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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 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**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, as of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $9,527,447,500 based upon the last sale price reported for the registrant's ordinary shares on such date on The Nasdaq Global Select Market. The calculation of the aggregate market value of voting and non-voting common equity excludes 1,548,177 ordinary shares of the registrant held by executive officers, directors and shareholders that the registrant concluded were affiliates of the registrant on that date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of February 22, 2023, a total of 63,331,430 ordinary shares, nominal value $0.0001 per share, of the registrant were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III, Items 10-14 of this Form 10-K is incorporated by reference to the registrant's definitive Proxy Statement for the 2023 Annual General Meeting of Shareholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A. If such Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Form 10-K, such information will be included in an amendment to this Form 10-K to be filed within such 120-day period.

JAZZ PHARMACEUTICALS PLC
2022 ANNUAL REPORT ON FORM 10-K

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We own or have rights to various copyrights, trademarks, and trade names used in our business in the U.S. and/or other countries, including the following: Jazz Pharmaceuticals®, Xyrem® (sodium oxybate) oral solution, Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, Epidiolex® (cannabidiol) oral solution, Epidyolex® (the trade name in Europe and other countries outside the U.S. for Epidiolex), Defitelio® (defibrotide sodium), Defitelio® (defibrotide), CombiPlex®, Vyxeos® (daunorubicin and cytarabine) liposome for injection, Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion, Zepzelca® (lurbinectedin), Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) and Sativex® (nabiximols) oral solution. This report also includes trademarks, service marks and trade names of other companies. Trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "propose," "intend," "continue," "potential," "possible," "strive," "seek," "designed," "goal", "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 factors in greater detail under Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. In addition, our goals and objectives are aspirational and are not guarantees or promises that such goals and objectives will be met. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this filing. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify our forward-looking statements by our cautionary statements. Except as required by law, we assume no obligation to update our forward-looking statements publicly, or to update the reasons that actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

SUMMARY RISK FACTORS

Below is a summary of material factors that make an investment in our ordinary shares speculative or risky. Importantly, this summary does not address all of the risks and uncertainties that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, as well as other risks and uncertainties that we face, can be found under "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. The below risk factor summary is qualified in its entirety by that more complete discussion of such risks and uncertainties. You should consider carefully the risks and uncertainties described under "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K as part of your evaluation of an investment in our ordinary shares.

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

- Delays or problems in the supply of our products for sale or for use in clinical trials, loss of our single source suppliers or failure to comply with manufacturing regulations could materially and adversely affect our business, financial condition, results of operations and growth prospects.
- Our future success depends on our ability to successfully develop and obtain and maintain regulatory approvals for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.
- We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these transactions.
- Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects.
- It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.
- We have incurred and may in the future incur substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products.
- Significant disruptions of information technology systems or data security breaches could adversely affect our business.
- We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products.
- If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.
- To continue to grow our business, we will need to commit substantial resources, which could result in future losses or otherwise limit our opportunities or affect our ability to operate and grow our business.

NOTE REGARDING COMPANY REFERENCE

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

PART I

Item 1. Business

Overview

Jazz Pharmaceuticals plc is a global biopharmaceutical company 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.

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.

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 seven years of age and older, and also approved by FDA in August 2021 for the treatment of idiopathic hypersomnia, or IH, in adults and launched in the U.S. in November 2021. Xywav contains 92% less sodium than Xyrem®;
- **Xyrem (sodium oxybate) oral solution**, a product approved by FDA and distributed in the U.S. for the treatment of cataplexy or EDS in patients with narcolepsy seven years of age and older; Jazz also markets Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. Xyrem is also approved and distributed in the European Union, or EU (EU market authorizations include Northern Ireland), Great Britain and other markets through a licensing agreement; and
- **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 and Great Britain (where it is marketed as Epidyolex®) and other markets listed in the table below, 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.

Oncology

- **Zepzelca® (lurbinectedin)**, a product approved by FDA in June 2020 under FDA's accelerated approval pathway and launched in the U.S. in July 2020 for the treatment of adult patients with metastatic small cell lung cancer, or SCLC, with disease progression on or after platinum-based chemotherapy; in Canada, Zepzelca received conditional approval in September 2021 for the treatment of adults with Stage III or metastatic SCLC, who have progressed on or after platinum-containing therapy;
- **Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)**, a product approved by FDA in June 2021 and launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia, or ALL, or lymphoblastic lymphoma, or LBL, in adults and pediatric patients aged one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase;

- **Vyxeos® (daunorubicin and cytarabine) liposome for injection**, a product approved in the U.S., Canada, EU, Great Britain and other markets listed in the table below (marketed as Vyxeos® liposomal in the EU, Great Britain and other markets) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia, or t-AML, or AML with myelodysplasia-related changes, or AML-MRC. An expanded indication was granted in the U.S. for the treatment of newly diagnosed t-AML or AML-MRC in pediatric patients aged 1 year and older; and
- **Defitelio® (defibrotide sodium)**, a product approved in the U.S. and Brazil for the treatment of hepatic veno-occlusive disease, or VOD, with renal or pulmonary dysfunction following hematopoietic stem cell transplantation, or HSCT, and in Japan for the treatment of hepatic sinusoidal obstruction syndrome (hepatic VOD). It is currently approved in the EU, Great Britain and other markets listed in the table below 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.

In 2022, consistent with our strategy, we continued to focus on research and development activities within our neuroscience and oncology therapeutic areas. For a summary of our ongoing research and development activities, see “Business—Research and Development” in this Part I, Item 1.

Our Commercialized Products

Neuroscience

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

Xywav. In July 2020, FDA approved Xywav for the treatment of both cataplexy and EDS in patients with narcolepsy. Narcolepsy is a chronic, debilitating neurological disorder characterized by EDS and the inability to regulate sleep-wake cycles normally. Since there is not currently a cure for narcolepsy and we believe there is unmet need in the patient population for long-term disease management, we believe that Xywav represents an important new therapeutic option for patients with this sleep disorder. Narcolepsy affects an estimated one in 2,000 people in the U.S., with symptoms typically appearing in childhood. There are five primary symptoms of narcolepsy, including EDS, cataplexy, disrupted nighttime sleep, sleep-related hallucinations, and sleep paralysis. While patients with narcolepsy may not experience all five symptoms, EDS, an essential symptom of narcolepsy, is present in all narcolepsy patients and is characterized by chronic, pervasive sleepiness as well as sudden irresistible and overwhelming urges to sleep (inadvertent naps and sleep attacks). Narcolepsy may affect many areas of life, including limiting a patient’s education and employment opportunities, and may lead to difficulties at work, school, or in daily life activities like driving, operating machinery or caring for children. Patients with narcolepsy may also suffer from significant medical comorbidities, including cardiac disorders, depression, suicide risk, anxiety, diseases of the digestive system and respiratory diseases.

Cataplexy, the sudden loss of muscle tone with retained consciousness, can be one of the most debilitating symptoms of narcolepsy. Cataplexy is present in approximately 70% of patients with narcolepsy. Cataplexy can range from slight weakness or a drooping of facial muscles to the complete loss of muscle tone resulting in postural collapse. It may also impair a patient’s vision or speech. Cataplexy is often triggered by strong emotions such as laughter, anger or surprise. Cataplexy can severely impair a patient’s quality of life and ability to function.

Narcolepsy patients, by virtue of their diagnosis, are at increased risk of cardiovascular events and disease, and the impact of sodium on cardiovascular health is well established. There is also extensive scientific evidence that reducing sodium consumption, which is a modifiable risk factor, is associated with clinically meaningful reductions in blood pressure and cardiovascular disease risk. Therefore, we believe that reducing sodium intake compared to the standard of care by 92% each and every day is a significant advancement for these patients. The 92% reduction of sodium translates into a reduction of approximately 1,000 to 1,500 milligrams per day for a patient prescribed Xyrem, depending on the dose. Our commercial efforts with respect to Xywav 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. When patients transition from Xyrem to Xywav, Xywav treatment is initiated at the same dose and regimen (gram for gram) and titrated as needed based on efficacy and tolerability. The label for Xywav, unlike Xyrem, does not include a warning to prescribers to monitor patients sensitive to sodium intake, including patients with heart failure, hypertension or renal impairment.

Our internal market research finds that health care providers and patients who understand the increased risk of cardiovascular disease faced by narcolepsy patients and who have been educated on the meaningful reduction in sodium from Xyrem to Xywav cite that meaningful reduction as a key reason for prescribing or starting on Xywav. In June 2021, FDA recognized seven years of Orphan Drug Exclusivity, or ODE, for Xywav in narcolepsy through July 21, 2027, stating 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.

In approving Xywav, FDA approved a risk evaluation and mitigation strategy, or REMS, to cover both Xywav and Xyrem. The Xywav and Xyrem REMS has the same requirements for both products and both products are also distributed by the central pharmacy through exclusive agreements described more fully below.

On August 12, 2021, FDA approved Xywav for the treatment of IH in adults. Xywav is the first and only FDA-approved therapy to treat IH. We initiated the U.S. commercial launch of Xywav for the treatment of IH in adults on November 1, 2021. In January 2022, FDA recognized seven years of ODE for Xywav in IH through August 12, 2028. IH is a debilitating neurologic sleep disorder characterized by chronic EDS (the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness), severe sleep inertia, and prolonged and non-restorative nighttime sleep. Although there are overlapping clinical features with other conditions, including narcolepsy, IH has its own specific diagnostic criteria. IH can significantly affect social, educational and occupational functioning. An estimated 37,000 people in the U.S. have been diagnosed with IH and are actively seeking healthcare.

We commenced the U.S. launch in November 2020. To date, we have entered into agreements for Xywav with all three major pharmacy benefit managers, or PBMs, in the U.S. and various other entities and have achieved benefit coverage for Xywav in both narcolepsy and IH indications for approximately 90% of commercial lives.

We have seen strong adoption of Xywav in narcolepsy since its launch in November 2020 and increasing adoption in IH since its launch in November 2021. In 2022, net product sales of Xywav were $958.4 million, which represented 26% of our total net product sales for the year. There were approximately 10,300 active patients on Xywav exiting the fourth quarter of 2022, including approximately 8,550 active patients with narcolepsy and approximately 1,750 active patients with IH. With respect to Xywav and Xyrem in the aggregate, the average number of active oxybate patients on therapy was approximately 18,000 in the fourth quarter of 2022.

Xyrem. Xyrem was approved in the U.S. for the treatment of cataplexy in adult patients with narcolepsy in 2002 and was approved for EDS in adult patients with narcolepsy in 2005. In October 2018, Xyrem was also approved in the U.S. for the treatment of cataplexy or EDS in pediatric narcolepsy patients ages seven and older. In its updated 2021 treatment guidelines, the American Academy of Sleep Medicine gives sodium oxybate a strong recommendation for the treatment of narcolepsy in adults. To support the development and commercialization of Xyrem internationally, we have a license and distribution agreement with UCB Pharma Limited, or UCB, across other countries. This agreement provides UCB and its affiliates with the sole right to commercialize Xyrem in exclusive territories for all indications.

In 2022, net product sales of Xyrem were $1.0 billion, which represented 28% of our total net product sales for the year.

Xywav and Xyrem REMS. Our marketing, sales and distribution of Xywav and Xyrem in the U.S. are subject to a REMS, which is required by FDA to mitigate the risks of serious adverse outcomes resulting from inappropriate prescribing, abuse, misuse and diversion of Xywav and Xyrem. Under this REMS, all of the Xywav and Xyrem sold in the U.S. must be dispensed and shipped directly to patients or caregivers through a central pharmacy. Xywav and Xyrem may not be stocked in retail pharmacies. Physicians and patients must complete an enrollment process prior to fulfillment of Xywav and Xyrem prescriptions, and each physician and patient must receive materials concerning the serious risks associated with Xywav and Xyrem before the physician can prescribe, or a patient can receive, the product. The central certified pharmacy must monitor and report instances of patient or prescriber behavior giving rise to a reasonable suspicion of abuse, misuse or diversion of Xywav and Xyrem, and maintains enrollment and prescription monitoring information in a central database. The central pharmacy ships the product directly to the patient (or caregiver) by a courier service.

We have had exclusive agreements with Express Scripts Specialty Distribution Services, Inc., or ESSDS, the central pharmacy for Xywav and Xyrem, to distribute Xywav and Xyrem in the U.S. and provide patient support services related to Xyrem since 2002. In December 2022, we entered into new agreements with ESSDS with a two-year term. Our current agreements with ESSDS, which expire on December 1, 2024, may be terminated by either party at any time without cause on 180 days’ prior written notice to the other party.

Epidiolex. On May 5, 2021, we acquired the entire issued share capital of GW. As a result, GW became an indirect wholly owned subsidiary of the Company. The aggregate consideration for the GW Acquisition was $7.2 billion. We acquired Epidiolex (Epidyolex outside the U.S.) in May 2021 as part of our acquisition of GW, which expanded our growing neuroscience business with a global, high-growth childhood-onset epilepsy franchise. We refer to the acquisition of GW as the GW Acquisition. 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 the prior approved indications, LGS and DS, to patients one year of age and older. The rolling European launch of Epidyolex is also underway following European Commission, or EC, 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. Epidyolex is now launched in all five key European markets: United Kingdom, Germany, Italy, Spain and France. The clobazam restriction is limited to the EU and Great Britain. Epidyolex was also approved for adjunctive therapy in seizures associated with TSC for patients 2 years of age and older in the EU in April 2021 and Great Britain in August 2021, and is approved for this indication in other markets. Outside the U.S. and Europe, Epidiolex/Epidyolex is approved in Israel, Australia and New Zealand. See “Research and Development” below for a discussion of clinical development activities for Epidiolex.

LGS and DS are severe childhood-onset, drug-resistant epilepsy syndromes. LGS and DS affect approximately 35,000-50,000 and approximately 10,000 individuals in the U.S., respectively. TSC is a rare genetic disorder that causes non-malignant tumors to form in many different organs and is a leading cause of genetic epilepsy. TSC affects approximately 50,000 individuals in the U.S. Epidiolex has received ODE to treat seizures associated with LGS and DS through 2025 and TSC through 2027.

Net product sales of Epidiolex/Epidyolex in 2022 were $736.4 million, which represented 20% of our total net product sales for the year.

In addition to our currently-marketed products, we previously marketed Sunosi® (solriamfetol) in the U.S., Europe and Canada. In March 2022, we entered into an agreement to divest Sunosi to Axsome Therapeutics, Inc., or Axsome. In May 2022, we completed the U.S. divestiture of Sunosi to Axsome and in November 2022, we completed the ex-U.S. divestiture. The Sunosi divestiture was intended to enable us to sharpen our focus on our highest strategic priorities. Further, we believed that Axsome is well positioned to deliver access to this important medicine and deliver value to us through anticipated royalties. For more information, see “*Sunosi Disposition*” in Note 3 of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

Oncology

Zepzelca. 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 believe there are opportunities for further growth in second-line share and overall demand, reflecting the significant unmet need and favorable Zepzelca product profile.

Our exclusive U.S. development and commercialization rights to Zepzelca were acquired through an exclusive license agreement we entered into with Pharma Mar, S.A., or PharmaMar, in December 2019. In October 2020, we entered into an amendment to the license agreement with PharmaMar to expand our exclusive license to include rights to develop and commercialize Zepzelca in Canada. The term of the amended license agreement extends on a licensed product-by-licensed product and country-by-country basis until the latest of: (i) expiration of the last PharmaMar patent covering Zepzelca in that country (subject to certain exclusions), (ii) expiration of regulatory exclusivity for Zepzelca in that country and (iii) 12 years after the first commercial sale of Zepzelca in that country. We have the right to terminate the amended license agreement at will upon a specified notice period, and either party can terminate the amended license agreement for the other party’s uncured material breach or bankruptcy. For a description of additional terms of the amended license agreement, including financial terms, see Note 3, Business Combinations, Asset Acquisitions and Collaborations—License Agreement of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

Zepzelca for injection (4 mg) is approved by FDA to treat adults with metastatic SCLC, with disease progression on or after platinum-based chemotherapy. Zepzelca is an alkylating drug that binds guanine residues within DNA. This triggers a cascade of events that can affect the activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in disruption of the cell cycle and eventual cell death. Zepzelca was granted orphan drug designation for SCLC by FDA in August 2018. In December 2019, PharmaMar submitted a New Drug Application, or NDA, to FDA for accelerated approval of Zepzelca for relapsed SCLC based on data from a Phase 2 trial, and in February 2020, FDA accepted the NDA for filing with priority review. In June 2020, FDA granted accelerated approval of Zepzelca for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy. Zepzelca is approved based on response rate and duration of response. After discussion with FDA, PharmaMar initiated a confirmatory trial in second-line SCLC in December 2021. 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, if positive, will serve as the confirmatory trial for Zepzelca to secure full approval in the U.S. See “Research and Development” below for a discussion of clinical development activities for Zepzelca.

In 2022, net product sales of Zepzelca were $269.9 million, which represented 7% of our total net product sales for the year.

Rylaze. Rylaze was approved by FDA in June 2021 under the Real-Time Oncology Review, or RTOR, program, and was launched in the U.S. in July 2021, for use as a component of a multi-agent chemotherapeutic regimen for the treatment of 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 serum asparaginase activity throughout the entire intended course of treatment. We developed Rylaze with the goal of addressing the needs of patients and health care providers for an innovative, high-quality *erwinia* asparaginase with reliable supply. Rylaze has been granted orphan drug designation for the treatment of patients with ALL or LBL. See “Research and Development” below for a discussion of clinical development activities for Rylaze.

The initial approved recommended dosage of Rylaze was for an intramuscular, or IM, administration of 25 mg/m2 every 48 hours. In November 2022, FDA approved a supplemental Biologics License Application, or sBLA, for a Monday/Wednesday/Friday, or M/W/F IM dosing schedule. See “Research and Development” below for a discussion of clinical development activities for Rylaze.

In 2022, net product sales of Rylaze were $281.7 million, which represented 8% of our total net product sales for the year.

Vyxeos. In 2017, we launched Vyxeos in the U.S. after FDA approved our NDA for the treatment of adults with newly-diagnosed t-AML or AML-MRC. In August 2018, the EC granted marketing authorization for Vyxeos and, as part of our rolling launch of Vyxeos in Europe, we are continuing to make pricing and reimbursement submissions in European countries. In March 2021, FDA approved a revised label to include a new indication to treat newly-diagnosed t-AML, or AML-MRC, in pediatric patients aged one year and older. AML is a rapidly progressing and life-threatening blood cancer that begins in the bone marrow, which produces most of the body's new blood cells. AML cells crowd out healthy cells and move aggressively into the bloodstream to spread cancer to other parts of the body. AML is a relatively rare disease representing about 1% of all new cancer cases and has the lowest survival rate of any form of leukemia. Patients with newly diagnosed t-AML or AML-MRC may have a particularly poor prognosis.

We have a number of ongoing development activities and continue to expand into new markets internationally. See “Research and Development” below for a discussion of clinical development activities for Vyxeos.

In 2022, Vyxeos product sales were $128.0 million, which represented 4% of our total net product sales for the year.

Defitelio. Defitelio is the first and only FDA approved treatment for patients with VOD, a potentially life-threatening complication of HSCT. In addition, it is currently approved in the EU, Great Britain and other markets. Stem cell transplantation is a frequently used treatment modality for hematologic cancers and other conditions in both adults and children. Certain conditioning regimens used as part of HSCT can damage the cells that line the hepatic vessels, which is thought to lead to the development of VOD, also referred to as SOS, a blockage of the small vessels in the liver, that can lead to liver failure and potentially result in significant dysfunction in other organs such as the kidneys and lungs. Severe VOD is the most extreme form of VOD and is associated with multi-organ failure and high rates of morbidity and mortality. An analysis of retrospective data, prospective cohort studies and clinical trials published between 1979 and 2007 found that the 100-day mortality rate in severe VOD cases is greater than 80%.

In 2022, Defitelio/defibrotide product sales were $194.3 million, which represented 5% of our total net product sales for the year.

Revenue Diversification

As part of our objective to reduce business risk by diversifying our revenue sources, we have been actively seeking to expand our commercial portfolio thorough a combination of launching internally developed therapies and therapies or commercial assets acquired through corporate development. In 2018, 75% of net product sales were generated by one product, Xyrem. For the year ended December 31, 2022, 63% of net product sales were generated from products that we launched or acquired since 2019, including Xywav, Epidiolex, Zepzelca, Rylaze, Sunosi[1] and Sativex[2].

[1] Net product sales of Sunosi U.S. are included until the date of divestment to Axsome on May 9, 2022.

[2] Sativex (nabiximols) is a product approved outside the U.S. for the treatment of adult patients with moderate to severe spasticity due to multiple sclerosis who have not responded adequately to other anti-spasticity medication. We continue to support the availability of Sativex in the 29 markets outside the U.S. where it is approved.

Our lead marketed products, listed below, are approved in countries around the world to improve patient care.

Product	Indication(s)	Initial Approval Date	Market(s)
NEUROSCIENCE			
Xywav® (calcium, magnesium, potassium, and sodium oxybates)	Treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy.	July 2020	U.S.
	Treatment of 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 LGS, DS or TSC, in patients 1 year of age and older.	June 2018	U.S.
	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, Israel, Australia and New Zealand
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.	April 2021	EU, Great Britain and Israel
ONCOLOGY			
Zepzelca® (lurbinectedin)	Treatment of adult patients with metastatic 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 ALL, and LBL, in adult and pediatric patients 1 month or older who have developed hypersensitivity to *E. coli*-derived asparaginase.	June 2021	U.S.
	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL, in adults and pediatric patients 1 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.	September 2022	Canada

Vyxeos® (daunorubicin and cytarabine) liposome for injection	Treatment of newly-diagnosed therapy-related t-AML or AML-MRC in adults and pediatric patients one year and older.	August 2017	U.S.
Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion	Treatment of adults with newly-diagnosed t-AML or AML-MRC.	August 2018	EU, Great Britain, Switzerland, Israel, Australia, South Korea
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)	Treatment of severe hepatic VOD, also known as SOS, following HSCT therapy.	October 2013	EU, Great Britain, Switzerland, Israel, Australia, South Korea, Saudi Arabia
Defitelio® (defibrotide sodium)	Treatment of adult and pediatric patients with hepatic VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT.	March 2016	U.S., Brazil
Defitelio® (defibrotide sodium)	Treatment of severe hepatic VOD, also known as SOS, following HSCT therapy. Treatment of hepatic sinusoidal obstruction syndrome (hepatic VOD).	July 2017	Canada
Defitelio® (defibrotide)		June 2019	Japan

*The Clobazam restriction limited to EU and Great Britain

**Accelerated approval received from FDA

***Conditional approval received from Health Canada

Research and Development

A key aspect of our strategy is our continued investment in expanding our research and development organization and initiatives. We actively explore new options for patients including novel compounds, small molecule advancements, biologics and innovative delivery technologies. We are focused on research and development activities within our neuroscience and oncology therapeutic areas, such as our expansion into movement disorders and solid tumors, and exploring and potentially investing in adjacent therapeutic areas.

