DISTRIBUTION SERVICES, INC.

By: /s/ Joshua B. Parker

Name: Joshua B. Parker

Title: VP

04/04/2022 | 1:56 PM CDT

RPM for JLD 4.4.22

EXHIBIT A

Trademarks

XYREM® (sodium oxybate)

866-XYREM88®

Jazz®

Jazz Pharmaceuticals, Inc.®

JP®

XYWAV®

JAZZ CARES®

MYWAV®

XYREM (SODIUM OXYBATE) ORAL SOLUTION CIII®

XYREM PATIENT SUCCESS PROGRAM®

XYREM SUCCESS PROGRAM®

And logos associated with the foregoing

EXHIBIT E

PRODUCT ID	DESCRIPTION	LOT NO.	PRICE SCHEDULE	UNITS	ORDERS
TOTAL ORDER					

Lot No.	Bottles	Orders

Lot No.	Half Bottles

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: May 4, 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: May 4, 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 March 31, 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: May 4, 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.