Our research and development activities encompass all stages of development and currently include clinical testing of new product candidates and activities related to clinical improvements of, or additional indications for, our existing marketed products. We also have active preclinical programs for novel therapies, including precision medicines in hematology and oncology, and our proprietary 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.

Our current and planned development activities in our neuroscience therapeutic area are focused on an additional indication for Epidiolex, and advancing novel therapies, including our product candidates suvecaltamide (JZP385), JZP150 and JZP441.

Epidiolex. Our neuroscience R&D efforts include the 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 August 2022. This trial is designed 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. We enrolled the first patient in a Phase 3 trial of Epidyolex for LGS, DS and TSC in Japan in October 2022.

Suvecaltamide. Suvecaltamide (JZP385) is a highly selective modulator of T-type calcium channels currently in development for the potential treatment of essential tremor, or ET. ET is the most common pathological movement disorder, and there have been no new approved therapies in more than 50 years. We acquired suvecaltamide in our acquisition of Cavion, Inc., or Cavion, a clinical-stage biotechnology company, in August 2019. We initiated a Phase 2b clinical trial of suvecaltamide in December 2021. In this multicenter, double-blind, randomized, placebo-controlled trial, we are evaluating the safety and efficacy of suvecaltamide in the treatment of adults with moderate to severe ET. The primary efficacy outcome measure is the change from baseline to Week 12 on the Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) composite outcome score, which represents items from the TETRAS-Activities of Daily Living and TETRAS-Performance Subscale, and measures the functional impact due to tremor. Additionally, in November 2022, we initiated a Phase 2 trial of suvecaltamide in patients with Parkinson's disease tremor.

JZP150. JZP150 is a fatty acid amide hydrolase, or FAAH, inhibitor program for the potential treatment of post-traumatic stress disorder, or PTSD, and associated symptoms. PTSD affects up to 8% of adults during their lifetime, and there are limited treatment options available. In October 2020, we entered into an asset purchase and exclusive license agreement with SpringWorks Therapeutics, Inc., or SpringWorks, under which we acquired SpringWorks' FAAH inhibitor program, including an assignment of SpringWorks' proprietary FAAH inhibitor PF-04457845, or PF-'845, now named JZP150. We initiated a Phase 2 clinical trial of JZP150 for PTSD in December 2021. In this trial, we are evaluating the safety and efficacy of JZP150 in the treatment of adults with PTSD as measured by improvement in the Clinician Administered Post Traumatic Stress Disorder (PTSD) Scale (CAPS-5) Total Symptom Severity Score, a validated clinical instrument for assessing the severity of PTSD symptoms.

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. 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 U.S., Europe and other territories for DSP-0187, now referred to as JZP441. In November 2022, we initiated a Phase 1 development program to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of JZP441 in sleep-deprived healthy volunteers. Our licensor, Sumitomo, initiated a Phase 1 trial in Japan in November 2021 to evaluate safety, tolerability and pharmacokinetics of JZP441 in healthy volunteers.

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

Our current and planned research and development activities in our oncology therapeutic area are focused on Zepzelca, including in combination with other therapeutic agents, Rylaze, Zanidatamab, Vyxeos, JZP815 and the research and development of new product candidates through our external collaborations.

Zepzelca. Within our oncology R&D program, there is a robust development plan being executed for Zepzelca.

In collaboration with F. Hoffmann-La Roche Ltd, or Roche, we have initiated a Phase 3 pivotal clinical trial in first-line extensive stage SCLC of Zepzelca in combination with Tecentriq® (atezolizumab). After discussion with FDA, our licensor PharmaMar initiated a confirmatory trial in second-line SCLC in December 2021. 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 either the first-line trial of Zepzelca in combination with Tecentriq or the PharmaMar trial could serve to confirm clinical benefit of Zepzelca and support full approval in the U.S.

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

Rylaze. The initial approved recommended dosage of Rylaze was for an IM administration of 25 mg/m^2 every 48 hours. In November 2022, FDA approved a sBLA with a M/W/F IM dosing schedule. In April 2022, we submitted an additional sBLA for intravenous, or IV, administration. In February 2023, we received a complete response letter from FDA requesting additional clinical data on the IV administration of Rylaze. There is no impact on the approved product labeling for Rylaze IM administration. We also submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, in May 2022 for M/W/F and every 48-hour dosing schedules and IV and IM administration.

Zanidatamab. Zanidatamab is an investigational HER2-targeted bispecific antibody. In October 2022, we entered into an exclusive licensing agreement with a subsidiary of Zymeworks Inc., or Zymeworks, providing us the right to acquire the development and commercialization rights to Zanidatamab across all indications in the U.S., Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks, and such agreement became effective on November 29, 2022. In December 2022, we exercised the option to continue with the exclusive development and commercialization rights to zanidatamab. In collaboration with Zymeworks, zanidatamab is currently being evaluated in Phase 1, Phase 2, and pivotal clinical trials as a treatment for patients with HER2-expressing cancers. These trials include a Phase 2 trial examining zanidatamab in combination with chemotherapy, in first-line patients with HER2-expressing metastatic gastroesophageal adenocarcinoma, or GEA, a Phase 3 randomized clinical trial, evaluating zanidatamab in combination with chemotherapy plus or minus tislelizumab as a first-line treatment for HER2-expressing GEA and a pivotal Phase 2 clinical trial evaluating zanidatamab monotherapy in patients with previously treated advanced or metastatic HER2-amplified biliary tract cancers, or BTC.

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

JZP815. JZP815 is a pan-RAF inhibitor for the treatment of solid tumors and hematologic malignancies that contain mutations in the mitogen-activated protein kinase, or MAPK, pathway. In October 2022, we enrolled our first patient in a Phase 1 study to investigate the safety, dosing, and initial antitumor activity of JZP815 in participants with advanced or metastatic solid tumors harboring alterations in the MAPK pathway.

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

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

- Codiak BioSciences, Inc., or Codiak, for an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize potential therapeutic candidates directed at up to three targets to be developed using Codiak's engEx™ precision engineering platform for exosome therapeutics;
- Ligand Pharmaceuticals Incorporated, or Ligand, for rights to JZP341, an early-stage long-acting e*rwinia* asparaginase;
- XL-protein GmbH, or XLp, for rights to use XLp's PASylation® technology to extend the plasma half-life of selected asparaginase product candidates;
- Redx Pharma plc, or Redx, for preclinical collaboration activities related to the Ras/Raf/MAP kinase pathway program that we purchased from Redx; and
- Werewolf Therapeutics, Inc., or Werewolf, for an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize Werewolf's investigational WTX-613, now referred to as JZP898. JZP898 is a differentiated, conditionally-activated interferon alpha, or IFNα, INDUKINE™ molecule.

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

Product Candidates	Description
NEUROSCIENCE	
Phase 3	
Epidiolex	EMAS, also known as Doose syndrome (ongoing trial) LGS, TSC and DS (ongoing trial in Japan)
Phase 2b	
Suvecaltamide (JZP385)	ET (ongoing trial)
Phase 2	
Suvecaltamide (JZP385)	Parkinson's disease tremor (ongoing trial)
JZP150	PTSD (ongoing trial)
JZP541	Irritability associated with autism spectrum disorders, or ASD (planned trial)
Additional cannabinoids	ASD (ongoing trial)
Phase 1	
JZP324	Oxybate extended-release formulation (planned trial)
JZP441*	Potent, highly selective oral orexin-2 receptor agonist (ongoing trials in Japan and the U.S.)
Additional cannabinoids	Neonatal hypoxic-ischemic encephalopathy (completed study) Neuropsychiatry targets (ongoing trial)
Preclinical	
Undisclosed targets	Neuroscience Cannabinoids
ONCOLOGY	
Regulatory Review	
Rylaze	ALL/LBL FDA approval in June 2021; approval for M/W/F IM dosing schedule in November 2022; received complete response letter from FDA requesting additional data on the IV administration of Rylaze in February 2023; submitted MAA to EMA in May 2022
Phase 3	
Zepzelca	First-line extensive stage SCLC in combination with Tecentriq (collaboration with Roche) (ongoing trial) Confirmatory Study (Pharma Mar study) (ongoing trial)
Zanidatamab	HER2-positive gastroesophageal adenocarcinoma, or GEA (ongoing trial)
Vyxeos	AML or high-risk Myelodysplastic Syndrome, or MDS (AML18) (cooperative group studies) (ongoing trial) Newly diagnosed adults with standard- and high-risk AML (AML Study Group cooperative group study) (ongoing study) Newly diagnosed pediatric patients with AML (Children's Oncology Group cooperative group study) (ongoing trial)
Pivotal Phase 2	
Zanidatamab	Previously treated, advanced HER2-expressing biliary tract cancer, or BTC (ongoing trial)
Phase 2	
Zepzelca	Basket trial including urothelial cancer, PD-NECs and HRD cancers (ongoing trial)
Vyxeos	High-risk MDS (European Myelodysplastic Syndromes) (cooperative group study) (ongoing trial) Newly diagnosed untreated patients with high-risk AML (cooperative group study) (planned trial)
Vyxeos + venetoclax	De novo or relapsed/refractory, or R/R, AML (MD Anderson collaboration study) (ongoing trial)
Zanidatamab	HER2-expressing GEA, BTC or colorectal cancer in combination with standard first-line chemotherapy (ongoing trial)

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

*Also known as DSP-0187

Commercialization Activities

We have direct Jazz commercial operations in the U.S., Europe, Australia and Canada and a network of commercial distributors that represent our commercial interests in other key markets across the globe. In the U.S., our products are commercialized through a number of teams, including a team of experienced, trained sales professionals who provide education and promote Xywav, Xyrem, Epidiolex, Zepzelca, Rylaze, Vyxeos and Defitelio to healthcare providers in the appropriate specialties for each product, a team that interacts with payors and institutions to ensure access and coverage for the products, and a team that distributes the products throughout the U.S. healthcare system (wholesalers, pharmacies, hospitals, and community and academic institutions) and provides patient services.

In Canada and in approved markets in Europe where we commercialize Defitelio and Vyxeos, we have a field force of hematology sales specialists. In markets where these products either are not approved or are unable to be promoted under local regulation, we have medical affairs personnel responsible for responding to medical information requests and for providing information consistent with local treatment protocols with respect to such products. In certain European markets, we have a sales team and a team of medical science liaisons supporting our rolling launch of Epidyolex. In addition, we directly market Xyrem and Zepzelca in Canada.

Other commercial activities include marketing related services, pricing and access, industry analytics and insights, distribution services and commercial support services. We employ third party vendors, such as advertising agencies, market research firms and suppliers of marketing and other sales support-related services, to assist with our commercial activities. We also provide reimbursement and patient assistance support for our U.S. markets.

We intend to scale the size of our sales force as appropriate to effectively reach our target audience in the specialty markets in which we currently operate. We promote Zepzelca, Rylaze, Vyxeos and Defitelio to many hematology and oncology specialists who operate in the same hospitals and outpatient clinical sites, and we believe that we benefit from operational synergies from this overlap. We expect that a potential launch of Rylaze in Europe, if approved, would be executed primarily through our existing team. Continued growth of our current marketed products and the launch of any future products may require a reevaluation of our field force and support organization in and outside the U.S.

Human Capital Management and Environment, Health and Safety

Jazz is committed to creating a company where the culture embodies our corporate purpose to innovate to transform the lives of patients and reflects our key goals: (1) be a great place to work; and (2) live our core values of *Integrity, Collaboration, Passion, Innovation, and Pursuit of Excellence.*

Employee Demographics. As of February 17, 2023, Jazz employed approximately 2,800 people worldwide, of which approximately 48% were employed in the U.S. and approximately 52% were employed outside the U.S. primarily in the U.K., Ireland and across the European Union, or EU. As an innovative biopharmaceutical company, we have over 700 full-time employees — representing approximately 25% of our global workforce — supporting our research and development activities. We consider our employee relations to be very good.

Diversity, Equity, Inclusion and Belonging. We make diversity, equity, inclusion and belonging, or DEIB, a priority because it is a key to unlocking the potential of our people and living our core values.

We strive to create a workplace culture that fosters the ability of our employees to be their authentic selves and contribute boldly. We aspire to have multi-dimensional diversity through our entire Jazz workforce. We seek to surround underrepresented groups with allies to enable all employees to thrive equitably. Our board of directors and management team are committed to fostering DEIB in all parts of our business.

Our DEIB strategy includes: (1) building a more diverse workforce in terms of gender identity, race, ethnicity and sexual orientation and that represent unique backgrounds, experiences, thoughts and talents; (2) investing in developing our diverse talent and driving equity; and (3) and creating a culture of inclusion and belonging.

We designed our Employee DEIB program to empower employees to guide and support our strategy and programs related to hiring diverse talent and using education and communication to continue fostering an inclusive environment.

We also have a DEIB Delegation, a committee of employees focused on helping to embed DEIB into all we do. Jazz ConcERTos, our employee resource teams, are self-led teams of employee volunteers with diverse backgrounds who come together to promote innovation through inclusion and to increase awareness of all dimensions of diversity. We believe that these groups will contribute positively to Jazz's culture and business success by working cross-functionally to drive innovation, helping to decrease unconscious bias, and encouraging employees to be their whole selves so they can perform at their best.

We have established goals related to increasing all dimensions of diversity, including representation of females and people of color, particularly at the leadership level (i.e., employees at executive director and above). In this regard, we have made some meaningful progress, as demonstrated by the following, as of February 17, 2023:

- 50% of our board of directors and 55% of our executive committee is diverse in terms of gender, ethnicity and sexual orientation.
- Females represent 54% of our global workforce and 46% at the leadership level (employees at executive director and above).
- In the U.S., people of color represent 33% of our U.S. workforce and 19% at the leadership level.

While we are proud of what we have accomplished to date, we remain committed to furthering our goals of providing a diverse, equitable and inclusive workplace that is supportive of all backgrounds, including among our broader leadership.

Employee Engagement. Jazz has a strong employee value proposition anchored in our shared commitment to our purpose to innovate to transform the lives of patients. We are committed to ensuring that we create a rich culture that provides a great place to work for our employees through company-wide efforts to connect employees to our shared purpose and to create an environment where our people feel valued, respected, and able to contribute to their full potential. We believe employee engagement and the power of our employee voices is foundational to strong performance. We have transparent and regular communication channels with our employees consisting of many forms – including all employee meetings, regular communication messages from executive leadership, town halls, top leadership forums, pulse check feedback mechanisms and engagement surveys.

Our employee feedback surveys are designed to help us measure overall employee engagement as well as gather insights on other important areas of our employee experience, and we consistently achieve participation rates above 75%. We consistently have high levels of engagement as measured by feelings of connection to our purpose, as well as Jazz being considered a good place to work by our employees. Our surveys also provide important insight into the areas where we have opportunities to focus, such as decision-making, planning and prioritizing work, and creating a greater sense of belonging. Our survey informs programs and activities aligned with achieving our corporate objectives and achieving our goal of evolving our operating culture for agility and scalability.

Our Community Beat teams are employee volunteers and representatives that promote company culture and create a sense of belonging and camaraderie among our employees. They foster programs and engagement activities on a local level to draw better connections to employees with the company strategy and business milestones, give back through community service, and promote different health and well-being initiatives.

Growth, Development and Total Rewards. Our talent strategy focuses on attracting the best talent, recognizing and rewarding the performance of our employees as defined by both *what* they accomplished and *how* they accomplished it, and continually developing our talent through new experiences and learning opportunities. We believe there is ample opportunity for growth and development at Jazz and there is not a one size fits all approach to growing our talent. We strive to create the best career experience for all of our employees, and encourage them to have regular dialogue with their leadership to create meaningful career development plans.

Our performance management process supports our culture of continual feedback and coaching, and ongoing growth and development through new experiences and learning. We encourage all employees to have an individual development plan to outline learning and growth interests and focus areas.

We leverage several digital learning platforms to provide on demand bite sized learning to all employees that can be accessed 24/7 on a range of topics from leadership, personal effectiveness and well-being. We deliver our “Harmonize” program to all managers to ensure they are grounded in our core Leadership Behaviors we expect all leaders to demonstrate (Instills Trust, Values Differences, Executes through Teams, Develops Talent, Drives Accountability and Provides and Receives Feedback).

In 2022, we continued to develop our top leadership, or Global Leadership Team (top 70 leaders), to build leadership excellence, strengthen relationships, and encourage cross functional collaboration in pursuit of our enterprise strategic goals. Additionally, we continue to focus on diverse early career talent by piloting an executive coaching program to support their development. We continue to offer tuition reimbursement in our major markets aimed at growth and career development.

Our management and leadership teams place significant focus and attention to diversity, capability development, and succession planning for critical roles. We regularly review talent development and succession plans for each of our functions to successfully maintain business operations and develop a pipeline of talent. We have goals concerning employee retention, diversity, and talent development.

We provide our employees with what we believe to be market competitive and locally relevant compensation and benefits that support our overarching strategy to attract, retain and reward highly talented employees in an extremely competitive and dynamic industry.

We strive to create a culture of health and well-being throughout the organization by offering a diverse and customizable set of programs focusing on employee experience, self-care, work-life balance, flexibility and early intervention. In addition to traditional employee benefits, Jazz supports employees and their families through access to a suite of innovative programs that are designed to enhance their physical, financial, emotional and social well-being. In 2022, we introduced an enhanced suite of differentiated global leave and time-off polices to address the needs of our diverse employee population through varying stages of life, including minimum standards for new parent leave (irrespective of gender or how a family is created), family caregiver leave, and bereavement leave. Additionally, in 2022, we launched a new global volunteer day, to provide employees time off with full pay to give back to their communities.

Workplace Safety & Employee Care. Workplace safety is always a top priority for Jazz. To create and sustain a safe and healthy workplace, we have implemented initiatives designed to address risk evaluation, education and training of employees, use of appropriate personal protective equipment, and compliance with relevant national and international health and safety standards.

We leverage an employee support framework focused on Care, Connection, Continuity and Consciousness (our “4Cs”) to enable our employees to live into our values and support one another while doing everything we can to deliver on our patient mission. Important to this framework are new leader expectations and tools given the rise and complexity of emerging employee demands and needs – including more flexibility to address personal needs, a greater connection to understand the whole person and their lives, and more active support surrounding social injustice. We provide productivity and collaboration tools and resources for employees working remotely, including training and toolkits to help leaders effectively lead and manage remote teams; increased flexibility within work schedules and leave programs to support employees caring for children and others; expanded employees assistance and mindfulness programs to help employees and their families manage anxiety, stress, and overall wellbeing; and increased investment in resources focused on inclusion and belonging.

Through direct input from employees, external insights and best practices, we developed our flexible working model and expanded the power of intentional collaboration and our ability to more effectively manage our global and highly distributed team workforce. This approach to work, called “Jazz Remix,” aims to provide eligible employees with the greatest flexibility and agility to globally connect, collaborate, innovate and perform.

Environment, Health and Safety. Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Ireland, the U.K. and Italy where we have manufacturing facilities. Our manufacturing activities involve the controlled storage, use and disposal of chemicals and solvents. Environmental and health and safety authorities in Ireland, the U.K. and Italy administer laws governing, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. In certain cases, such laws, directives and regulations may impose strict liability for pollution of the environment and contamination resulting from spills, disposals or other releases of hazardous substances or waste. Costs, damages and/or fines may result from the presence, investigation and remediation of such contamination at properties currently or formerly owned, leased or operated by us or at off-site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination.

We seek to operate our manufacturing facilities in an environmentally responsible way to protect our people, our business, our environment and the local communities in which we operate. In light of the potential impact of our business on the environment, we have adopted a number of internal environmental policies and management systems designed to manage our operations in compliance with applicable laws, directives and regulations on environmental protection and in support of environmental sustainability and local biodiversity. Our environmental policies and management systems include procedures for assessing compliance with applicable environmental laws and regulations and reporting incidents of non-compliance to applicable governmental authorities. For example, we have environmental policies governing our manufacturing facilities in Ireland, the U.K. and Italy, which demonstrate our commitment to environmental sustainability and require us to minimize resource use (e.g., energy and water) and waste generation, optimize the use of raw materials, and undertake continuous improvement in environmental performance, with an emphasis on pollution prevention.

Competition

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

With respect to competition we face from generic drugs, certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. Generic competition often results in decreases in the prices at which branded products can be sold.

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

- *Xywav and Xyrem*. Xywav and Xyrem are approved by FDA and marketed in the U.S. for the treatment of both cataplexy and EDS in both adult and pediatric patients with narcolepsy. We and others have launched products to treat EDS in narcolepsy and may in the future launch products to treat cataplexy in narcolepsy that are competitive with or disrupt the market. An authorized generic version of sodium oxybate launched in January 2023 and in the future we expect competition from other authorized generic and generic versions of sodium oxybate. For a description of generic versions of sodium oxybate and/or new products for the treatment of cataplexy and/or EDS that currently compete or could in the future compete with, or otherwise disrupt the market for, Xywav and Xyrem, as well as a description of our settlement agreements with abbreviated new drug application, or ANDA, filers, see the risk factor under the heading "*The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products and product candidates would adversely affect sales of our oxybate products and product candidates*" in Part I, Item 1A of this Annual Report on Form 10-K.

  In addition to generic competition, Xywav and Xyrem may face competition in the future from other new sodium oxybate formulations for treatment of narcolepsy. In July 2022, Avadel Pharmaceuticals plc, or Avadel, announced that it had received tentative FDA approval of FT218, an extended-release formulation of sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy, and pending disposition of our REMS patent, Avadel stated that it is seeking to accelerate full approval. For additional information on litigation involving this matter, see "*Avadel Patent Litigation*" in Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Moreover, Avadel has announced that it has obtained an orphan drug designation from FDA related to its extended-release sodium oxybate formulation. To obtain approval in light of the prior

approval of our oxybate products and to obtain its own Orphan Drug Exclusivity for FT218 if approved, we believe Avadel will have to show clinical superiority to Xywav, which requires establishing that FT218 has greater effectiveness, greater safety, or otherwise makes a major contribution to patient care when compared to our products. We cannot predict the timing of full approval of Avadel's sodium oxybate product or how FDA will evaluate any clinical superiority arguments that either we or Avadel may make, but in any event, we expect to face competition from Avadel.

Non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy or IH (Xywav is the first and only FDA-approved therapy to treat IH), including new market entrants, even if not directly competitive with Xywav or Xyrem, could have the effect of changing treatment regimens and payor or formulary coverage of Xywav or Xyrem in favor of other products, and indirectly materially and adversely affect sales of Xywav and Xyrem. Xywav and Xyrem may face increased competition from new branded entrants to treat EDS or cataplexy in narcolepsy such as pitolisant, which has been approved by FDA for the treatment of both cataplexy and EDS in adult patients with narcolepsy. Pitolisant is also in late-stage development for the treatment of IH. Other companies have announced that they have product candidates in various phases of development to treat the symptoms of narcolepsy, such as Axsome's reboxetine, and various companies are performing research on orexin agonists for the treatment of sleep disorders, including Takeda Pharmaceutical Company Limited and Alkermes plc.

In addition, we are also aware that prescribers often prescribe branded or generic medications for cataplexy before prescribing or instead of prescribing oxybate therapy, and that payors often require patients to try such medications before they will cover Xywav or Xyrem, even if they are not approved for this use. For example, prescribers often treat mild cataplexy with drugs that have not been approved by FDA for this indication, including tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors. We are also aware that branded or generic stimulants may be prescribed off-label for treatment of EDS in narcolepsy. Wake-promoting agents modafinil and armodafinil, including both branded and generic equivalents, are approved for the treatment of EDS in narcolepsy and other conditions, and may be used in conjunction with or instead of Xywav or Xyrem.

- Epidiolex. Patients in the U.S. suffering from seizures associated with DS or LGS are treated with a variety of FDA-approved products, including clobazam, clonazepam, valproate, lamotrigine, levetiracetam, rufinamide, topiramate, ethosuximide, and zonisamide. FDA approved Zogenix, Inc.'s low-dose fenfluramine, or Fintepla, in DS in June 2020, and for LGS in March 2022. In March 2022, UCB S.A. announced that it had completed its acquisition of Zogenix. FDA approved Marinus Pharmaceuticals, Inc.'s ganaxolone for the treatment of seizures associated with cyclin-dependent kinase-like 5 deficiency disorder in March 2022. Ovid Therapeutics Inc./Takeda Pharmaceutical Company Limited and Eisai Company Limited are developing therapies for treating Developmental and Epileptic Encephalopathies (includes DS and LGS). Stiripentol has been approved in Europe for several years to treat DS and was approved in 2018 by the FDA. Zynerba Pharmaceuticals, Inc. is developing a topical formulation of cannabidiol, or CBD, for which it is working with FDA on a path forward on CONNECT-FX data for Zygel in Fragile X syndrome. There are a number of public and private companies in the early stages of developing genetic therapies for DS, including Stoke Therapeutics, Inc., which has an antisense oligonucleotide, STK-001, in early clinical trials.

  In addition, there are non-FDA approved CBD preparations being made available from companies in the medical marijuana industry, which might attempt to compete with Epidiolex. While federal law prohibits the sale and distribution of most marijuana products not approved or authorized by FDA, the vast majority of states and the District of Columbia have legalized either CBD or marijuana for either recreational or medical use, or both. Under the U.S. Farm Bill, enacted in late 2018, certain extracts and other material derived from cannabis are no longer controlled under the Federal Controlled Substances Act, or CSA. However, the marketing of such products as a food, dietary supplement, or for medical purposes remains subject to FDA requirements. With respect to the marketing of CBD as a food or dietary supplement, in January 2023 FDA concluded that the existing regulatory frameworks for foods and supplements were not appropriate for CBD products and denied three citizen petitions that had asked the agency to conduct rulemaking to allow the marketing of CBD products as dietary supplements. In addition, Congressional efforts related to legalization of marijuana continue. Although our business is distinct from that of entities marketing FDA-unapproved marijuana and CBD-containing dietary supplement, future legislation or federal government action authorizing the sale, distribution, use, and insurance reimbursement of non-FDA approved marijuana or CBD products could increase competition for and adversely affect our ability to generate sales of Epidiolex and our cannabinoid product candidates.

  We are aware of: exploratory research into the effects of tetrahydrocannabinol, often referred to as THC, and CBD drug formulations; discovery research within the pharmaceutical industry into synthetic agonists and antagonists of CB1 and CB2 receptors; companies that supply synthetic cannabinoids and cannabis extracts to researchers for pre-clinical and clinical investigation; and various companies that cultivate cannabis plants with a view to supplying

herbal cannabis or nonpharmaceutical cannabis-based formulations to patients. These activities have not been approved by the FDA but may in the future compete with our products.

Moreover, we expect that Epidiolex will face competition from generic products in the future. In November and December 2022, we received notices from various ANDA filers that they have each filed with FDA an ANDA for a generic version of Epidiolex (cannabidiol) oral solution. In January 2023, we filed patent infringement suits against these ANDA filers. For a description of this litigation, see "*Epidiolex Patent Litigation*" in Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. As a result of these lawsuits, we expect that a stay of approval of up to 30 months will be imposed by FDA on these ANDA filers.

- *Zepzelca.* Zepzelca faces competition from topotecan, which is also an approved treatment in second line SCLC in the U.S., as well as other regimens for relapsed SCLC currently recommended in compendia guidelines, including rechallenge with first line platinum chemotherapy. There are also a number of products and immunotherapies for the treatment of second line SCLC in various phases of development.
- *Rylaze.* Rylaze may face competition from Erwinase, which was previously approved and commercialized by Jazz as a treatment for ALL patients with hypersensitivity to *E. coli*-derived asparaginase. In April 2020, Porton Biopharma Limited, or PBL, granted Clinigen Group plc, or Clinigen, a global license for Erwinase. However, in December 2021, Clinigen announced that FDA issued a complete response letter to PBL's BLA for Erwinaze, indicating that the BLA cannot be approved in its current form. Rylaze may also face competition from other companies who have developed or are developing new treatments for ALL. In addition, some new asparaginase treatments could reduce the rate of hypersensitivity in patients with ALL, and new treatment protocols are being developed and approved for ALL that may not include asparaginase-containing regimens, including some for the treatment of relapsed or refractory ALL patients.
- *Vyxeos*. With respect to Vyxeos, there are a number of alternative established therapies in AML. A key consideration in the treatment of AML patients is the patient's suitability for chemotherapy. The AML patient population studied in the Vyxeos Phase 3 clinical trial supporting our NDA included 60-75 year old fit patients, or those deemed able to tolerate intensive induction chemotherapy. Prior to Vyxeos, the most widely recognized option for the treatment of newly-diagnosed t-AML and AML-MRC in fit patients was cytarabine in combination with daunorubicin, known as 7+3, which is still used today in this population, along with other intensive chemotherapy regimens, particularly in patients under the age of 60. Also, since Vyxeos was approved, several other products have been approved by FDA or are in development as treatment options for newly diagnosed AML patients eligible for intensive chemotherapy, such as targeted agents (e.g. midostaurin, enasidenib and ivosidenib), immunotherapies (e.g., gemtuzumab ozogamicin and chimeric antigen receptor T-cell therapy), and agents disrupting leukemia cell survival (e.g., glasdegib). We are also aware of the increasing use of venetoclax combined with either a hypomethylating agent or low-dose cytarabine, a treatment approved by FDA in newly diagnosed AML patients who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.
- *Defitelio*. While there is currently no direct competition to Defitelio to treat severe VOD, changes in the types of conditioning regimens used as part of HSCT may affect the incidence of VOD diagnosis and demand for Defitelio.

An important part of our corporate strategy is to build a diversified product pipeline, including by acquiring or in-licensing and developing, or partnering to license and develop, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. Our ability to continue to grow our product portfolio requires that we compete successfully with other pharmaceutical companies, many of which may have substantially greater financial sales and marketing resources, to acquire or in-license products and product candidates.

Customers

In the U.S., Xywav and Xyrem are sold to one certified specialty pharmacy, ESSDS, that ships Xywav and Xyrem directly to patients. Also in the U.S., Epidiolex is sold to specialty pharmacies, wholesalers and specialty distributors. Defitelio is sold to hospital customers through subsidiary specialty distributors of McKesson Corporation, or McKesson. Zepzelca, Rylaze and Vyxeos are sold to customers through subsidiary specialty distributors of McKesson, AmerisourceBergen Corporation, or ABC, and Cardinal Health, Inc., or Cardinal. We have distribution services agreements made in the ordinary course of business with McKesson, ABC and Cardinal and a pharmacy services agreement with ESSDS that provides for the distribution of Xywav and Xyrem to patients. For more information regarding our relationship with ESSDS, see "Business—Our Commercialized Products—Xyrem" in this Part I, Item 1. Purchases are made on a purchase order basis.

In certain countries in Europe, Defitelio and Vyxeos are sold pursuant to marketing authorizations. We distribute these products through Durbin PLC, a U.K.-based wholesaler and distributor, and O&M Movianto Nederland BV, our centralized European logistics services provider, to hospitals and local wholesalers in Europe where we market these products directly and,

in other markets in Europe and elsewhere where we do not market these products directly, to local distributors and wholesalers. In certain countries in Europe, Epidyolex is sold pursuant to marketing authorizations. We distribute Epidyolex through a variety of wholesalers and distributors. In countries where there is no marketing authorization, Defitelio, Vyxeos and Epidyolex are available pursuant to named patient programs, temporary use authorizations or similar authorizations in accordance with local regulations controlling the medical use of unapproved products.

We directly market Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. Xyrem is also sold in 21 countries by UCB (which has rights to market Xyrem in 54 countries).

Manufacturing

We have a manufacturing and development facility in Athlone, Ireland where we manufacture Xywav and Xyrem, a manufacturing and development facility in Kent Science Park, U.K. where we produce Epidiolex/Epidyolex, and a manufacturing plant in Villa Guardia, Italy where we produce defibrotide drug substance. We currently do not have our own commercial manufacturing or packaging capability for our other products, product candidates or their active pharmaceutical ingredients, or APIs. As a result, our ability to develop and supply products in a timely and competitive manner depends on third party suppliers being able to meet our ongoing commercial and clinical trial needs for API, other raw materials, packaging materials and finished products. Our manufacturing facilities currently continue to be operational with essential staff onsite and office-based staff working onsite and remotely as business needs require.

Lead Marketed Products

Xywav. Xywav is manufactured at our Athlone facility. Xywav, like Xyrem, is a Schedule III controlled substance in the U.S. The API of Xywav are the calcium, magnesium, potassium and sodium salts of gamma-hydroxybutyric acid (as gamma-hydroxybutyric acid is the API for Xyrem), which are Schedule I controlled substances in the U.S. As a result, Xywav and Xyrem are subject to regulation by the U.S. Drug Enforcement Administration, or DEA, under the CSA, and its manufacturing and distribution are highly restricted. Quotas from the DEA are required in order to manufacture or procure calcium, magnesium, potassium and sodium salts of gamma-hydroxybutyric acid in the U.S. For information related to DEA quota requirements, see “Business—Government Regulation—Other Post-Approval Pharmaceutical Product Regulation—Controlled Substance Regulations” in this Part I, Item 1.

Xyrem. Xyrem is manufactured by us in our Athlone facility and by Patheon Pharmaceuticals Inc., which we refer to together with its affiliates as Patheon, under a Master Manufacturing Services Agreement, or the Patheon Agreement, entered into with Patheon in 2015. We manufacture Xyrem in our Athlone facility for most of our U.S. commercial supply and rely on Patheon to supply Xyrem for other markets, though we are not required to purchase Xyrem exclusively from Patheon. The current term of the Patheon Agreement will expire in December 2024, subject to further automatic two-yearly extensions if Patheon is then providing manufacturing services for any product, unless either party provides prior notice of termination. In addition, we may terminate the Patheon Agreement for any reason upon 12 months’ prior written notice.

Siegfried USA, LLC and its European affiliates, or Siegfried, supply sodium oxybate, the API of Xyrem, to Patheon and our Athlone facility. Although Siegfried has been our only supplier of sodium oxybate since 2012, we have the right to purchase a portion of our worldwide requirements of sodium oxybate from other suppliers. The agreement with Siegfried expires in April 2024, subject to automatic three-year extensions until either party provides advance notice of its intent to terminate the agreement. During the term of the agreement and, under certain circumstances for 18 months after the agreement terminates, Siegfried is not permitted to manufacture sodium oxybate for any other company.

Epidiolex. Epidiolex/Epidyolex is manufactured by us in our Kent Science Park facility in the U.K. Epidiolex is a pharmaceutical formulation comprising highly purified plant-derived CBD. We cultivate our cannabinoid plants in the U.K. under highly controlled and standardized conditions.

Zepzelca. Zepzelca is manufactured by Baxter Oncology GmbH, or Baxter. The current term of the agreement with Baxter will expire in December 2025 and will then be subject to automatic two-year extensions, unless either party provides advance notice of its intent to terminate the agreement. PharmaMar retains manufacturing rights for the API for U.S. and Canadian commercial supply of Zepzelca. We also entered into a manufacturing agreement for ongoing commercial supply of the drug product Zepzelca with GP Pharm S.A.

Rylaze. Rylaze is currently manufactured by Patheon, and the API of Rylaze is manufactured by AGC Biologics A/S. The initial term of the agreement with Patheon will expire in December 2025 and will then be subject to automatic two-year extensions, unless either party provides advance notice of its intent to terminate the agreement. The initial term of the agreement with AGC Biologics A/S will expire in October 2026 and will then be subject to automatic three-year extensions, unless either party provides advance notice of its intent to terminate the agreement.

Vyxeos. Vyxeos is manufactured by Baxter, which is a sole source supplier from a single site location, using our CombiPlex technology platform. CombiPlex products represent formulations with increased manufacturing complexities

associated with producing drug delivery vehicles encapsulating two or more drugs that are maintained at a fixed ratio and, in the case of Vyxeos, two drugs that are co-encapsulated in a freeze-dried liposomal format. Our manufacturing agreement with Baxter expires in August 2025, subject to automatic three-year renewal terms, unless either party provides advance notice of its intent to terminate the agreement. While other contract manufacturers may be able to produce Vyxeos, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. The marketing authorization in the EU for Vyxeos also requires us to comply with certain manufacturing-related post-approval commitments.

Defitelio. We are our own sole supplier of, and we believe that we are currently the sole worldwide producer of, defibrotide API. We manufacture defibrotide API from porcine DNA in a single facility located in Villa Guardia, Italy. Patheon currently processes defibrotide API into its finished vial form under a specific product agreement entered into under a separate agreement with Patheon. Patheon is the sole provider of our commercial and clinical supply of Defitelio; however, we are not required to purchase Defitelio exclusively from Patheon. If Patheon does not or is not able to supply us with Defitelio for any reason, it may take time and resources to implement and execute the necessary technology transfer to another processor, and such delay could negatively impact our anticipated revenues from Defitelio and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

Product Candidates

For discussion of the challenges we face with respect to supply of our products and product candidates, see the risk factor under the heading "*Delays or problems in the supply of our products for sale or for use in clinical trials, loss of our single source suppliers or failure to comply with manufacturing regulations could materially and adversely affect our business, financial condition, results of operations and growth prospects*" in Part I, Item 1A of this Annual Report on Form 10-K.

Patents and Proprietary Rights

We actively seek to patent, or to acquire or obtain licenses to third party patents, to protect our products and product candidates and related inventions and improvements that we consider important to our business. We own a portfolio of U.S. and non-U.S. patents and patent applications and have licensed rights to a number of issued patents and patent applications. Our owned and licensed patents and patent applications cover or relate to our products and product candidates, including certain formulations, used to treat particular conditions, distribution methods and methods of administration, drug delivery technologies and delivery profiles and methods of making and use. Patents extend for varying periods according to the date of the patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The patent laws of non-U.S. countries differ from those in U.S., and the degree of protection afforded by non-U.S. patents may be different from the protection offered by U.S. patents. In addition to patents, our products and product candidates are in some instances protected by various regulatory exclusivities. For a description of those exclusivities and their regulatory background, see "Business—Government Regulation—Marketing Exclusivity—The Hatch-Waxman Act" in this Part I, Item 1.

The patents, patent applications and regulatory exclusivities that relate to our marketed products include:

- *Xywav.* We have 13 U.S. patents that relate to Xywav. These patents expire from 2033 to 2037. In addition, we have patent applications that relate to Xywav for use in additional indications that would, if issued, expire between 2040 and 2041. Xywav has been granted ODE by FDA to treat narcolepsy through 2027 and to treat IH through 2028.
- Xyrem. We currently have six issued patents in the U.S. relating to Xyrem listed in FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Our patents relate to Xyrem's restricted distribution system and a drug-drug interaction, or DDI, between Xyrem and divalproex sodium. In October 2018, as a result of FDA's grant of pediatric exclusivity, an additional six months was added to the original expiration dates of all of our Orange Book-listed patents that existed at that time. As a result, our Orange Book-listed patents have periods of exclusivity between December 2022 (with an additional six months for pediatric exclusivity) and September 2033. Some of our Xyrem patents have been subject to patent litigation with the companies who filed ANDAs seeking to market a generic version of Xyrem, including challenge through the inter partes review, or IPR, procedures of the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office, or USPTO. Some IPR petitions were dismissed by the PTAB. However, in July 2018, the United States Court of Appeals for the Federal Circuit upheld on appeal PTAB decisions finding that six patents associated with the Xywav and Xyrem REMS and three claims of a seventh REMS patent were unpatentable. As a result, we will not be able to enforce patents or claims that the PTAB found unpatentable. Although we have settled all patent litigation against the nine companies that filed ANDAs, it is possible that additional companies may challenge our U.S. patents for Xyrem in the future. For a description of our Xyrem settlements, see the risk factor under the heading "The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products and product candidates would adversely affect sales of our oxybate products and product candidates" in Part I, Item 1A of this Annual Report on Form 10-K. For additional information on litigation involving or Orange Book-listed patents, see

"*Avadel Patent Litigation*" in Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K

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

- *Epidiolex.* Our patent portfolio relating to the use of CBD in the treatment of epileptic encephalopathies includes 90 distinct patent families that are either granted or filed. Most of the patent families in this portfolio claim the use of CBD in the treatment of particular childhood epilepsy syndromes, seizure sub-types and interactions with other concomitantly dosed anti-seizure drugs. To date, we have obtained 25 issued U.S. patents, including patents with claims for the use of CBD for the treatment of convulsive, drop and atonic seizures associated with both LGS and DS, an oral composition of CBD, as well as the use of CBD with clobazam, and the teaching that dose adjustment may be needed when concomitantly prescribed. These issued patents are directly aligned with the Epidiolex label, and we have listed them in the Orange Book. The patents currently listed in the Orange Book have expiry between 2035 and 2041. We have filed corresponding patent applications in many jurisdictions worldwide, including Europe, UK, Canada, Japan, Mexico, Australia and New Zealand. The USPTO has granted a patent based on data that demonstrates that Epidiolex provides a benefit over synthetic CBD in an animal model of epilepsy, which has an expiry date of 2039 and we have listed it in the Orange Book. Epidiolex has received ODE to treat seizures associated with LGS and DS through 2025 and TSC through 2027.
- *Zepzelca*. In December 2019, we entered into an exclusive license agreement with PharmaMar pursuant to which we obtained exclusive U.S. development and commercialization rights to Zepzelca. In October 2020, we entered into the amended license agreement which expanded our exclusive license to include rights to develop and commercialize Zepzelca in Canada. We have a portfolio of in-licensed U.S. and Canadian patents for lurbinectedin relating to compositions, methods of use, and processes. For example, one U.S. patent (expiring in 2024) covers a genus of compounds, including lurbinectedin, and use in treating various cancers. A request for a patent term extension for this U.S. patent has been filed and, if granted, would extend to 2029. A request for extension (CSP) has also been filed in Canada. Zepzelca has also been granted ODE for the treatment of adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy until 2027 and new chemical entity exclusivity until 2025 in the U.S.
- *Rylaze*. In 2016, we obtained worldwide rights from Pfenex, Inc., including Pfenex's patent rights relating to Rylaze, to develop and commercialize multiple early-stage hematology product candidates, including a license to two U.S. process patents relating to Rylaze, with respective expirations in 2026 and 2038. Pfenex has been acquired by Ligand Pharmaceuticals Incorporated. Rylaze has been granted orphan drug designation for the treatment of patients with ALL or LBL. We have two patent application families relating to dosing regimens. One covers the dosing regimen (25mg/m2 intramuscularly every 48 hours), while the other covers various dosing regimens of interest. If issued, these would expire in 2040 and 2042, respectively. Another application relating to formulations of asparaginase would expire in 2042 if issued.
- *Vyxeos.* We have a portfolio of U.S. and non-U.S. patents and patent applications for Vyxeos and the CombiPlex technology platform relating to various compositions and methods of making and use. These include seven U.S. patents covering Vyxeos compositions and methods of use expiring between 2025 and 2034 and two U.S. patents covering CombiPlex (which also cover Vyxeos) expiring in January 2027. These patents are listed in the Orange Book. Vyxeos has been granted ODE by FDA until August 2024, seven years from its FDA approval, for the treatment of adults with newly-diagnosed t-AML or AML-MRC. In March 2021, FDA approved an expanded label for Vyxeos for the treatment of t-AML or AML-MRC in pediatric patients 1 year and older. In addition, Vyxeos has been granted orphan drug designation by the EC until August 2028, ten years from its EC approval for the treatment of adults with newly-diagnosed t-AML or AML-MRC and was approved by Health Canada for treatment of adults with newly diagnosed t-AML or AML-MRC in April 2021.
- *Defitelio*. The unique process of deriving defibrotide from porcine DNA is extensive and uses both chemical and biological processes that rely on complex characterization methods. We have U.S. and non-U.S. patents and patent applications relating to various compositions, methods of use and methods of characterization, with the issued patents expiring at various times between 2021 and 2035. One U.S. patent is listed in the Orange Book and an additional allowed patent is expected to be Orange Book listed in 2022. Defibrotide has been granted ODE by FDA to treat and prevent VOD until March 2023. Defibrotide has also been granted orphan drug designation by the EC and the Korean Ministry of Food and Drug Safety to treat and prevent VOD, by the Commonwealth of Australia-Department of Health for the treatment of VOD and by the EC for the prevention of acute Graft-versus-Host Disease, or aGvHD,

and have also received approvals in Canada, Brazil and Switzerland. We acquired the rights to defibrotide for the treatment and prevention of VOD in North America, Central America and South America from Sigma-Tau Pharmaceuticals, Inc. in 2014.

The patents and/or patent applications that relate to our product candidates include:

- *Suvecaltamide (JZP385)*. Through the acquisition of Cavion in 2019, we obtained a portfolio of U.S. and non-U.S. patents and patent applications, including rights relating to compositions and methods of using suvecaltamide. The portfolio includes a U.S. composition of matter patent relating to suvecaltamide, which expires in 2027, but which can be extended to 2032 depending on regulatory approval. Two further U.S. patents to the treatment of specific conditions (Angelman Syndrome and memory and cognitive disorders) provide supplemental protection to 2038.
- *JZP150*. Through the asset purchase and exclusive license agreement with SpringWorks in 2020, we obtained a license to a portfolio of U.S. and non-U.S. patents and patent applications, including rights relating to compositions and methods of using JZP150. The portfolio includes a U.S. composition of matter patent relating to JZP150, which expires in 2029.
- *JZP441*. Through a license agreement with Sumitomo Pharma Co., Ltd. in 2022, we obtained a license to a portfolio of U.S. and non-U.S. patents and patent applications, including rights relating to compositions and methods of using JZP441. The portfolio contains a U.S. composition of matter patent relating to JZP441, which expires in 2040 (excluding any adjustments or extensions).
- *JZP815*. Through a collaboration agreement and an asset purchase agreement with Redx in 2019, we acquired a portfolio of U.S. and non-U.S. patents and patent applications, including rights relating to compositions and methods of using JZP815. The portfolio contains a U.S. composition of matter patent relating to JZP815, which expires in 2035 (excluding any adjustments or extensions).
- *Zanidatamab*. Through a license agreement with Zymeworks BC Inc. in 2022, we obtained a license to a portfolio of U.S. and non-U.S. patents and patent applications, including rights relating to compositions and methods of using zanidatamab. The portfolio contains a U.S. composition of matter patent relating to zanidatamab, which expires in 2034 (excluding any adjustments or extensions).

In addition, we have rights to a number of trademarks and service marks, and pending trademark and service mark applications, in the U.S. and elsewhere in the world to further protect the proprietary position of our products. For a discussion of the challenges we face in obtaining or maintaining patent and/or trade secret protection, see the risk factors under the heading “Risks Related to Our Intellectual Property” in Part I, Item 1A of this Annual Report on Form 10-K.

Government Regulation

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

Testing and Approval of Pharmaceutical Products

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

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

- conducting preclinical laboratory and animal testing and submitting the results to FDA in an investigational new drug, or IND, application requesting approval to test the product candidate in human clinical trials;
- conducting adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate in the desired indication;
- submitting an NDA, supplemental New Drug Application, or sNDA, or Biologics License Application, or BLA, as appropriate, to FDA seeking approval for a specific indication; and

- completing inspections by FDA of the facilities where the product candidate is manufactured, analyzed and stored to demonstrate compliance with current Good Manufacturing Practices, or cGMP, and any requested FDA audits of the clinical trial sites that generated the data supporting the application.

Human clinical trials conducted before approval of a product generally proceed in three sequential phases, although the phases may overlap. In Phase 1, the initial introduction of the product candidate in humans, the product candidate is typically tested to assess metabolism, pharmacokinetics, pharmacological actions and tolerability, including side effects associated with increasing doses. Phase 2 usually involves clinical trials in a limited patient population to determine the effectiveness of the product candidate for a particular indication or indications, dosage tolerance and optimum dosage and to identify common adverse effects and safety risks. If a product candidate demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2, Phase 3 clinical trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of patients. Clinical trials must be conducted in accordance with specific protocols, as well as FDA requirements related to conducting the trials and recording and reporting the results, commonly referred to as good clinical practices, to ensure that the resulting data are credible and accurate and that the trial participants are adequately protected. FDA enforces good clinical practices through periodic inspections of trial sponsors, clinical investigators and trial sites.

Once an NDA, sNDA or BLA has been compiled and submitted, FDA performs an initial review before it accepts the application for filing. FDA may refuse to file an application and/or request additional information before acceptance. Once accepted for filing, FDA begins an in-depth review of the application. Under the current goals and policies agreed to by FDA under the Prescription Drug User Fee Act, or PDUFA, for a new molecular entity, FDA has ten months from the filing decision in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing decision for a priority application. FDA does not always meet its PDUFA goal dates, and in certain circumstances, the PDUFA goal date may be extended.

FDA also has various programs, including Fast Track, Priority Review, Breakthrough Therapy and Accelerated Approval (Subpart H and E), RTOR pilot program, that are intended to expedite the process for reviewing certain applications and/or provide for approval on the basis of surrogate endpoints or restricted distribution. Generally, products may be eligible for one or more of these programs if they are intended for serious or life-threatening diseases or conditions, have potential to address unmet medical needs, or may provide meaningful benefit over existing treatments. For example, FDA granted Vyxeos Breakthrough Therapy and Fast Track designations and granted Priority Review with respect to our NDA for Vyxeos for the treatment of t-AML and AML-MRC that was approved in August 2017. In addition, a priority review voucher, or PRV, may be used to obtain priority review by FDA for one of our future regulatory submissions. We used the PRV we acquired in May 2018 to obtain priority review for our Xywav for the treatment of IH sNDA, which was approved by FDA in August 2021. In June 2020, FDA granted Accelerated Approval to Zepzelca for relapsed SCLC. In December 2020, we initiated the submission of a BLA for Rylaze for ALL under the RTOR pilot program, which was approved by FDA in June 2021.

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

Even if a product is approved, the approval may be subject to limitations based on FDA's interpretation of the data submitted in the application. For example, as a condition of approval, FDA may require the sponsor to agree to certain post-marketing requirements, such as conducting Phase 4, or post-approval, clinical trials to gain additional safety data or to document a clinical benefit in the case of products approved under Accelerated Approval regulations. FDA's approval of the NDA for Defitelio included a number of post-marketing commitments and requirements, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. For its approval of Vyxeos, FDA required that we conduct a safety study to characterize infusion-related reactions in patients treated with Vyxeos and a clinical trial to determine dosing to minimize toxicity in patients with moderate and severe renal impairment. Further, FDA granted Accelerated Approval to Zepzelca for relapsed SCLC based on data from a Phase 2 trial, which approval is contingent upon verification and description of clinical benefit in a post-marketing clinical trial.

In addition, if FDA determines that a REMS is necessary to ensure that the benefits of the product outweigh the risks, a sponsor may be required to include a proposed REMS (either as part of the application or after approval), which may include a patient package insert or a medication guide to provide information to consumers about the product's risks and benefits; a plan for communication to healthcare providers; or conditions on the product's prescribing or distribution referred to as elements to assure safe use. Xywav and Xyrem are required to have a REMS. For more discussion regarding the Xywav and Xyrem REMS, see the risk factors under the headings "*The distribution and sale of our oxybate products are subject to significant*

regulatory restrictions, including the requirements of a REMS, and these regulatory requirements subject us to risks and uncertainties, any of which could negatively impact sales of Xywav and Xyrem" and "Risks Related to Our Intellectual Property" in Part I, Item 1A of this Annual Report on Form 10-K.

The EU and many individual countries have regulatory structures similar to the U.S. for conducting preclinical and clinical testing and applying for marketing approval or authorization, although specifics may vary widely from country to country. Clinical trials in the EU must be conducted in accordance with the requirements of the EU Clinical Trials Regulation and applicable good clinical practice standards. In the EU, there are several procedures for requesting marketing authorization which can be more efficient than applying for authorization on a country-by-country basis. There is a "centralized" procedure allowing submission of a single marketing authorization application to the European Medicines Agency, or EMA. If the EMA issues a positive opinion, the EC will grant a centralized marketing authorization that is valid in all EU member states and three of the four European Free Trade Association countries (Iceland, Liechtenstein and Norway). The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products and biotechnology-derived medicinal products, and optional for others. There is also a "decentralized" procedure allowing companies to file identical applications to several EU member states simultaneously for product candidates that have not yet been authorized in any EU member state and a "mutual recognition" procedure allowing companies that have a product already authorized in one EU member state to apply for that authorization to be recognized by the competent authorities in other EU member states. The U.K.'s withdrawal from the EU on January 31, 2020, commonly referred to as Brexit, has created uncertainty concerning the future relationship between the U.K. and the EU. Among the changes that have had a direct impact are that Great Britain (England, Scotland and Wales) is now treated as a third country. To mitigate the immediate impact of this in December 2020, the EU and U.K. reached an agreement in principle on the framework for their future relationship, the EU-U.K. Trade and Cooperation Agreement, or TCA. With regard to EU regulations, Northern Ireland continues to follow the EU regulatory rules. As part of the TCA, the EU and the U.K. recognize Good Manufacturing Practice, or GMP, inspections carried out by the other party and the acceptance of official GMP documents issued by the other party. The TCA also encourages, although it does not oblige, the parties to consult one another on proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The U.K. has unilaterally agreed to accept EU batch testing and batch release until January 2023. In December 2022, the U.K. announced its decision to make permanent the approach of maintaining a list of approved countries for import into Great Britain which require no import testing or U.K. "qualified person" release certification. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the U.K. must be retested and re-released when entering the EU market for commercial use. As regards marketing authorizations, Great Britain has introduced a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland, however, continues to be covered by the marketing authorizations granted by the EC.

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

In the EU, if an applicant can demonstrate that comprehensive data on the efficacy and safety of the product under normal conditions of use cannot be provided due to certain specified objective and verifiable reasons, products may be granted marketing authorization "under exceptional circumstances." A marketing authorization granted under exceptional circumstances is valid for five years, subject to an annual reassessment of conditions imposed by the EC. The marketing authorization in the EU for Defitelio was granted under exceptional circumstances because it was not possible to obtain complete information about the product due to the rarity of the disease and because ethical considerations prevented conducting a study directly comparing Defitelio with best supportive care or a placebo. As a result, the marketing authorization requires us to comply with a number of post-marketing obligations, including obligations relating to the manufacture of the drug substance and finished product, the submission of data concerning patients treated with the product collected through a third-party patient registry and the establishment of a multi-center, multinational and prospective observational patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use. We are in the process of conducting the post-authorization study in the EU to provide further data on long-term safety, health outcomes and patterns of utilization of Defitelio in normal use.

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

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes, modifying a REMS, or making certain additional labeling claims, are subject to further regulatory review and approval. Obtaining approval for a new indication generally requires that additional clinical studies be conducted to demonstrate that the product is safe and effective for the new intended use. Such regulatory reviews can result in denial or modification of the planned changes, or requirements to conduct additional tests or evaluations that can substantially delay or increase the cost of the planned changes.

Manufacture of Pharmaceutical Products

The manufacturing process for pharmaceutical products is highly regulated, and regulators may shut down manufacturing facilities that they believe do not comply with regulations. We and the third party suppliers of our products are subject to cGMP, which are extensive regulations governing manufacturing processes, stability testing, recordkeeping and quality standards as defined by FDA, the EC, the EMA, competent authorities of EU member states and other regulatory authorities. FDA also periodically inspects manufacturing facilities and the sponsor's and manufacturer's records related to manufacturing, and assesses compliance with cGMP. Following such inspections, FDA may issue notices on Form FDA 483 and warning letters. In addition to Form FDA 483 notices and warning letters, failure to comply with the statutory and regulatory requirements may result in suspension of manufacturing, product seizure, withdrawal of the product from the market, administrative, civil and criminal penalties, among other enforcement remedies both in the U.S. and in non-U.S. countries.

In the EU, a manufacturing authorization is required to manufacture medicinal products, and the manufacturing authorization holder must comply with various requirements set out in applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing products and their APIs, including APIs manufactured outside of the EU with the intention of importing them into the EU. In addition to inspection reports, manufacturers and marketing authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in cases of non-compliance with the EU or EU member states' requirements applicable to manufacturing.

Sales and Marketing of Pharmaceutical Products

Advertising and Promotional Activities

FDA regulates advertising and promotional activities for products in the U.S., requiring advertising, promotional materials and labeling to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. FDA actively investigates allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. FDA routinely issues informal and more formal communications such as untitled letters or warning letters interpreting its authority over these matters. While such communications may not be considered final agency decisions, many companies may decide not to contest the agency's interpretations so as to avoid disputes with FDA, even if they believe the claims they were making to be truthful, not misleading and otherwise lawful.

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

Fraud and Abuse

We are also subject to numerous fraud and abuse laws and regulations globally. In the U.S., there are a variety of federal and state laws restricting certain marketing practices in the pharmaceutical industry pertaining to healthcare fraud and abuse, including anti-kickback laws and false claims laws. Our sales, marketing, patient support and medical activities may be subject to scrutiny under these laws. The U.S. federal healthcare program Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving anything of value to induce (or in return for) the referral of business, including the purchase, recommendation or prescription of a particular drug reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and patients, prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common manufacturer business arrangements and activities from prosecution and administrative sanction, the exemptions and safe harbors are drawn narrowly

and are subject to regulatory revision or changes in interpretation by the U.S. Department of Justice, or DOJ, and the Office of Inspector General of the U.S. Department of Health and Human Services, or OIG. Practices or arrangements that involve remuneration may be subject to scrutiny if they do not qualify for an exemption or safe harbor. For example, in November 2020, the OIG issued a Special Fraud Alert to highlight certain inherent risks of remuneration related to speaker programs sponsored by drug and device companies, which do not fall under either safe harbor or statutory exception protection. The Special Fraud Alert sent a clear signal that speaker programs will be subject to potentially heightened enforcement scrutiny, in particular for those programs with certain characteristics identified as risk factors by OIG, including meals exceeding modest value or where alcohol is made available; lack of substantive or new content presented; programs held at venues not conducive to the exchange of educational information; repeat attendees or attendees without a legitimate business interest; sales or marketing influence on speaker selection; and excessive speaker compensation. Violations of the federal Anti-Kickback Statute may be established without providing specific intent to violate the statute, and may be punishable by civil, criminal, and administrative fines and penalties, damages, imprisonment, and/or exclusion from participation in federal healthcare programs.

The federal civil False Claims Act prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of federal funds, or knowingly making, or causing to be made, a false statement to get a false claim paid. A claim resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of themselves and the federal government alleging violations of the statute and to share in any monetary recovery. Violations of the False Claims Act may result in significant financial penalties (including mandatory penalties on a per claim or statement basis), treble damages and exclusion from participation in federal health care programs.

Pharmaceutical companies are subject to other federal false claim and statements laws, some of which extend to non-government health benefit programs. For example, the healthcare fraud provisions under the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations, or HIPAA, impose criminal liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program, including private third party payors, or falsifying or covering up a material fact or making any materially false or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Violations of HIPAA fraud provisions may result in criminal, civil and administrative penalties, fines and damages, including exclusion from participation in federal healthcare programs.

The majority of individual states also have statutes or regulations similar to the federal anti-kickback law and the False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Other states restrict whether and when pharmaceutical companies may provide meals to health care professionals or engage in other marketing-related activities, and certain states and cities require identification or licensing of sales representatives.

Other Post-Approval Pharmaceutical Product Regulation

Safety Reporting/Pharmacovigilance

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

FDA and the competent authorities of the EU member states on behalf of the EMA also periodically inspect our records related to safety reporting. Following such inspections, FDA may issue notices on FDA Form 483 and warning letters that could cause us to modify certain activities. An FDA Form 483 notice, if issued, can list conditions FDA investigators believe may have violated relevant FDA regulations or guidance. Failure to adequately and promptly correct the observation(s) can result in a warning letter or other regulatory enforcement action. Similarly, the EMA's Pharmacovigilance Risk Assessment Committee may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps. Non-compliance can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Sunshine Act and Transparency Laws

The Physician Payment Sunshine Act requires tracking of payments and transfers of value to physicians and teaching hospitals and ownership interests held by physicians and their families, and reporting to the federal government and public disclosure of these data. Beginning in 2022, reporting is required of information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. A number of states now require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to healthcare providers in the states. Government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports.

Outside the U.S., interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products, which is prohibited in the EU, is governed by the national anti-bribery laws of the EU member states, as described below in "Business—Government Regulation—Anti-Corruption Legislation" in this Part I, Item 1. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states, or industry codes of conduct, require that payments made to physicians be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her competent professional organization, and/or the competent authorities of the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Controlled Substance Regulations

A drug product approved by FDA may be subject to scheduling as a controlled substance under the CSA depending on the drug's potential for abuse. Controlled substances that are pharmaceutical products are subject to a high degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. may be classified as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse. The API of Xywav and Xyrem, oxybate salts, are regulated by the DEA as Schedule I controlled substances, and Xywav and Xyrem are regulated as Schedule III controlled substances. Certain product candidates we are developing contain controlled substances as defined in the CSA. Drug products approved by FDA that contain cannabis or cannabis extracts may be controlled substances and will be rescheduled to Schedules II-V after approval, or, like Epidiolex, removed completely from the schedules by operation of other laws.

The DEA limits the quantity of certain Schedule I and II controlled substances that may be manufactured and procured in the U.S. in any given calendar year through a quota system and, as a result, quotas from the DEA are required in order to manufacture and package sodium oxybate and Xyrem in the U.S. Accordingly, we require DEA quotas for Siegfried, our U.S. based sodium oxybate supplier, to procure sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to obtain the sodium oxybate from Siegfried in order to manufacture and supply us with Xyrem. Xywav and Xyrem manufactured at our plant in Ireland enters the U.S. as a Schedule III drug and thus does not require a manufacturing quota.

As Schedule III drugs, Xywav and Xyrem are also subject to DEA import volume limits and state regulations relating to manufacturing, storage, distribution and physician prescription procedures, including limitations on prescription refills. In addition, the third parties who perform our clinical and commercial manufacturing, distribution, dispensing and clinical studies for Xywav and Xyrem are required to maintain necessary DEA registrations and state licenses. The DEA periodically inspects facilities for compliance with its rules and regulations.

Other Regulations

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

Anti-Corruption Legislation

Our business activities outside of the U.S. are subject to the U.S. Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional

conduct or rules of other countries in which we operate, including the U.K. Bribery Act of 2010, or the U.K. Bribery Act. The FCPA and similar anti-corruption laws in other countries generally prohibit the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to U.S. or non-U.S. government officials in order to improperly influence any act or decision, secure an improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The U.K. Bribery Act prohibits giving, offering, or promising bribes to any person, including U.K. and non-U.K. government officials and private persons, as well as requesting, agreeing to receive, or accepting bribes from any person. In addition, under the U.K. Bribery Act, companies that carry on a business or part of a business in the U.K. may be held liable for bribes given, offered or promised to any person, including U.K. and non-U.K. government officials and private persons in any country, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Liability is strict, with no element of a corrupt state of mind, but a defense of having in place adequate procedures designed to prevent bribery is available. As described above, our business is heavily regulated and therefore involves significant interaction with government officials in many countries. Additionally, in certain countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers may be subject to the FCPA, the U.K. Bribery Act and similar laws. Recently the Securities and Exchange Commission, or SEC, and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We engage in ongoing efforts designed to ensure our compliance with these laws, including due diligence, training, policies, procedures, and internal controls. However, there is no certainty that all employees and third party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of our suppliers and other third party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits.

Data Protection and Privacy

We are subject to data protection and privacy laws and regulations globally, which restrict the processing of personal data. The legislative and regulatory landscape for privacy and data security continues to evolve with an increased attention in countries globally that could potentially affect our business. In particular, we are subject to the EU General Data Protection Regulation, which imposes penalties up to 4% of annual global revenue, and the California Consumer Privacy Act of 2018. These laws and regulations applicable to our business, increase potential enforcement and litigation activity. In order to manage these evolving risks, we have adopted a global privacy program that governs the processing of personal data across our business.

Marketing Exclusivity

The Hatch-Waxman Act

The marketing approval process described above for the U.S. is premised on the applicant being the owner of, or having obtained a right of reference to, all of the data required to prove the safety and effectiveness of a drug product. This type of marketing application, sometimes referred to as a “full” or “stand-alone” NDA, is governed by Section 505(b)(1) of the United States Federal Food, Drug, and Cosmetic Act, or FDCA. A Section 505(b)(1) NDA contains full reports of investigations of safety and effectiveness, which includes the results of preclinical and clinical trials, together with detailed information on the manufacture and composition of the product, in addition to other information. As an alternative, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, provides two abbreviated approval pathways for certain drug products.

The first path, under Section 505(b)(2) of the FDCA, usually is used for the approval of a product that is similar, but not identical, to a previously-approved brand-name product, referred to as the reference listed drug, or RLD. Under this path, the applicant is permitted to rely to some degree on FDA’s finding that the RLD is safe and effective and must submit its own product-specific data on safety and effectiveness only to the extent necessary to bridge the differences between the products. The second abbreviated path established under the Hatch-Waxman Act is for the approval of generic drugs. Section 505(j) of the FDCA permits the submission of an ANDA for a generic version of an approved, brand-name drug. Generally, an ANDA must contain data and information showing that the proposed generic product and the RLD (i) have the same active ingredient, in the same strength and dosage form, to be delivered via the same route of administration, (ii) are intended for the same uses, and (iii) are bioequivalent. This data and information are provided instead of data and information independently demonstrating the proposed generic product’s safety and effectiveness.

The Hatch-Waxman Act requires an ANDA or a Section 505(b)(2) NDA applicant to certify that there are no patents listed for that product in the Orange Book, or that for each Orange Book-listed patent either the listed patent has expired, the listed patent will expire on a particular date and approval is sought after patent expiration, or the listed patent is invalid or will

not be infringed by the manufacture, use or sale of the new product. A certification that approval is sought after patent expiration is called a "Paragraph III Certification." A certification that the new product will not infringe the RLD's Orange Book-listed patents, or that such patents are invalid, is called a "Paragraph IV Certification." If a relevant patent covers an approved method of use, an ANDA or Section 505(b)(2) NDA applicant can also file a statement, called, in the case of an ANDA, a "section viii statement," that the application does not seek approval of the method of use covered by the listed patent. With such a statement, the applicant must "carve out" the protected method of use (typically an indication and related material) from the proposed product's labeling. If the applicant makes a Paragraph III Certification, the ANDA or the Section 505(b)(2) NDA will not be approved until the listed patents claiming the RLD have expired.

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

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

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

In the EU, innovative medicinal products that are subject to marketing authorization on the basis of a full dossier qualify for eight years' data exclusivity upon marketing authorization and an additional two years' market exclusivity. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced. However, the generic product or biosimilar products cannot be marketed in the EU for a further two years thereafter. The overall ten-year period may be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Orphan Drug and Other Exclusivities

Some jurisdictions, including the U.S., may designate drugs or biologics for relatively small patient populations as orphan drugs. FDA grants orphan drug designation to drugs or biologics intended to treat a rare disease or condition, which is one that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals, but for which there is no reasonable expectation that the cost of developing the product and making it available in the U.S. for the disease or condition will be recovered from U.S. sales of the product. Orphan drug designation does not shorten the duration of the regulatory review process or lower the approval standards, but can provide important benefits, including consultation with FDA. If a product is approved for its orphan designated use, it may be entitled to ODE, which blocks FDA from approving for seven years any other application for a product that is the same drug for the same indication. If there is a previously-approved product that is the

same drug for the same indication, orphan drug designation requires the sponsor to provide a plausible hypothesis of clinical superiority over the approved product, whereas ODE requires the sponsor to actually demonstrate clinical superiority. Clinical superiority can be established by way of greater efficacy, greater safety, or making a major contribution to patient care. Additionally, a later product can be approved if the sponsor holding ODE consents, or cannot adequately supply the market. ODE does not prevent approval of another sponsor's application for different indications or uses of the same drug, or for different drugs for the same indication. Defibrotide has been granted ODE by FDA to treat and prevent VOD until March 2023. Vyxeos has been granted ODE by FDA for the treatment of AML until August 2024. Epidiolex has received ODE to treat seizures associated with LGS and DS through 2025 and TSC through 2027. In June 2021, FDA, recognized seven years of ODE for Xywav stating that Xywav is clinically superior to Xyrem by means of greater safety due to reduced chronic sodium burden. Xywav has been granted ODE by FDA to treat narcolepsy through 2027 and to treat IH through 2028. Rylaze has been granted ODE for the treatment of patients with ALL or LBL until 2028.

Biologic products approved under a BLA are subject to the Biologics Price Competition and Innovation Act, or BPCIA, which authorizes an abbreviated approval pathway for a biological product that is "biosimilar" to an already approved biologic, or reference product. The BPCIA provides periods of exclusivity that protect a reference product from competition by biosimilars. FDA may not accept a biosimilar application for review until four years after the date of first licensure of the reference product, and the biosimilar cannot be licensed until 12 years after the reference product was first licensed.

Under certain circumstances, the exclusivity periods applicable to drugs and biologics and the patent-related protections applicable to drugs may be eligible for a six-month extension if the sponsor submits pediatric data that fairly respond to a written request from FDA for such data. This exclusivity may be granted even if the data does not support a pediatric indication. We consider seeking pediatric exclusivity for our products whenever appropriate. For example, in response to a written request from FDA, we conducted a Phase 3 clinical trial to assess the safety and efficacy of Xyrem in children and adolescents aged seven to 17 who have narcolepsy with cataplexy, and submitted study results in a supplement to the Xyrem NDA, seeking approval for this indication. In October 2018, FDA approved the sNDA and notified us that we had been granted pediatric exclusivity, extending by six months the preclusive effect of our Orange Book-listed patents for Xyrem, as well as the three-year regulatory exclusivity period granted to the Xyrem pediatric indication because of the clinical studies that were necessary for approval of the sNDA.

In the EU, orphan drug designation may be granted to products that can be used to treat life-threatening diseases or chronically debilitating conditions with an incidence of no more than five in 10,000 people or that, for economic reasons, would be unlikely to be developed without incentives. Orphan designated medicinal products are entitled to a range of benefits during the development and regulatory review process and ten years of market exclusivity in all EU member states upon approval. As in the U.S., a similar medicinal product with the same orphan indication may be approved, notwithstanding orphan product exclusivity, if the exclusivity holder gives consent or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity granted in relation to the original orphan medicinal product may, in addition, be reduced to six years if it can be demonstrated, on the basis of available evidence, that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity. Defibrotide has been granted orphan drug designation by the EC for the treatment of VOD and prevention of GvHD until October 2023, by the Korean Ministry of Food and Drug Safety to treat and prevent VOD, and by the Commonwealth of Australia-Department of Health for the treatment of VOD. Vyxeos has been granted orphan drug designation by the EC until August 2028. We also received Orphan Designation from EMA's Committee for Orphan Medicinal Products, or COMP, for Epidyolex for DS, LGS and TSC, and the COMP reconfirmed the designation for DS, LGS and TSC upon EC's approval.

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

Pricing and Reimbursement

Successful commercialization of our products depends in significant part on adequate financial coverage and reimbursement from third party payors, including governmental payors (such as the Medicaid and Medicare programs in the U.S.), managed care organizations and private health insurers. Third party payors decide which drugs will be reimbursed and establish reimbursement and co-pay levels and conditions for reimbursement. Third party payors are increasingly challenging the prices charged for medical products and services by examining their cost effectiveness, as demonstrated in pharmacoeconomic and/or clinical studies, in addition to their safety and efficacy. In some cases, for example, third party payors try to encourage the use of less expensive products, when available, through their prescription benefits coverage and reimbursement, co-pay and prior authorization policies. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third party payors may require prior approval before covering a specific product, or may require patients and health care providers to try other covered products first. Third party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. For

certain categories of products, third party payors, principally through contracted pharmacy benefit managers, or PBMs, negotiate rebates with drug manufacturers for inclusion of products on their formularies in specific positions or coverage criteria. Beginning in the third quarter of 2019, we have been entering into agreements with certain PBMs or similar organizations to provide rebates for our products where coverage was provided and products were listed in certain formulary positions, among other conditions.

Medicaid is a joint federal and state program that is administered by the states for low-income and disabled beneficiaries. Medicare is a federal program that is administered by the federal government covering individuals age 65 and over as well as those with certain disabilities. Medicare Part B pays physicians who administer our products. Under the Medicaid Drug Rebate Program, as a condition of having federal funds made available to the states for our drugs under Medicare Part B, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. Medicaid rebates are based on pricing data we report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services, or CMS, the federal agency that administers the Medicaid Drug Rebate Program and Medicare. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all applicable sales and associated rebates, discounts and other price concessions. If we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. We are required to provide average sales price, or ASP, information for certain of our products to CMS on a quarterly basis. The ASP is calculated based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. This information is used to compute Medicare payment rates, with rates for Medicare Part B drugs outside the hospital outpatient setting and in the hospital outpatient setting consisting of ASP plus a specified percentage.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the Public Health Service's 340B program, or the 340B program, in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program, which is administered by the Health Resources and Services Administration, or HRSA, requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered drugs used in an outpatient setting. These 340B covered entities include certain qualifying community health clinics, a variety of entities that receive health services grants from the Public Health Service, and multiple categories of hospitals, including children's hospitals, critical access hospitals, free standing cancer hospitals and hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. A regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities became effective on January 1, 2019. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis and HRSA then publishes them to 340B covered entities. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

A provision in The American Rescue Plan Act of 2021 eliminates, effective January 2024, the statutory cap on rebates drug manufacturers are required to pay under the Medicaid Drug Rebate Program. Since 2010, the total Medicaid rebate amount a drug manufacturer is required to pay under the Medicaid Drug Rebate Program has been capped at 100 percent of the Average Manufacturer Price. The elimination of the cap on rebates means that manufacturer discounts to Medicaid may rise beginning in 2024 and, in certain circumstances, rebates could exceed the amount that state Medicaid programs pay for the drug. This policy change will have the greatest impact on drugs whose prices have reached the 100 percent Average Manufacturer Price rebate cap. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under the program, which could negatively affect our business and financial condition.

Effective January 2023, a provision of the Infrastructure Investment and Jobs Act requires a manufacturer of single source drugs or biologicals in single-use packages or single dose containers to pay a refund on discarded amounts of drug under Medicare Part B where the discarded amount exceeds an applicable threshold.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we also participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. Under this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a

price to certain federal agencies that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non-federal average manufacturer price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts, which can change and evolve over time.

In addition, in the U.S., drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny, including with respect to companies that have increased the price of products after acquiring those products from other companies. There are numerous ongoing efforts at the federal and state level seeking to indirectly or directly regulate drug prices to reduce overall healthcare costs using tools such as price ceilings, value-based pricing and increased transparency and disclosure obligations. Numerous states have passed or are considering legislation that requires or purports to require companies to report pricing information, including proprietary pricing information. For example, in 2017, California adopted a prescription drug price transparency state bill requiring advance notice of and an explanation for price increases of certain drugs that exceed a specified threshold. Similar bills have been previously introduced at the federal level and additional legislation could be introduced this year.

Similar to what is occurring in the U.S., political, economic and regulatory developments outside of the U.S. are also subjecting the healthcare industry to fundamental changes and challenges. Pressure by governments and other stakeholders on prices and reimbursement levels continue to exist. In various EU member states we expect to be subject to continuous cost-cutting measures, such as voluntary and temporary sales rebates, lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. Health technology assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including countries representing major markets. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally compares attributes of individual medicinal products, as compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. In December 2021, the EC adopted a HTA regulation intended to boost cooperation among EU member states in assessing health technologies, including new medicinal products. The regulation will apply to all EU member states from January 2025 provides that EU member states will be able to use common HTA tools, methodologies, and procedures across the EU. Individual EU member states will continue to be responsible for drawing conclusions on the overall value of a new health technology for their healthcare system, and pricing and reimbursement decisions.

In the EU, our products are marketed through various channels and within different legal frameworks. The making available or placing on the EU market of unauthorized medicinal products is generally prohibited. However, the competent authorities of the EU member states may exceptionally and temporarily allow and reimburse the supply of such unauthorized products, either on a named patient basis or through a compassionate use process, to individual patients or a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorized medicinal product. Such reimbursement may no longer be available if authorization for named patient or compassionate use programs expire or is terminated or if marketing authorization is granted for the product. In some EU member states, authorization and reimbursement policies may also delay commercialization of our products, or may adversely affect our ability to sell our products on a profitable basis. After initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or arbitrage between low-priced and high-priced EU member states.

For more information, including with respect to recent legal developments regarding the Medicaid Drug Rebate Program, Medicare Part B, and the 340B program, see the risk factors under the headings *"Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and group purchasing organizations, which could diminish our sales or affect our ability to sell our products profitably; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement that could diminish our sales," "The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition"* and *"If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects"* in Part I, Item 1A of this Annual Report on Form 10-K.

Patient Copay Assistance and Free Product Programs

We have various patient programs to help patients access and pay for our products, including co-pay coupons for certain products, services that help patients determine their insurance coverage for our products, and a free product program. We also make grants to independent charitable foundations that help financially needy patients with their premium, and co-pay and co-insurance obligations. There has been enhanced scrutiny of company-sponsored patient assistance programs, including co-pay assistance programs and donations to third-party charities that provide such assistance, as well as reimbursement support offerings.

The OIG has established guidelines for pharmaceutical manufacturers who make donations to charitable organizations providing co-pay assistance to Medicare patients. Such donations are unlikely to run afoul of the anti-kickback laws provided that the organizations receiving donations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. In 2016 and 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of charitable organizations that provide financial assistance to Medicare patients. In April 2019, we finalized our civil settlement agreement with the DOJ and OIG, and entered into a corporate integrity agreement requiring us to maintain our ongoing corporate compliance program and obligating us to implement or continue, as applicable, a set of defined corporate integrity activities to ensure compliance with OIG's policies around charitable contributions for a period of five years from the effective date of the corporate integrity agreement.

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc was formed under the laws of Ireland (registered number 399192) as a private limited liability company in March 2005 under the name Azur Pharma Limited and was subsequently re-registered as a public limited company under the name Azur Pharma Public Limited Company, or Azur Pharma, in October 2011. On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma were combined in a merger transaction, in connection with which Azur Pharma was re-named Jazz Pharmaceuticals plc and we became the parent company of and successor to Jazz Pharmaceuticals, Inc.

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

Available Information

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

We file or furnish pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as applicable, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, amendments to those reports, proxy statements and other information electronically with the SEC. Through a link on our website, we make copies of our periodic and current reports, amendments to those reports, proxy statements and other information available, free of charge, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this Annual Report on Form 10-K.

Item 1A. Risk Factors

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

Risks Related to Our Lead Products and Product Candidates

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

Historically, our business has been substantially dependent on Xyrem and our financial results have been significantly influenced by sales of Xyrem. Our operating plan assumes that Xywav, our oxybate product launched in November 2020, will remain the treatment of choice for patients who can benefit from oxybate treatment. While we expect that our business will continue to be substantially dependent on oxybate product sales, there is no guarantee that we can maintain oxybate sales at or near historical levels, or that oxybate sales will continue to grow. In this regard, our ability to maintain or increase oxybate product sales and realize the anticipated benefits from our investment in Xywav are subject to a number of risks and uncertainties as discussed in greater detail below, including those related to the launch of Xywav for the treatment of idiopathic hypersomnia, or IH, in adults and adoption in that indication; competition from the recent introduction of an authorized generic

version of sodium oxybate and in the future from additional authorized generic versions of sodium oxybate and generic versions of sodium oxybate and new products for treatment of cataplexy and/or excessive daytime sleepiness, or EDS, in narcolepsy in the U.S. market and from other competitors; 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 Xyrem and/or Xywav, including from pending antitrust and intellectual property litigation; and continued acceptance of Xywav and Xyrem by physicians and patients. A significant decline in oxybate sales could cause us to reduce our operating expenses or seek to raise additional funds, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including on our ability to acquire, in-license or develop new products to grow our business.

The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products and product candidates would adversely affect sales of our oxybate products and product candidates.

New treatment options for cataplexy and EDS in narcolepsy have been commercially launched, and in the future, other products may be launched that are competitive with or disrupt the market for our oxybate products.

Nine companies have sent us notices that they had filed abbreviated new drug applications, or ANDAs, seeking approval to market a generic version of Xyrem, and we have filed and settled patent lawsuits with all nine companies. To date, the U.S. Food and Drug Administration, or FDA, has approved or tentatively approved four of these ANDAs, and we believe that it is likely that FDA will approve or tentatively approve some or all of the others. Pursuant to our patent litigation settlement with the first filer, a wholly owned subsidiary of Hikma Pharmaceuticals PLC, or Hikma, Hikma launched an authorized generic product, or AG Product, in the U.S. beginning on January 1, 2023. Accordingly, beginning in January 2023, Xywav and Xyrem face competition from an authorized generic version of sodium oxybate and in the future, we expect to compete with other authorized generic and generic versions of sodium oxybate. Hikma has a right to elect to continue to sell the Hikma AG Product, with royalties back to us, for a total of up to five years. We will receive a meaningful royalty from Hikma on net sales of the Hikma AG Product, with the royalty rate increasing during the initial six month term based on increased net sales of the Hikma AG Product; if Hikma elects to extend the term for the remainder of the first year, the rate will become fixed. There will also be a substantial increase in the royalty rate should the term be extended beyond one year. We will also be paid for supply of the Hikma AG Product and will be reimbursed by Hikma for a portion of the services costs associated with the operation of the Xywav and Xyrem REMS and distribution of the Hikma AG Product. We also granted Hikma a license to launch its own generic sodium oxybate product as early as six months after it has the right to sell the Hikma AG Product, but if it elects to launch its own generic product, Hikma will no longer have the right to sell the Hikma AG Product. In our settlements with Amneal Pharmaceuticals LLC, or Amneal, Lupin Inc., or Lupin, and Par Pharmaceutical, Inc., or Par, we granted each party the right to sell a limited volume of an AG Product in the U.S. beginning on July 1, 2023 and ending on December 31, 2025, with royalties back to us. AG Products will be distributed through the same risk evaluation and mitigation strategy, or REMS, as Xywav and Xyrem. We also granted each of Amneal, Lupin and Par a license to launch its own generic sodium oxybate product under its ANDA on or after December 31, 2025, or earlier under certain circumstances, including the circumstance where Hikma elects to launch its own generic product. If Amneal, Lupin or Par elects to launch its own generic product under such circumstance, it will no longer have the right to sell an AG Product. In our settlements with each of the other five ANDA filers, we granted each a license to launch its own generic sodium oxybate product under its ANDA on or after December 31, 2025, or earlier under certain circumstances, including circumstances where Hikma launches its own generic sodium oxybate product. It is possible that additional companies may file ANDAs seeking to market a generic version of Xyrem which could lead to additional patent litigation or challenges with respect to Xyrem.

Any ANDA holder launching an AG Product or another generic sodium oxybate product will independently establish the price of the AG Product and/or its own generic sodium oxybate product and determine the types of discounts or rebates they will offer parties that purchase or pay for the product. Generic competition often results in decreases in the net prices at which branded products can be sold. A component of drug pricing is the manufacturer’s list price for a drug to wholesalers or direct purchasers in the U.S. (without discounts, rebates or other reductions) referred to as the Wholesale Acquisition Cost, or WAC. In this regard, Hikma launched the Hikma AG Product at a WAC that was less than 15% lower than the WAC for Xyrem. After any introduction of a generic product, whether or not it is an AG Product, a significant percentage of the prescriptions written for Xyrem will likely be filled with the generic product. Certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. This would result in reduction in sales of, and revenue from, Xyrem, although we would continue to receive royalties and other revenue based on sales of an AG Product in accordance with the terms of our settlement agreements.

Other companies may develop sodium oxybate products for treatment of narcolepsy, using an alternative formulation or a different delivery technology, and seek approval in the U.S. using a new drug application, or NDA, approval pathway under Section 505(b)(2) and referencing the safety and efficacy data for Xyrem. For example, in July 2022, Avadel Pharmaceuticals plc, or Avadel, announced that it had received tentative approval of FT218, an extended-release formulation of sodium oxybate

which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy, and pending disposition of our REMS patent, Avadel stated that it is seeking to accelerate full approval. For additional information on litigation involving this matter, see "*Avadel Patent Litigation*" in Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Moreover, Avadel has announced that it has obtained an orphan drug designation from FDA related to its extended-release sodium oxybate formulation. To obtain approval in light of the prior approval of our oxybate products and to obtain its own Orphan Drug Exclusivity for FT218 if approved, we believe Avadel will have to show clinical superiority to Xywav, which requires establishing that FT218 has greater effectiveness, greater safety, or otherwise makes a major contribution to patient care when compared to our products. We cannot predict the timing of full approval of Avadel's sodium oxybate product or how FDA will evaluate any clinical superiority arguments that either we or Avadel may make, but in any event, we expect to face competition from Avadel.

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

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

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

We expect that the approval and launch of the Hikma AG Product, another AG Product or other generic version of Xyrem and the approval and launch of any other sodium oxybate product (including Avadel's FT218) or alternative product that treats narcolepsy could have a material adverse effect on our sales of Xywav and Xyrem and on our business, financial condition, results of operations and growth prospects.

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

The active pharmaceutical ingredient, or API, of Xywav and Xyrem, is a form of gamma-hydroxybutyric acid, or GHB, a central nervous system depressant known to be associated with facilitated sexual assault as well as with respiratory depression and other serious side effects. As a result, FDA requires that we maintain a REMS with elements to assure safe use, or ETASU, for Xywav and Xyrem to help ensure that the benefits of the drug in the treatment of cataplexy and EDS in narcolepsy outweigh the serious risks of the drug. The REMS imposes extensive controls and restrictions on the sales and marketing of Xywav and Xyrem that we are responsible for implementing. Any failure to demonstrate our substantial compliance with our REMS obligations, or a determination by FDA that the REMS is not meeting its goals, could result in enforcement action by FDA, lead to changes in our REMS obligations, negatively affect sales of Xywav or Xyrem, result in additional costs and expenses for us and/or require us to invest a significant amount of resources, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

FDA will evaluate the Xywav and Xyrem REMS on an ongoing basis and will require modifications as may be appropriate. We cannot predict whether FDA will request, seek to require or ultimately require modifications to, or impose additional requirements on, the Xywav and Xyrem REMS, including in connection with the submission of new oxybate products or indications, the introduction of authorized generics, or to accommodate generics, or whether FDA will approve modifications to the Xywav and Xyrem REMS that we consider warranted. Any modifications approved, required or rejected by FDA could change the safety profile of Xywav or Xyrem, and have a significant negative impact in terms of product liability, public acceptance of Xywav or Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers'

willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our oxybate business. Modifications approved, required or rejected by FDA could also make it more difficult or expensive for us to distribute Xywav or Xyrem, make distribution easier for oxybate competitors, disrupt continuity of care for Xywav or Xyrem patients and/or negatively affect sales of Xywav or Xyrem.

We depend on outside vendors, including Express Scripts Specialty Distribution Services, Inc., the central certified pharmacy, to distribute Xywav and Xyrem in the U.S., provide patient support services and implement the requirements of the Xywav and Xyrem REMS. If the central pharmacy fails to meet the requirements of the Xywav and Xyrem REMS applicable to the central pharmacy or otherwise does not fulfill its contractual obligations to us, moves to terminate our agreement, refuses or fails to adequately serve patients, or fails to promptly and adequately address operational challenges or challenges in implementing REMS modifications, the fulfillment of Xywav or Xyrem prescriptions and our sales would be adversely affected. If we change to a new central pharmacy, new contracts might be required with government payors and other insurers who pay for Xywav or Xyrem, and the terms of any new contracts could be less favorable to us than current agreements. In addition, any new central pharmacy would need to be registered with the U.S. Drug Enforcement Administration, or DEA, and certified under the REMS and would also need to implement the particular processes, procedures and activities necessary to distribute under the Xywav and Xyrem REMS. Transitioning to a new pharmacy could result in product shortages, which would negatively affect sales of Xywav and Xyrem, result in additional costs and expenses for us and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

In its approval of Hikma's ANDA, FDA waived the requirement of a single shared REMS between the brand drug and generic versions, approving Hikma's ANDA with a generic sodium oxybate REMS separate from the Xywav and Xyrem REMS, except for the requirement that the generic sodium oxybate REMS program pharmacies contact the Xywav and Xyrem REMS by phone to verify and report certain information. The generic sodium oxybate REMS was approved with the condition that it be open to all future sponsors of ANDAs or NDAs for sodium oxybate products. A sodium oxybate distribution system that is less restrictive than the Xywav and Xyrem REMS, such as the generic sodium oxybate REMS or another branded sodium oxybate REMS, could increase the risks associated with oxybate distribution. Because patients, consumers and others may not differentiate generic sodium oxybate from Xyrem or differentiate between the different REMS programs, any negative outcomes, including risks to the public, caused by or otherwise related to a separate sodium oxybate REMS, could have a significant negative impact in terms of product liability, our reputation and good will, public acceptance of Xywav or Xyrem as a treatment for cataplexy and EDS in narcolepsy, and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our oxybate business.

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

REMS programs have increasingly drawn public scrutiny from the U.S. Congress, the Federal Trade Commission, or FTC, the United States Patent and Trademark Office, or USPTO, and FDA, with allegations that such programs are used as a means of improperly blocking or delaying competition. In December 2019, as part of the Further Consolidated Appropriations Act of 2020, the U.S. Congress passed legislation known as the Creating and Restoring Equal Access To Equivalent Samples Act, or CREATES. CREATES is intended to prevent companies from using REMS and other restricted distribution programs as a means to deny potential competitors access to product samples that are reasonably necessary to conduct testing in support of an application that references a listed drug or biologic, and provides such potential competitors a potential private right of action if the innovator fails to timely provide samples upon request. CREATES also grants FDA additional authority regarding approval of generic products with REMS. A further example of continued interest in REMS oversight came from the USPTO in collaboration with FDA in November 2022, when they published a Request for Comment, or RFC, in the Federal Register that asked, "What policy considerations or concerns should the USPTO and the FDA explore in relation to the patenting of risk evaluation and mitigation strategies associated with certain FDA-approved products?" The comments for this RFC closed on February 6, 2023.

It is possible that the FTC, FDA or other governmental authorities could claim that, or launch an investigation into whether, we are using our REMS programs in an anticompetitive manner or have engaged in other anticompetitive practices, whether under CREATES or otherwise. The Federal Food, Drug and Cosmetic Act further states that a REMS ETASU shall

not be used by an NDA holder to block or delay generic drugs or drugs covered by an application under Section 505(b)(2) from entering the market. In its 2015 letter approving the Xyrem REMS, FDA expressed concern that we were aware that the Xyrem REMS is blocking competition. From June 2020 to May 2022, we were served with a number of lawsuits that included allegations that we had used the Xyrem REMS to delay approval of generic sodium oxybate. In December 2020, these cases were centralized and transferred to the United States District Court for the Northern District of California, where the multidistrict litigation will proceed for the purpose of discovery and pre-trial proceedings. For additional information on these lawsuits, see Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. It is possible that additional lawsuits will be filed against us making similar or related allegations or that governmental authorities could commence an investigation. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

Any failure to demonstrate our substantial compliance with the REMS or any other applicable regulatory requirements to the satisfaction of FDA or another regulatory authority could result in such regulatory authorities taking actions in the future which could have a material adverse effect on oxybate product sales and therefore on our business, financial condition, results of operations and growth prospects.

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

Our ability to maintain or increase sales of Epidiolex/Epidyolex (cannabidiol) is subject to many risks. There are many factors that could cause the commercialization of Epidiolex to be unsuccessful, including a number of factors that are outside our control. The commercial success of Epidiolex depends on the extent to which patients and physicians accept and adopt Epidiolex as a treatment for seizures associated with Lennox-Gastaut syndrome, Dravet syndrome and Tuberous Sclerosis Complex, and we do not know whether our or others' estimates in this regard will be accurate. Physicians may not prescribe Epidiolex and patients may be unwilling to use Epidiolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex in the market, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex. In the future, we expect Epidiolex to face competition from generic cannabinoids. In November and December 2022, we received notices from various ANDA filers that they have each filed with FDA an ANDA for a generic version of Epidiolex (cannabidiol) oral solution. In January 2023, we filed patent infringement suits against these ANDA filers. As a result of these lawsuits, a stay of approval of up to 30 months will be imposed by FDA on these ANDA filers. For additional information see "*Epidiolex Patent Litigation*" in Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

While we expect our oxybate products and Epidiolex/Epidyolex to remain our largest products, our success also depends on our ability to effectively commercialize our other existing products and potential future products.

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

Our ability to realize the anticipated benefits from our investment in Zepzelca is subject to a number of risks and uncertainties, including our ability to successfully commercialize Zepzelca in the U.S. and Canada; adequate supply of Zepzelca to meet demand; availability of favorable treatment pathway designations pricing and adequate coverage and reimbursement; the limited experience of, and need to educate, physicians in the use of Zepzelca for the treatment of metastatic small cell lung cancer, or SCLC; the potential for negative trial data read-outs in ongoing or future Zepzelca clinical trials; our and Pharma Mar, S.A., or PharmaMar's, ability to maintain accelerated approval or successfully complete a confirmatory study of Zepzelca; and our ability to educate health care providers about Zepzelca in the treatment of relapsed, metastatic SCLC in the U.S. and

patients' access to lung cancer screening, diagnosis and treatment. Our ability to realize the anticipated benefits from our investments in Rylaze is subject to a number of uncertainties, including our ability to successfully commercialize Rylaze in the U.S. including creating awareness among health care professionals and ensuring that patients with acute lymphoblastic leukemia or lymphoblastic lymphoma will be given the appropriate course of therapy and dosing regimen based on current FDA approval. Our ability to realize the anticipated benefits from our investment in Vyxeos is subject to a number of risks and uncertainties, including our ability to differentiate Vyxeos from other liposomal chemotherapies and generically available chemotherapy combinations with which physicians and treatment centers are more familiar; acceptance by hospital pharmacy and therapeutics committees in the U.S., the EU and other countries; the increasing complexity of the acute myeloid leukemia, or AML, landscape requiring changes in patient identification and treatment selection, including diagnostic tests and monitoring that clinicians may find challenging to incorporate; the use of new and novel compounds in AML that are either used off-label or are only approved for use in combination with other agents and that have not been tested in combination with Vyxeos; the increasing use of venetoclax, which received full FDA approval in October 2020 for AML treatment; the limited size of the population of high-risk AML patients who may potentially be indicated for treatment with Vyxeos; the availability of adequate coverage, pricing and reimbursement approvals; and competition from new and existing products and potential competition from products in development. Our ability to maintain and grow sales and to realize the anticipated benefits from our investment in Defitelio is subject to a number of risks and uncertainties, including continued acceptance by hospital pharmacy and therapeutics committees in the U.S., the EU and other countries; the continued availability of favorable pricing and adequate coverage and reimbursement; the limited experience of, and need to educate, physicians and other health care providers in recognizing, diagnosing and treating hepatic veno-occlusive disease, or VOD, particularly in adults; the possibility that physicians recognizing VOD symptoms may not initiate or may delay initiation of treatment while waiting for those symptoms to improve, or may terminate treatment before the end of the recommended dosing schedule; and the limited size of the population of VOD patients who are indicated for treatment with Defitelio (particularly if changes in hematopoietic stem cell transplantation treatment protocols reduce the incidence of VOD diagnosis and demand for Defitelio).

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

Our products compete, and our product candidates may in the future compete, with currently existing therapies, including authorized generic and generic drugs, product candidates currently under development by us and others and/or future product candidates, including new chemical entities that may be safer or more effective or more convenient than our products. Any products that we develop may be commercialized in competitive markets, and our competitors, which include large global pharmaceutical companies and small research-based companies and institutions, may succeed in developing products that render our products obsolete or noncompetitive. Many of our competitors, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources than we do. Smaller or earlier stage companies may also prove to be significant competitors, particularly through focused development programs and collaborative arrangements with large, established companies. In addition, many of our competitors deploy more personnel to market and sell their products than we do, and we compete with other companies to recruit, hire, train and retain pharmaceutical sales and marketing personnel. If our sales force and sales support organization are not appropriately resourced and sized to adequately promote our products, the commercial potential of our current and any future products may be diminished. In any event, the commercial potential of our current products and any future products may be reduced or eliminated if our competitors develop or acquire and commercialize generic or branded products that are safer or more effective, are more convenient or are less expensive than our products. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

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

Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and other organizations; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement, either of which could diminish our sales or adversely affect our ability to sell our products profitably.

In both U.S. and non-U.S. markets, our ability to successfully commercialize and achieve market acceptance of our products depends in significant part on adequate financial coverage and reimbursement from third party payors, including governmental payors (such as the Medicare and Medicaid programs in the U.S.), managed care organizations and private health insurers. Without third party payor reimbursement, patients may not be able to obtain or afford prescribed medications. In addition, reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a significant impact on the prescribing physicians' willingness and ability to prescribe our products. The demand for, and the

profitability of, our products could be materially harmed if state Medicaid programs, the Medicare program, other healthcare programs in the U.S. or elsewhere, or third party commercial payors in the U.S. or elsewhere deny reimbursement for our products, limit the indications for which our products will be reimbursed, or provide reimbursement only on unfavorable terms.

As part of the overall trend toward cost containment, third party payors often require prior authorization for, and require reauthorization for continuation of, prescription products or impose step edits, which require prior use of another medication, usually a generic or preferred brand, prior to approving coverage for a new or more expensive product. Such restrictive conditions for reimbursement and an increase in reimbursement-related activities can extend the time required to fill prescriptions and may discourage patients from seeking treatment. We cannot predict actions that third party payors may take, or whether they will limit the access and level of reimbursement for our products or refuse to provide any approvals or coverage. From time to time, third party payors have refused to provide reimbursement for our products, and others may do so in the future.

Third party payors increasingly examine the cost-effectiveness of pharmaceutical products, in addition to their safety and efficacy, when making coverage and reimbursement decisions. We may need to conduct expensive pharmacoeconomic and/or clinical studies in order to demonstrate the cost-effectiveness of our products. If our competitors offer their products at prices that provide purportedly lower treatment costs than our products, or otherwise suggest that their products are safer, more effective or more cost-effective than our products, this may result in a greater level of access for their products relative to our products, which would reduce our sales and harm our results of operations. In some cases, for example, third party payors try to encourage the use of less expensive generic products through their prescription benefit coverage and reimbursement and co-pay policies. Because some of our products compete in a market with both branded and generic products, obtaining and maintaining access and reimbursement coverage for our products may be more challenging than for products that are new chemical entities for which no therapeutic alternatives exist.

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

In many countries outside the U.S., procedures to obtain price approvals, coverage and reimbursement can take considerable time after the receipt of marketing authorization. Many European countries periodically review their reimbursement of medicinal products, which could have an adverse impact on reimbursement status. In addition, we expect that legislators, policymakers and healthcare insurance funds in the EU member states will continue to propose and implement cost-containing measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative to branded products, and/or branded products available through parallel import to keep healthcare costs down. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU member states, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including those representing the larger markets. The HTA process, which is currently governed by national laws in each EU member state, is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU member states, although beginning in January 2025, the EU HTA regulation will apply; this regulation aims to harmonize the clinical benefit assessment of HTA across the EU. If we are unable to maintain favorable pricing and reimbursement status in EU member states that represent significant markets, our anticipated revenue from and growth prospects for our products in the EU

could be negatively affected. For example, the European Commission, or EC, granted marketing authorization for Vyxeos in August 2018 and for Epidyolex in September 2019, and, as part of our rolling launches of Vyxeos and Epidyolex in Europe, we are making pricing and reimbursement submissions in European countries. If we experience setbacks or unforeseen difficulties in obtaining favorable pricing and reimbursement decisions, including as a result of regulatory review delays, planned launches in the affected EU member states would be delayed, which could negatively impact anticipated revenue from and growth prospects for Vyxeos and Epidyolex.

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

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U.S. We expect there will continue to be legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably, as governmental oversight and scrutiny of biopharmaceutical companies is increasing. For example, we anticipate that the U.S. Congress, state legislatures, and federal and state regulators may adopt or accelerate adoption of new healthcare policies and reforms intended to curb healthcare costs, such as federal and state controls on reimbursement for drugs (including under Medicare, Medicaid and commercial health plans), new or increased requirements to pay prescription drug rebates and penalties to government health care programs, and additional pharmaceutical cost transparency policies that aim to require drug companies to justify their prices through required disclosures. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under the program, which could negatively affect our business and financial condition. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are currently capped at 100 percent of average manufacturer price, but, effective January 1, 2024, this cap will be lifted, which could adversely affect our rebate liability.

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

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

If new healthcare policies or reforms intended to curb healthcare costs are adopted or if we experience negative publicity with respect to pricing of our products or the pricing of pharmaceutical drugs generally, the prices that we charge for our products may be affected, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted. We have periodically increased the price of our products, including Xywav and Xyrem most recently in January 2023, and there is no guarantee that we will make similar price adjustments to our products in the future or that price adjustments we have taken or may take in the future will not negatively affect our sales volumes and revenues. There is no guarantee that such price adjustments will not negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our products, which could limit the prices that we charge for our products, limit the commercial opportunities for our products and/or negatively impact revenues from sales of our products.

Government investigations or U.S. Congressional oversight with respect to drug pricing or our other business practices could cause us to incur significant expense and could distract us from the operation of our business and execution of our

strategy. Any such investigation or hearing could also result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. For example, in July 2022, we received a subpoena from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to Xyrem and U.S. Patent No. 8,772,306 ("Method of Administration of Gamma Hydroxybutyrate with Monocarboxylate Transporters"), product labeling changes for Xyrem, communications with FDA and the U.S. Patent and Trademark Office, pricing of Xyrem, and other related documents. For more information, see the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products*" in this Part I, Item 1A.

We expect that legislators, policymakers and healthcare insurance funds in Europe and other international markets will continue to propose and implement cost-containing measures to keep healthcare costs down. These measures could include limitations on the prices we will be able to charge for our products or the level of reimbursement available for these products from governmental authorities or third party payors as well as clawbacks and revenue caps. For example, in the U.K., the cap on National Health Service, or NHS, spending on branded medicines agreed between the U.K. government and industry for 2019 to 2023 has remained unaltered despite higher than expected growth in NHS use of branded medicines, resulting in significant increases to the industry level revenue clawback rate payable on sales of branded medicines to the NHS. In the EU, a trend in some EU member states is for medicinal products to be reimbursed based on competitor products and not in relation with the value or the cost of the product. A proposal for EU pharmaceutical reform also includes cooperation with the relevant national authorities of the EU member states on pricing and reimbursement. Further, an increasing number of European and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

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

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

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

  and the view of patients, law enforcement agencies, physicians and regulators of our products as being the same or similar to illicit products;
- relative convenience and ease of administration;
- with respect to Xywav and Xyrem, physician and patient assessment of the burdens associated with obtaining or maintaining the certifications required under the Xywav and Xyrem REMS;
- the cost of treatment in relation to alternative treatments, including generic products; and
- the availability of financial or other assistance for patients who are uninsured or underinsured.

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

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

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of process controls required to consistently produce the API and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. We and our suppliers may encounter difficulties in production, including difficulties with the supply of manufacturing materials, production costs and yields, process controls, quality control and quality assurance, including testing of stability, impurities and impurity levels and other product specifications by validated test methods, and compliance with strictly enforced U.S., state and non-U.S. regulations. In addition, we and our suppliers are subject to FDA's current Good Manufacturing Practices, or cGMP, requirements, federal and state controlled substances obligations and equivalent rules and regulations prescribed by non-U.S. regulatory authorities. If we or any of our suppliers encounter manufacturing, quality or compliance difficulties with respect to any of our products, whether due to the ongoing military conflict in Ukraine and related sanctions imposed against Russia (including as a result of disruptions of global shipping, the transport of products, energy supply, cybersecurity incidents and banking systems as well as of our ability to control input costs) or otherwise, we may be unable to obtain or maintain regulatory approval or meet commercial demand for such products, which could adversely affect our business, financial condition, results of operations and growth prospects. In addition, we could be subject to enforcement action by regulatory authorities for our failure to comply with cGMP with respect to the products we manufacture in our facilities as well as for our failure to adequately oversee compliance with cGMP by any of our third party suppliers operating under contract. Moreover, failure to comply with applicable legal and regulatory requirements subjects us and our suppliers to possible regulatory action, including restrictions on supply or shutdown, which may adversely affect our or a supplier's ability to supply the ingredients or finished products we need.

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

In part due to the limited market size for our products and product candidates, we have a single source of supply for most of our marketed products, product candidates and their APIs. Single sourcing puts us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties. If one of our suppliers fails or refuses to supply us for any reason, it would take a significant amount of time and expense to implement and execute the necessary technology transfer to, and to qualify, a new supplier. FDA and similar international or national regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and certain packaging materials used in our products. If there are delays in qualifying new suppliers or facilities or a new supplier is unable to meet FDA's or similar international regulatory body's requirements for approval, there could be a shortage of the affected products for the marketplace or for use in clinical studies, or both, which could negatively impact our anticipated revenues and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

We are responsible for the manufacture and supply of Epidiolex/Epidyolex and other cannabinoid product candidates for commercial use and for use in clinical trials. The manufacturing of Epidiolex/Epidyolex and our product candidates necessitates compliance with Good Manufacturing Practice, or GMP, and other regulatory requirements in jurisdictions internationally. Our ability to successfully manufacture Epidiolex/Epidyolex and other cannabinoid product candidates involves cultivation of botanical raw material from specific cannabinoid plants, extraction and purification processes, manufacture of finished products and labeling and packaging, which includes product information, tamper evidence and anti-counterfeit features, under tightly controlled processes and procedures. In addition, we must ensure chemical consistency among our batches, including clinical batches and, if approved, marketing batches. Demonstrating such consistency may require typical manufacturing controls as well as clinical data. We must also ensure that our batches conform to complex release specifications. We have a second site at which we can grow the specific cannabinoid plants that produce the CBD used in Epidiolex/Epidyolex, a second site at which we can extract CBD from botanical raw material and a second site at which we can crystallize the purified CBD from the liquid plant extract. A number of our product candidates (excluding Epidiolex/Epidyolex) consist of a complex mixture manufactured from plant materials, and because the release specifications may not be identical in all countries, certain batches may fail release testing and not be able to be commercialized. If we are unable to

manufacture Epidiolex/Epidyolex or other product candidates in accordance with regulatory specifications, including GMP or if there are disruptions in our manufacturing process due to damage, loss or otherwise, or failure to pass regulatory inspections of our manufacturing facilities, we may not be able to meet current demand or supply sufficient product for use in clinical trials, and this may also harm our ability to commercialize Epidiolex/Epidyolex and our product candidates on a timely or cost-competitive basis, if at all. Our manufacturing program requires significant time and resources and may not be successful, may lead to delays, interruptions to supply or may prove to be more costly than anticipated.

Vyxeos is manufactured by Baxter Oncology GmbH, or Baxter, which is a sole source supplier from a single site location. There have been batch failures due to mechanical, component, raw materials and other issues in the production of Vyxeos, and batches have been produced that have otherwise not been in compliance with applicable specifications. We are continuing to work with Baxter and others to address manufacturing complexities related to Vyxeos. Moreover, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. Consequently, engaging an alternate manufacturer may be difficult, costly and time-consuming. If we fail to obtain a sufficient supply of Vyxeos in accordance with applicable specifications on a timely basis, our sales of Vyxeos, our future maintenance and potential growth of the market for this product, our ability to conduct ongoing and future clinical trials of Vyxeos, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Rylaze drug substance is manufactured by AGC Biologics A/S at its facility in Copenhagen, Denmark and the drug product is manufactured and packaged by Patheon at its facility in Greenville, North Carolina. Both sites have ample capacity to support forecast demand and we have secured supply for more than one year's forecast demand. To successfully manufacture Rylaze, the manufacturer must have an adequate master and working cell bank. If we fail to obtain a sufficient supply of Rylaze in accordance with applicable specifications on a timely basis, our sales of Rylaze, our future maintenance and potential growth of the market for this product, our competitive advantage over competing products that have supply constraints, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

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

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

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

Our future success depends on our ability to successfully develop and obtain and maintain regulatory approvals for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.

The testing, manufacturing and marketing of our products require regulatory approvals, including approval from FDA and similar bodies in Europe and other countries. If FDA, the European Medicines Agency, or EMA, or the competent authorities of the EU member states or other European countries determine that our quality, safety or efficacy data do not warrant marketing approval for a product candidate, we could be required to conduct additional clinical trials as a condition to receiving approval, which could be costly and time-consuming and could delay or preclude the approval of our application. Our inability to obtain and maintain regulatory approval for our product candidates in the U.S. and internationally and to successfully commercialize new products that are approved would prevent us from receiving a return on our investments and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Even if we receive regulatory approval of a product, regulatory authorities may impose significant labeling restrictions or requirements, including limitations on the dosing of the product, requirements around the naming or strength of a product, restrictions on indicated uses for which we may market the product, the imposition of a boxed warning or other warnings and precautions, and/or the requirement for a REMS or equivalent obligation imposed in a European or other foreign country to ensure that the benefits of the drug outweigh the risks. FDA requires a REMS and a boxed warning for Xywav and Xyrem, and similar restrictions could be imposed on other products in the future. Our receipt of approval for narrower indications than sought, restrictions on marketing through a REMS or equivalent obligation imposed in a European or other foreign country, or

significant labeling restrictions or requirements in an approved label such as a boxed warning, could have a negative impact on our ability to recoup our research and development costs and to successfully commercialize that product, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Regulatory authorities may also impose post-marketing obligations as part of their approval, which may lead to additional costs and burdens associated with commercialization of the product and may pose a risk to maintaining approval of the product. We are subject to certain post-marketing requirements and commitments in connection with the approval of certain of our products, including Epidiolex/Epidyolex, Defitelio, Vyxeos, Rylaze and Zepzelca. These post-marketing requirements and commitments include satisfactorily conducting multiple post-marketing clinical trials and safety studies. Failure to comply with these post-marketing requirements could result in withdrawal of our marketing approvals for the applicable product and/or other civil or criminal penalties. For example, FDA granted accelerated approval to Zepzelca for relapsed SCLC based on data from a Phase 2 trial, which approval is contingent upon verification and description of clinical benefit in a post-marketing clinical trial. We and our licensor PharmaMar are committed to the further study of lurbinectedin, both as a single agent and in combination, and have reached agreement with FDA regarding a confirmatory clinical development program. Our inability to confirm its clinical benefit could result in the withdrawal of approval of Zepzelca, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In any event, if we are unable to comply with our post-marketing obligations imposed as part of the marketing approvals in the U.S., the EU, or other countries, our approval may be varied, suspended or revoked, product supply may be delayed and our sales of our products could be materially adversely affected.

Epidiolex has been administered only to a limited number of patients and in limited populations in clinical trials. While FDA and EC granted approval of Epidiolex/Epidyolex based on the data included in GW's NDA, supplemental NDA and marketing authorization application, we do not know whether the results will be consistent with those resulting from administration of the drug to a large number of patients. New data relating to Epidiolex/Epidyolex, including from adverse event reports and post-marketing studies in the U.S. and Europe, and from other ongoing clinical trials, may result in changes to the product label and/or imposition of a REMS and may adversely affect sales, or result in withdrawal of Epidiolex/Epidyolex from the market. FDA, EMA and regulatory authorities in other jurisdictions may also consider the new data in reviewing Epidiolex/Epidyolex marketing applications for indications other than our approved uses in other jurisdictions or impose additional post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales of Epidiolex/Epidyolex. If we are not successful in the clinical development of our product candidates, if we are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, or if sales of an approved product do not reach the levels we expect, our anticipated revenue from our product candidates would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

In addition to continued investment in our research and development pipeline, we intend to grow our business by acquiring or in-licensing, and developing, including with collaboration partners, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. However, we may be unable to identify or consummate suitable acquisition or in-licensing opportunities, and this inability could impair our ability to grow our business. Other companies, many of which may have substantially greater financial, sales and marketing resources, compete with us for these opportunities. Even if appropriate opportunities are available, we may not be able to successfully identify them, or we may not have the financial resources necessary to pursue them.

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

- the need to incur substantial debt and/or engage in dilutive issuances of equity securities to pay for acquisitions;
- the need to comply with regulatory requirements, including in some cases clearance from the Federal Trade Commission;

- the potential disruption of our historical core business;
- the strain on, and need to continue to expand, our existing operational, technical, financial and administrative infrastructure;
- the difficulties in integrating acquired products and product candidates into our portfolio;
- the difficulties in assimilating employees and corporate cultures;
- the failure to retain key managers and other personnel;
- the need to write down assets or recognize impairment charges;
- the diversion of our management's attention to integration of operations and corporate and administrative infrastructures; and
- any unanticipated liabilities for activities of or related to the acquired business or its operations, products or product candidates.

As a result of these or other factors, products or product candidates we acquire, or obtain licenses to, may not produce the revenues, earnings or business synergies that we anticipated, may not result in regulatory approvals, and may not perform as expected. For example, in May 2021, we made a substantial investment in Epidiolex and certain other products and technologies acquired in our acquisition of GW. The total consideration paid by us for the entire issued share capital of GW was $7.2 billion. The success of our acquisition of GW will depend, in part, on our ability to realize the anticipated benefits from the acquisition, which benefits may not be realized at the expected levels 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. In this regard, in the third quarter of 2022, we recorded a $133.6 million asset impairment charge as a result of the decision to discontinue the nabiximols program that we acquired as part of our acquisition of GW. In any event, failure to manage effectively our growth through acquisitions or in-licensing transactions could adversely affect our growth prospects, business, results of operations and financial condition.

Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects.

As a condition to regulatory approval, each product candidate must undergo extensive and expensive preclinical studies and clinical trials to demonstrate that the product candidate is safe and effective. The results at any stage of the development process may lack the desired safety, efficacy or pharmacokinetic characteristics. If FDA determines that the safety or efficacy data included in any marketing application we submit do not warrant marketing approval for the affected product or product candidate, we may be required to conduct additional preclinical studies or clinical trials, which could be challenging to perform, costly and time-consuming. Even if we believe we have successfully completed testing, FDA or any equivalent non-U.S. regulatory agency may determine our data is not sufficiently compelling to warrant marketing approval for the indication(s) sought, if at all, and may require us to engage in additional clinical trials or provide further analysis which may be costly and time-consuming. Any adverse events or other data generated during the course of clinical trials of our product candidates and/or clinical trials related to additional indications for our commercialized products could result in action by FDA or an equivalent non-U.S. regulatory agency, which may restrict our ability to sell, or adversely affect sales of, currently marketed products, or such events or other data could otherwise have a material adverse effect on a related commercial product, including with respect to its safety profile. Any failure or delay in completing such clinical trials could materially and adversely affect the maintenance and growth of the markets for the related marketed products, which could adversely affect our business, financial condition, results of operations and overall growth prospects.

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

- difficulty identifying, recruiting or enrolling eligible patients, often based on the number of clinical trials, particularly with enrollment criteria targeting the same patient population, and in rare diseases with small patient populations;
- difficulty identifying a clinical development pathway, including viable indications and appropriate clinical trial protocol design, particularly where there is no applicable regulatory precedent;
- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;

- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidate for use in trials;
- delays or failures in reaching agreement on acceptable terms with prospective study sites;
- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board, known as an ethics committee in Europe, to conduct a clinical trial at a prospective study site;
- failure of our clinical trials and clinical investigators, including contract research organizations or other third parties assisting us with clinical trials, to satisfactorily perform their contractual duties, meet expected deadlines and comply with FDA and other regulatory agencies' requirements, including good clinical practices;
- unforeseen safety issues;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites; or
- insufficient funds to complete the trials.

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

Risks Related to Our Intellectual Property

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

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

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

- our patent applications, or those of our licensors or partners, may not result in issued patents;
- others may independently develop similar or therapeutically equivalent products without infringing our patents, or those of our licensors, such as products that are not covered by the claims of our patents, or for which fall outside the exclusive rights granted under our license agreements;
- our issued patents, or those of our licensors or partners, may be held invalid or unenforceable as a result of legal challenges by third parties or may be vulnerable to legal challenges as a result of changes in applicable law;
- our patents covering certain aspects of our products or the distribution thereof could be delisted from FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or Orange Book, as a result of challenges by third parties before FDA or the courts;
- competitors may manufacture products in countries where we have not applied for patent protection or that have a different scope of patent protection or that do not respect our patents; or
- others may be issued patents that prevent the sale of our products or require licensing and the payment of significant fees or royalties.

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

Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property portfolio. Any patent may be challenged, and potentially invalidated or held unenforceable, including through patent litigation or through administrative procedures that permit challenges to patent validity. Patents can also be circumvented, potentially including by an ANDA or Section 505(b)(2) application that avoids infringement of our intellectual property.

In June 2021, we received notice from Lupin that it has filed with FDA an ANDA for a generic version of Xywav. The notice from Lupin included a "paragraph IV certification" with respect to ten of our patents listed in FDA's Orange Book for Xywav on the date of our receipt of the notice. A paragraph IV certification is a certification by a generic applicant that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product. In April 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. Additionally, in November and December 2022, ten companies sent us notices that they had filed ANDAs seeking approval to market a generic version of Epidiolex, which notices each included a "paragraph IV certification" with respect to certain of our patents listed in FDA's Orange Book for Epidiolex on the date of the receipt of the applicable notice. For additional information on litigation involving these matters, see Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

We have settled patent litigation with nine companies seeking to introduce generic versions of Xyrem in the U.S. by granting those companies licenses to launch their generic products (and in certain cases, an authorized generic version of Xyrem) in advance of the expiration of the last of our patents. Notwithstanding our Xyrem patents and settlement agreements, additional third parties may also attempt to introduce generic versions of Xyrem, Xywav or other sodium oxybate products for treatment of cataplexy and/or EDS in narcolepsy that design around our patents or assert that our patents are invalid or otherwise unenforceable. Such third parties could launch a generic or 505(b)(2) product referencing Xyrem before the dates provided in our patents or settlement agreements. For example, we have several method of use patents listed in the Orange Book, that expire in 2033 that cover treatment methods included in the Xyrem label related to a drug-drug interaction, or DDI, with divalproex sodium. Although FDA has stated, in granting a Citizen Petition we submitted in 2016, that it would not approve any sodium oxybate ANDA referencing Xyrem that does not include the portions of the currently approved Xyrem label related to the DDI patents, we cannot predict whether a future ANDA filer, or a company that files a Section 505(b)(2) application for a drug referencing Xyrem, may pursue regulatory strategies to avoid infringing our DDI patents notwithstanding FDA's response to the Citizen Petition, or whether any such strategy would be successful. Likewise, we cannot predict whether we will be able to maintain the validity of these patents or will otherwise obtain a judicial determination that a generic or other sodium oxybate product, its package insert or the generic sodium oxybate REMS or another separate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents a future ANDA filer or other company introducing a different sodium oxybate product from marketing its product, or instead require that party to pay damages in the form of lost profits or a reasonable royalty.

On May 13, 2021, we filed a patent infringement suit against Avadel and several of its corporate affiliates in the United States District Court for the District of Delaware. The suit alleges that Avadel's product candidate FT218 will infringe five of our patents related to controlled release formulations of oxybate and the safe and effective distribution of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe these patents, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents. For additional information on litigation involving this matter, see "*Avadel Patent Litigation*" in Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

Since Xyrem's regulatory exclusivity has expired in the EU, we are aware that generic or hybrid generic applications have been approved by various EU regulatory authorities, and additional generic or hybrid generic applications may be submitted and approved.

We also currently rely on trade secret protection for several of our products, including Defitelio, and product candidates. Trade secret protection does not protect information or inventions if another party develops that information or invention independently, and establishing that a competitor developed a product through trade secret misappropriation rather than through legitimate means may be difficult to prove. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality and invention agreements with our employees, consultants, advisors and partners. Nevertheless, our employees, consultants, advisors and partners may unintentionally or willfully disclose our proprietary information to competitors, and we may not have adequate remedies for such disclosures. Moreover, if a dispute arises with our employees, consultants, advisors or partners over the ownership of rights to inventions, including jointly developed intellectual property, we could lose patent protection or the confidentiality of our proprietary information, and possibly also lose the ability to pursue the development of certain new products or product candidates.

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

Our ability, and that of our partners, to successfully commercialize any approved products will depend, in part, on our ability to obtain patents, enforce those patents and operate without infringing the proprietary rights of third parties. If we choose to go to court to stop a third party from infringing our patents, our licensed patents or our partners' patents, that third party has the right to ask the court or an administrative agency to rule that these patents are invalid and/or should not be enforced. These lawsuits and administrative proceedings are expensive and consume time and other resources, and we may not be successful in these proceedings or in stopping infringement. In addition, the inter partes review process, or IPR, or a post grant review process under the Leahy-Smith America Invents Act permits any person, whether they are accused of infringing the patent at issue or not, to challenge the validity of certain patents through a proceeding before the Patent Trial and Appeal Board, or PTAB, of the U.S. Patent and Trademark Office.

There is a risk that a court could decide that our patents or certain claims in our patents are not valid or infringed, and that we do not have the right to stop a third party from using the inventions covered by those claims. In addition, the PTAB may invalidate a patent, as happened with six of our patents covering the Xywav and Xyrem REMS, which were invalidated through the IPR process. In addition, even if we prevail in establishing that another product infringes a valid claim of one of our patents, a court may determine that we can be compensated for the infringement in damages, and refuse to issue an injunction. As a result, we may not be entitled to stop another party from infringing our patents for their full term.

Litigation involving patent matters is frequently settled between the parties, rather than continuing to a court ruling, and we have settled patent litigation with all nine Xyrem ANDA filers. The FTC has publicly stated that, in its view, certain types of agreements between branded and generic pharmaceutical companies related to the settlement of patent litigation or the manufacture, marketing and sale of generic versions of branded drugs violate the antitrust laws and has commenced investigations and brought actions against some companies that have entered into such agreements. In particular, the FTC has expressed its intention to take aggressive action to challenge settlements that include an alleged transfer of value from the brand company to the generic company (so-called "pay for delay" patent litigation settlements). The U.S. Congress and state legislatures have also identified pharmaceutical patent litigation settlements as potential impediments to generic competition and have introduced, and in states like California passed, legislation to regulate them. Third party payors have also challenged such settlements on the grounds that they increase drug prices. Because there is currently no precise legal standard with respect to the lawfulness of such settlements, many pharmaceutical companies, including us, have faced extensive litigation over whether patent litigation settlements they have entered into are reasonable and lawful. From June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with Hikma and other ANDA filers violate state and federal antitrust and consumer protection laws. For additional information on these lawsuits, see Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs in the class action complaints were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Parties to such settlement agreements in the U.S. are required by law to file the agreements with the FTC and the U.S. Department of Justice, or DOJ, for review. Accordingly, we have submitted our patent litigation settlement agreements to the FTC and the DOJ for review. We may receive formal or informal requests from the FTC regarding our ANDA litigation settlements, and there is a risk that the FTC may commence a formal investigation or action against us, which could divert the attention of management and cause us to incur significant costs, regardless of the outcome. Any claim or finding that we or our business partners have failed to comply with applicable laws and regulations could be costly to us and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

A third party may claim that we or our manufacturing or commercialization partners are using inventions covered by the third party's patent rights, or that we or such partners are infringing, misappropriating or otherwise violating other intellectual property rights, and may go to court to stop us from engaging in our normal operations and activities, including making or selling our products. Such lawsuits are costly and could affect our results of operations and divert the attention of management and development personnel. There is a risk that a court could decide that we or our partners are infringing, misappropriating or otherwise violating third party patent or other intellectual property rights, which could be very costly to us and have a material adverse effect on our business. If we are sued for patent infringement, we would need to demonstrate that our products or methods do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid or unenforceable, which we may not be able to do.

If we were found to infringe upon a patent or other intellectual property right, or if we failed to obtain or renew a license under a patent or other intellectual property right from a third party, or if a third party that we were licensing technologies from

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

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

The first NDA applicant with an orphan drug designation for a particular active moiety to treat a specific disease or condition that receives FDA approval is usually entitled to a seven-year exclusive marketing period in the U.S. for that drug, for that indication. We rely in part on this Orphan Drug Exclusivity and other regulatory exclusivities to protect Xywav, Epidiolex, Zepzelca, Defitelio, Vyxeos and, potentially, our other products and product candidates from competitors, and we expect to continue relying in part on these regulatory exclusivities in the future. The duration of our regulatory exclusivity period could be impacted by a number of factors, including FDA's later determination that our request for orphan designation was materially defective, that the manufacturer is unable to supply sufficient quantities of the drug, that the extension of the exclusivity period established by the Improving Regulatory Transparency for New Medical Therapies Act does not apply, or the possibility that we are unable to successfully obtain pediatric exclusivity. There is no assurance that we will successfully obtain orphan drug designation for other products or product candidates or other rare diseases or that a product candidate for which we receive orphan drug designation will be approved, or that we will be awarded orphan drug exclusivity upon approval as, for example, FDA may reconsider whether the eligibility criteria for such exclusivity have been met and/or maintained. Moreover, a drug product with an active moiety that is different from that in our drug candidate or, under limited circumstances, the same drug product, may be approved by FDA for the same indication during the period of marketing exclusivity. The limited circumstances include a showing that the second drug is clinically superior to the drug with marketing exclusivity through a demonstration of superior safety or efficacy or that it makes a major contribution to patient care. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for the same indication before us, approval of our product candidate would be blocked during the period of marketing exclusivity unless we could demonstrate that our product candidate is clinically superior to the approved product. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for a different orphan indication, this may negatively impact the market opportunity for our product candidate. There have been legal challenges to aspects of FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, including whether two drugs are the same drug product, and future challenges could lead to changes that affect the protections potentially afforded our products in ways that are difficult to predict. In the future, there is the potential for legislative changes or additional legal challenges to FDA's orphan drug regulations and policies, and it is uncertain how such challenges might affect our business.

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

Other Risks Related to Our Business and Industry

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

We are headquartered in Dublin, Ireland and have offices in multiple locations, including the U.S., the U.K., Italy and Canada. We may further expand our international operations into other countries in the future, either organically or by

acquisition. Conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including:

- the diverse regulatory, financial and legal requirements in the countries where we are located or do business, and any changes to those requirements;
- the impact of Brexit on trade relations between the EU and the U.K.;
- challenges inherent in efficiently managing employees and commercial partners in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and employment law and other regulations, as well as maintaining positive interactions with our unionized employees;
- costs of, and liabilities for, our international operations, products or product candidates;
- additional exposure to foreign currency exchange risk from non-U.S. operations;
- political and economic instability, such as the instability caused by Russia's invasion of Ukraine; and
- public health risks, such as the COVID-19 pandemic and potential related effects on supply chain, travel and employee health and availability.

In addition, there can be no guarantee that we will effectively manage the increasing, global complexity of our business without experiencing operating inefficiencies or control deficiencies. Our failure to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

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

Significant disruptions of our, our third party vendors' and/or business partners' information technology systems or security breaches, including in our remote work environment, could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal data), and could result in financial, legal, business and reputational harm to us. Any such event that leads to unauthorized access, use or disclosure of personal data, including personal data regarding our patients or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal data. This could disrupt our business, result in increased costs or loss of revenue, and/or result in significant legal and financial exposure. In addition, security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may further harm us. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business. In addition, failure to maintain effective internal accounting controls related to security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and subject us to regulatory scrutiny.

We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products.

FDA and Equivalent Non-U.S. Regulatory Authorities

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

We monitor adverse events resulting from the use of our products, as do the regulatory authorities, and we file periodic reports with the authorities concerning adverse events. The authorities review these events and reports, and if they determine that any events and/or reports indicate a trend or signal, they can require a change in a product label, restrict sales and marketing and/or require conduct or other actions, potentially including variation, withdrawal or suspension of the marketing authorization, any of which could result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. FDA, the competent authorities of the EU member states on behalf of the EMA, and the competent authorities of other European countries, also periodically inspect our records related to safety reporting. The EMA's Pharmacovigilance Risk Assessment Committee may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps or advise that the existing marketing authorization be varied, suspended or revoked. Failure to adequately and promptly correct the observation(s) can result in further regulatory enforcement action, which could include the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

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

FDA, the competent authorities of the EU member states and other European countries, and other governmental authorities require advertising and promotional materials to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. Regulatory authorities actively investigate allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. A determination that we have promoted an approved product for off-label uses could subject us to significant liability, including civil and administrative financial penalties and other remedies as well as criminal financial penalties, other sanctions and imprisonment. Even if we are not determined to have engaged in off-label promotion, an allegation that we have engaged in such activities could have a significant impact on our sales, business and financial condition. The U.S. government has also required companies to enter into complex corporate integrity agreements and/or non-prosecution agreements that impose significant reporting and other burdens on the affected companies. Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could subject us to a range of regulatory actions and/or civil or criminal penalties that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

Other Regulatory Authorities

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

We are subject to numerous fraud and abuse laws and regulations globally and our sales, marketing, patient support and medical activities may be subject to scrutiny under these laws and regulations. These laws are described in "Business—Government Regulation" in Part I, Item 1 of this Annual Report on Form 10-K for the year ended December 31, 2022. While we maintain a comprehensive compliance program to try to ensure that our practices and the activities of our third-party contractors and employees fall within the scope of available statutory exceptions and regulatory safe harbors whenever possible, and otherwise comply with applicable laws, regulations or guidance, regulators and enforcement agencies may disagree with our assessment or find fault with the conduct of our employees or contractors. In addition, existing regulations are subject to regulatory revision or changes in interpretation by the DOJ or OIG. For example, in November 2020, the OIG issued a Special Fraud Alert to highlight certain inherent fraud and abuse risks associated with speaker fees, honorariums and expenses paid by pharmaceutical and medical device companies to healthcare professionals participating in company-sponsored events. The Special Fraud Alert sent a clear signal that speaker programs will be subject to potentially heightened enforcement scrutiny.

Many companies have faced government investigations or lawsuits by whistleblowers who bring a *qui tam* action under the False Claims Act on behalf of themselves and the government for a variety of alleged improper marketing activities, including providing free product to customers expecting that the customers would bill federal programs for the product, providing consulting fees, grants, free travel and other benefits to physicians to induce them to prescribe the company's products, and inflating prices reported to private price publication services, which are used to set drug reimbursement rates under government healthcare programs. In addition, the government and private whistleblowers have pursued False Claims Act cases against pharmaceutical companies for causing false claims to be submitted as a result of the marketing of their products for unapproved uses or violations of the federal anti-kickback statute. If we become the subject of a government False Claims Act or other investigation or whistleblower suit, we could incur substantial legal costs (including settlement costs) and business disruption responding to such investigation or suit, regardless of the outcome.

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

Public reporting under the Physician Payment Sunshine Act, or Sunshine provisions, and other similar state laws, the requirements of which are discussed in "Business—Government Regulation" in Part I, Item 1 of this Annual Report on Form 10-K for the year ended December 31, 2022, has resulted in increased scrutiny of the financial relationships between industry, teaching hospitals, physicians and other health care providers. Such scrutiny may negatively impact our ability to engage with physicians and other health care providers on matters of importance to us. In addition, government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports. If the data reflected in our reports are found to be in violation of any of the Sunshine provisions or any other U.S. federal, state or local laws or regulations that may apply, or if we otherwise fail to comply with the Sunshine provisions or similar requirements of state or local regulators, we may be subject to significant civil, and administrative penalties, damages or fines.

We have various programs to help patients access our products, including patient assistance programs, which include co-pay coupons for certain of our products, assistance to help patients determine their insurance coverage for our products, and a free product program. Co-pay coupon programs for commercially insured patients, including our program for Xyrem, have received negative publicity related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives, and some states have imposed restrictions on manufacturer co-pay programs when therapeutic equivalents are available. In September 2014, the OIG issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal Anti-Kickback Statute and other laws if they do not take appropriate steps to exclude Medicare Part D beneficiaries from using co-pay coupons. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, including Xyrem, and therefore could have a material adverse effect on our sales, business and financial condition.

We have established programs to consider grant applications submitted by independent charitable organizations, including organizations that provide co-pay support to patients who suffer from the diseases treated by our drugs. The OIG has issued guidance for how pharmaceutical manufacturers can lawfully make donations to charitable organizations who provide

co-pay assistance to Medicare patients, provided that such organizations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. In April 2019, we finalized our civil settlement agreement with the DOJ and OIG and entered into a corporate integrity agreement requiring us to maintain our ongoing corporate compliance program and obligating us to implement or continue, as applicable, a set of defined corporate integrity activities for a period of five years from the effective date of the corporate integrity agreement. Although we have structured our programs to follow available guidance and the requirements of our corporate integrity agreement, if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, such facts could be used as the basis for an enforcement action against us by the federal government or other enforcement agencies or private litigants, or we could become liable for payment of certain stipulated penalties or could be excluded from participation in federal health care programs, which would have a material adverse effect on our sales, business and financial condition.

Our business activities outside of the U.S. are subject to the U.S. Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act of 2010, or the U.K. Bribery Act. In certain countries, the health care providers who prescribe pharmaceuticals are employed by their government and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers may be subject to regulation under the FCPA, the U.K. Bribery Act and equivalent national laws in other countries. As an example, recently the U.S. Securities and Exchange Commission and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. Violation of these laws by us or our suppliers and other third party agents for which we may be liable may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

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

We are also subject to federal, state, national and international laws and regulations governing the privacy and security of health related and other personal data we collect and maintain (e.g., Section 5 of the Federal Trade Commission Act, the California Consumer Privacy Act and the EU's General Data Protection Regulation). These laws and regulations are evolving and subject to interpretation, and may impose limitations on our activities or otherwise adversely affect our business.

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

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

We participate in the Medicaid Drug Rebate Program, the 340B program, the U.S. Department of Veterans Affairs, Federal Supply Schedule, or FSS, pricing program, and the Tricare Retail Pharmacy program, and have obligations to report the average sales price for certain of our drugs to the Medicare program. All of these programs are described in more detail under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1 of this Annual Report on Form 10-K. For calendar quarters beginning January 1, 2022, manufacturers are required to report the average sales price for drugs under the Medicare program regardless of whether they are enrolled in the Medicaid Drug Rebate Program. In addition, starting in 2023, manufacturers must pay refunds to Medicare for single source drugs or biologicals, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Statutory or regulatory changes or guidance from the Centers for Medicare & Medicaid Services, or CMS, could affect the average sales price calculations for our products and the resulting Medicare payment rate and could negatively impact our results of operations. Further, starting in January 2023, the IRA establishes a Medicare Part B inflation rebate scheme, under which, generally speaking, manufacturers will owe rebates if the

average sales price of a Part B drug increases faster than the pace of inflation. Failure to timely pay a Part B inflation rebate is subject to a civil monetary penalty.

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

Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. CMS could also decide to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS to be incomplete or incorrect. Moreover, failure to pay refunds for discarded drug under the refund program could subject us to civil monetary penalties of 125 percent of the refund amount.

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

The Health Resources and Services Administration, or HRSA, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective in January 2019. Implementation of this regulation could affect our obligations and potential liability under the 340B program in ways we cannot anticipate. We are also required to report the 340B ceiling prices for our covered outpatient drugs to HRSA, which then publishes them to 340B covered entities. Any charge by HRSA that we have violated this regulation or other requirements of the program could negatively impact our financial results. Moreover, HRSA newly established an administrative dispute resolution, or ADR, process under a final regulation effective January 2021, for claims by covered entities that a manufacturer engaged in overcharging, including claims that a manufacturer limited the ability of a covered entity to purchase the manufacturer’s drugs at the 340B ceiling price, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. Under the ADR final rule which became effective in January 2021, an ADR proceeding could potentially subject us to discovery by covered entities and other onerous procedural requirements and could result in additional liability. This ADR regulation has been challenged in separate litigation instituted by PhRMA and by pharmaceutical manufacturers in multiple federal courts. In November 2022, HRSA issued a notice of proposed rulemaking that proposes changes to the ADR process, which could negatively affect us. In addition, HRSA could decide to terminate a manufacturer’s agreement to participate in the 340B program for a violation of that agreement or other good cause shown, in which case the manufacturer’s covered outpatient drugs may no longer be eligible for federal payment under the Medicaid or Medicare Part B program.

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

Medicare Part D generally provides coverage to enrolled Medicare patients for self-administered drugs (*i.e.*, drugs that are not administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and, subject to detailed program rules and government oversight, each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time to time. The prescription drug plans negotiate pricing with manufacturers and pharmacies and may condition formulary placement on the availability of

manufacturer discounts. In addition, manufacturers, including us, are currently required to provide to CMS a 70% discount on brand name prescription drugs utilized by Medicare Part D beneficiaries when those beneficiaries are in the coverage gap phase of the Part D benefit design. Civil monetary penalties could be due if we fail to offer discounts to beneficiaries under the Medicare Part D coverage gap discount program. The IRA sunsets the coverage gap discount program starting in 2025 and replaces it with a new manufacturer discount program. Failure to pay a discount under this new program will be subject to a civil monetary penalty. In addition, starting in October 2022, the IRA establishes a Medicare Part D inflation rebate scheme, under which, generally speaking, manufacturers will owe additional rebates if the average manufacturer price of a Part D drug increases faster than the pace of inflation. Failure to timely pay a Part D inflation rebate is subject to a civil monetary penalty.

The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be capped by reference to, among other things, a specified non-federal average manufacturer price starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and/or a civil monetary penalty. This or any other legislative change could impact the market conditions for our products. We further expect continued scrutiny on government price reporting from Congress, agencies, and other bodies.

Pursuant to applicable law, knowing provision of false information in connection with price reporting under the U.S. Department of Veterans Affairs, FSS or Tricare Retail Pharmacy, or Tricare, programs can subject a manufacturer to civil monetary penalties. These program obligations also contain extensive disclosure and certification requirements. If we overcharge the government in connection with our arrangements with FSS or Tricare, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Product liability and product recalls could harm our business.

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

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

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

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

Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Ireland, the U.K. and Italy where we have manufacturing facilities. If an accident or contamination involving pollutants or hazardous substances occurs, an injured party could seek to hold us liable for any damages that result and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance with sufficient coverage on acceptable terms, or at all. Costs, damages and/or fines may result from the presence, investigation and remediation of such contamination at properties currently or formerly owned, leased or operated by us or at off-site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination.

Risks Related to Controlled Substances

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

Xyrem and Xywav and certain product candidates we are developing contain controlled substances as defined in state law and the federal CSA. Controlled substances are subject to a number of requirements and restrictions under the CSA and implementing regulations, including certain registration, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V substances. Schedule I substances by definition have a high potential for abuse, no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. which contain a controlled substance are listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Schedule I and II drugs are subject to the strictest controls under the CSA, including manufacturing and procurement quotas, heightened security requirements and additional criteria for importation. In addition, dispensing of Schedule II drugs is restricted. For example, they may not be refilled without a new prescription.

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

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

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

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

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

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

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

Our cannabinoid research and manufacturing facilities are located exclusively in the U.K. In the U.K., licenses to cultivate, possess and supply cannabis for medical research are granted by the U.K. government on an annual basis. Although our licenses have been renewed each year since 1998, they may not in the future, in which case we may not be able to carry on our research and development program in the U.K. In addition, we are required to maintain our existing commercial licenses to cultivate, produce and supply cannabis. However, if the U.K. government were not prepared to renew such licenses, we would be unable to manufacture and distribute our products on a commercial basis in the U.K. or beyond. In order to carry out research in countries other than the U.K., similar licenses to those outlined above are required to be issued by the relevant authority in each country. In addition, we will be required to obtain licenses to export from the U.K. and to import into the recipient country. To date, we have obtained necessary import and export licenses to over 30 countries. Although we have an established track record of successfully obtaining such licenses as required, this may change in the future, which could materially and adversely affect our business, results of operations, financial condition and growth prospects.

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

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

Risks Related to Our Financial Condition and Results

We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.

As of December 31, 2022, we had total indebtedness of approximately $5.8 billion. Our substantial indebtedness may:

- limit our ability to use our cash flow or borrow additional funds for working capital, capital expenditures, acquisitions, investments or other general business purposes;
- require us to use a substantial portion of our cash flow from operations to make debt service payments;
- limit our flexibility to plan for, or react to, changes in our business and industry, or our ability to take specified actions to take advantage of certain business opportunities that may be presented to us;
- expose us to the risk of increased interest rates as certain of our borrowings, including borrowings under the credit agreement, are at variable rates of interest;
- result in dilution to our existing shareholders in the event exchanges of our exchangeable senior notes are settled in our ordinary shares;
- place us at a competitive disadvantage compared to our less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay investments and capital expenditures, seek additional capital or restructure or refinance our debt. These alternative measures may not be successful and may not permit us to meet our debt service obligations. In the absence of such cash flows and resources, we could face substantial liquidity problems and might be required to dispose of material assets or operations to meet our debt service and other obligations. In addition, if we are unable to repay amounts under our secured credit agreement or senior secured notes, the credit agreement lenders and note holders could proceed against the collateral granted to them to secure that debt, which would seriously harm our business.

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

The credit agreement and the indenture governing our senior secured notes contain various covenants that, among other things, limit our ability and/or our restricted subsidiaries' ability to:

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

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

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

As a result of these restrictions, we may be:

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

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

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

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

The scope of our business and operations has grown substantially, including through a series of business combinations and acquisitions. To continue to grow our business over the longer term, we plan to commit substantial resources to product acquisition and in-licensing, product development, clinical trials of product candidates and expansion of our commercial, development, manufacturing and other operations. Acquisition opportunities that we pursue could materially affect our liquidity and capital resources and may require us to incur additional indebtedness, seek equity capital or both. Our ability to raise additional capital may be adversely impacted by worsening global economic conditions and the recent disruptions to, and

volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures or otherwise. In addition, under Irish law we must have authority from our shareholders to issue any ordinary shares, including ordinary shares that are part of our authorized but unissued share capital, and we currently have such authorization. Moreover, as a matter of Irish law, when an Irish public limited company issues ordinary shares to new shareholders for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders on a pro-rata basis, unless this statutory pre-emption obligation is dis-applied, or opted-out of, by approval of its shareholders. At our annual general meeting of shareholders in July 2022, our shareholders voted to approve our proposal to dis-apply the statutory pre-emption obligation on terms that are substantially more limited than our general pre-emption opt-out authority that had been in effect prior to August 4, 2021. This current pre-emption opt-out authority is due to expire in December 2023. If we are unable to obtain further pre-emption authorities from our shareholders in the future, or otherwise continue to be limited by the terms of new pre-emption authorities approved by our shareholders in the future, our ability to use our unissued share capital to fund in-licensing, acquisition or other business opportunities, or to otherwise raise capital, could be adversely affected. In any event, an inability to borrow or raise additional capital in a timely manner and on attractive terms could prevent us from expanding our business or taking advantage of acquisition opportunities and could otherwise have a material adverse effect on our business and growth prospects. In addition, if we use a substantial amount of our funds to acquire or in-license products or product candidates, we may not have sufficient additional funds to conduct all of our operations in the manner we would otherwise choose.

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

Our intangible assets and goodwill are significant and are subject to an impairment analysis whenever events or changes in circumstances indicate the carrying amount of the asset may not be recoverable. Additionally, goodwill and indefinite-lived assets are subject to an impairment test at least annually. Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. For example, in the third quarter of 2022, we recorded a $133.6 million asset impairment charge as a result of the decision to discontinue our nabiximols program. Our results of operations and financial position in future periods could be negatively impacted should future impairments of intangible assets or goodwill occur.

Our financial results have been and may continue to be adversely affected by foreign currency exchange rate fluctuations.

Because our financial results are reported in U.S. dollars, we are exposed to foreign currency exchange risk as the functional currency financial statements of non-U.S. subsidiaries are translated to U.S. dollars for reporting purposes. To the extent that revenue and expense transactions are not denominated in the functional currency, we are also subject to the risk of transaction losses. For example, because our product sales outside of the U.S. are primarily denominated in the euro, our sales of those products have been and may continue to be adversely affected by fluctuations in foreign currency exchange rates. Given the volatility of exchange rates, as well as our expanding operations, there is no guarantee that we will be able to effectively manage currency transaction and/or translation risks, which could adversely affect our operating results. Although we utilize foreign exchange forward contracts to manage currency risk primarily related to certain intercompany balances denominated in non-functional currencies, our efforts to manage currency risk may not be successful.

Changes in our effective tax rates could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries in North America, the U.K. and a number of other foreign jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various jurisdictions where we operate. Our effective tax rate may fluctuate depending on a number of factors, including, but not limited to, the distribution of our profits or losses between the jurisdictions where we operate and changes to or differences in interpretation of tax laws. For example, our income tax expense for the year ended December 31, 2021 included an expense of $259.9 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory tax rate in the U.K. following enactment of the U.K. Finance Act 2021.

We are subject to reviews and audits by the U.S. Internal Revenue Service, or IRS, and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure, transfer pricing arrangements and tax positions through an audit or lawsuit. Responding to or defending against challenges from taxing authorities could be expensive and consume time and other resources. If we are unsuccessful, we may be required to pay additional taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our products or seek to raise additional funds. Any of these actions could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Changes to tax laws relating to multinational corporations could adversely affect us.

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

Ireland, the U.S. and other countries in which we and our affiliates do business could change on a prospective or retroactive basis, and any such changes could adversely affect us.

One example is the OECD's initiative in the area of "base erosion and profit shifting," or BEPS. Many countries have implemented or begun to implement legislation and other guidance to align their international tax rules with the OECD's BEPS recommendations. In addition, the OECD has been working on an extension of the BEPS project, referred to as BEPS 2.0, focusing on (1) global profit allocation and (2) a global minimum tax rate. In particular, the OECD has released a framework proposal reflecting the agreement of over 140 jurisdictions, including Ireland, to implement a global minimum tax rate of 15% for large multinational corporations on a jurisdiction-by-jurisdiction basis. In December 2022, the EU agreed to implement this global minimum tax rate for EU member states by the start of 2024 and therefore Ireland will be required to introduce these new rules from the start of 2024.

Further, on August 16, 2022, President Biden signed the IRA into law, which, among other things, introduced new tax provisions, including a 15 percent corporate alternative minimum tax for certain large corporations, and a one percent excise tax on certain share repurchases by publicly traded corporations, including certain repurchases by specified domestic affiliates of publicly traded foreign corporations. These provisions will be effective for 2023. The IRS has issued limited guidance on the corporate alternative minimum tax, the excise tax and the other provisions in the IRA, and this guidance has yet to be finalized. We are currently evaluating the effect of the new law on our financial results. The U.S. and other jurisdictions in which we operate continue to consider other changes in tax laws that apply to multinationals which, if enacted, could adversely impact our tax provision, cash tax liability and effective tax rate.

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

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

Our ability to use net operating losses and carryforward tax losses to offset potential taxable income is limited under applicable law and could be subject to further limitations if we do not generate taxable income in a timely manner or if certain "ownership change" provisions of applicable law result in further limitations.

Our ability to use net operating losses, or NOLs, to offset potential future taxable income and related income taxes that would otherwise be due also depends on our ability to generate future income that is taxable in the U.S. before the NOLs expire. We cannot predict with certainty when, or whether, our U.S. affiliates will generate sufficient taxable income to use all of the NOLs. In addition, the use of NOLs to offset potential future taxable income and related income taxes that would otherwise be due is subject to limitations under the "ownership change" provisions of Sections 382 and 383 of the Code and similar state provisions. Additionally, U.K. carryforward tax losses may become subject to limitations in the event of certain changes in the ownership interest of significant shareholders where there is also a major change in the nature of conduct of a trade or business within a specified period of time. These limitations may cause us to lose or forfeit additional NOLs or carryforward tax losses before we can use these attributes. Subsequent ownership changes and changes to the U.S. federal or state or U.K. tax rules with respect to the use of NOLs and carryforward tax losses may further affect our ability to use these losses in future years.

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

In July 2017, the Financial Conduct Authority, or FCA, the authority that regulates the London Inter-bank Offered Rate, or LIBOR, announced that it intended to stop compelling banks to submit rates for the calculation of LIBOR after 2021. FCA

also announced that certain of the commonly used USD LIBOR tenors will continue to be published until June 30, 2023; however, the Federal Reserve, Federal Deposit Insurance Corporation and the Office of the Comptroller of Currency in the U.S. as well as the FCA announced that all market participants should stop using LIBOR in new contracts after December 31, 2021, subject to limited exemptions for loans and derivative products. Accordingly, new contracts entered into after December 31, 2021, must utilize an alternative reference rate. Our credit agreement is indexed to USD LIBOR. Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate, may adversely affect interest rates on our current or future indebtedness. Any transition process may involve, among other things, increased volatility or illiquidity in markets for instruments that rely on LIBOR, reductions in the value of certain instruments or the effectiveness of related transactions such as hedges, increased borrowing costs, uncertainty under applicable documentation, or difficult and costly consent processes. Furthermore, the transition away from LIBOR may result in increased expenses, may impair our ability to refinance our indebtedness or hedge our exposure to floating rate instruments, or may result in difficulties, complications or delays in connection with future financing efforts, any of which could adversely affect our financial condition and results of operations.

Risks Related to Our Ordinary Shares

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

The stock market in general, including the market for life sciences companies, has experienced extreme price and trading volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies, which has resulted in decreased market prices, notwithstanding the lack of a fundamental change in the underlying business models of those companies. Worsening economic conditions and other adverse effects or developments may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. The market price for our ordinary shares is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market, industry and other factors, including the risk factors described in this “Risk Factors” section.

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

In addition, the market price of our ordinary shares may decline if the effects of our acquisition of GW and other strategic transactions on our financial or operating results are not consistent with the expectations of financial analysts or investors. The market price of our ordinary shares could also be affected by possible sales of our ordinary shares by holders of our exchangeable senior notes who may view our exchangeable senior notes as a more attractive means of equity participation in our company and by hedging or arbitrage trading activity involving our ordinary shares by the holders of our exchangeable senior notes.

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

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

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

Our articles of association, Irish law, our credit agreement and the indentures governing our senior secured notes and exchangeable senior notes contain provisions that could delay or prevent a takeover of us by a third party.

Our articles of association could delay, defer or prevent a third party from acquiring us, despite the possible benefit to our shareholders, or otherwise adversely affect the price of our ordinary shares. In addition to our articles of association, several mandatory provisions of Irish law could prevent or delay an acquisition of us. We are also subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in our shares in certain circumstances. Furthermore, our credit agreement limits our ability to enter into certain fundamental changes, and the indentures governing our senior secured notes and exchangeable senior notes require us to offer to repurchase such notes for cash if we undergo certain fundamental changes. Additionally, in certain circumstances, the indentures governing our exchangeable senior notes require us to increase the exchange rate for a holder of our exchangeable senior notes in connection with a fundamental change. A takeover of us may trigger a default under the credit agreement or the requirement that we offer to purchase our senior secured notes or exchangeable senior notes and/or increase the exchange rate applicable to our exchangeable senior notes, which could make it more costly for a potential acquirer to engage in a business combination transaction with us.

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

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

We expect to continue to opportunistically seek access to additional capital to license or acquire additional products, product candidates or companies to expand our operations or for general corporate purposes. To the extent we raise additional capital by issuing equity securities or securities convertible into or exchangeable for ordinary shares, our shareholders may experience substantial dilution. We may sell ordinary shares, and we may sell convertible or exchangeable securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell such ordinary shares, convertible or exchangeable securities or other equity securities in subsequent transactions, existing shareholders may be materially diluted.

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

We do not currently plan to pay cash dividends in the foreseeable future. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, compliance with the terms of the credit agreement and the indenture governing our senior secured notes, and other factors our board of directors deems relevant. Accordingly, holders of our ordinary shares must rely on increases in the trading price of their shares for returns on their investment in the foreseeable future. In addition, in the event that we pay a dividend on our ordinary shares, in certain circumstances, as an Irish tax resident company, some shareholders may be subject to withholding tax, which could adversely affect the price of our ordinary shares.

General Risk Factors

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

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

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

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

Item 1B. Unresolved Staff Comments

There are no material unresolved written comments that were received from the SEC staff 180 days or more before the end of our 2022 fiscal year relating to our periodic or current reports under the Securities Exchange Act of 1934, as amended.

Item 2. Properties

Our corporate headquarters are located in Dublin, Ireland, and our U.S. operations are located in Palo Alto, California, Carlsbad, California and Philadelphia, Pennsylvania. In addition to our owned manufacturing and development facilities and our leased administrative, manufacturing and development facilities, we also have dedicated growing facilities operated by contract partners. The following table contains information about our significant properties as of December 31, 2022:

Type	Location	Approximate Square Feet	Lease / Contract Expiration Date
Administrative office	Dublin, Ireland	45,000	2036
Administrative office	Palo Alto, United States	99,000	2029
Administrative office	Carlsbad, United States	52,000	2023-2027
Administrative office	Philadelphia, United States	60,000	2029
Administrative office	Oxford, United Kingdom	26,000	2028
Administrative office	Cambridge, United Kingdom	22,000	2030-2031
Administrative office	London, United Kingdom	7,000	2028
Administrative office and laboratory	Villa Guardia (Como), Italy	34,000	2023
Manufacturing and development	Athlone, Ireland	58,000	Owned
Manufacturing and development	Villa Guardia (Como), Italy	45,000	Owned
Manufacturing and development	Southern United Kingdom	156,000	2023-2033
Growing facility	Eastern United Kingdom	1,960,000	2026
Growing facility	Northern United Kingdom	915,000	2025
Growing facility	Southern United Kingdom	165,000	2028
Growing facility under construction	Southern United Kingdom	370,000	2035

In addition, we have offices in Canada, Japan, Australia, France and elsewhere in Europe.

We believe that our existing properties are in good condition and suitable for the conduct of our business. As we continue to expand our operations, we may need to lease additional or alternative facilities.

Item 3. Legal Proceedings

The information required to be set forth under this Item 3 is incorporated by reference to Note 14, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our ordinary shares trade on The Nasdaq Global Select Market under the trading symbol "JAZZ."

Holders of Ordinary Shares

As of February 22, 2023, there were 898 holders of record of our ordinary shares. Because almost all of our ordinary shares are held by brokers, nominees and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Dividends

In 2022 and 2021, we did not declare or pay cash dividends on our common equity. Under Irish law, dividends may only be paid, and share repurchases and redemptions must generally be funded only out of, "distributable reserves." In addition, the terms of our credit agreement restrict our ability to make certain restricted payments, including dividends and other distributions by us in respect of our ordinary shares, subject to, among other exceptions, (1) a general exception for dividends and restricted payments up to $30 million in the aggregate and (2) an exception that allows for restricted payments, subject to a cap equal to the sum of (i) $100 million plus (ii) so long as our secured leverage ratio (as defined in our credit agreement) does not exceed 3:1 after giving pro forma effect to the restricted payment, a formula-based amount tied to our consolidated net income; provided that such cap applies only if our total leverage ratio (as defined in our credit agreement) exceeds 2:1 after giving pro forma effect to the restricted payment. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our consolidated financial condition, results of operations, capital requirements, compliance with the terms of our credit agreement or other future borrowing arrangements, and other factors our board of directors deems relevant.

Unregistered Sales of Equity Securities

Except as previously reported in our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the Securities and Exchange Commission, or SEC, during the year ended December 31, 2022, there were no unregistered sales of equity securities by us during the year ended December 31, 2022.

Irish Law Matters

As we are an Irish incorporated company, the following matters of Irish law are relevant to the holders of our ordinary shares.

Irish Restrictions on Import and Export of Capital

Except as indicated below, there are no restrictions on non-residents of Ireland dealing in Irish domestic securities, which includes ordinary shares of Irish companies. Dividends and redemption proceeds also continue to be freely transferable to non-resident holders of such securities. The Financial Transfers Act, 1992 gives power to the Minister for Finance of Ireland to restrict financial transfers between Ireland and other countries and persons. Financial transfers are broadly defined and include all transfers that would be movements of capital or payments within the meaning of the treaties governing the member states of the European Union. The acquisition or disposal of interests in shares issued by an Irish incorporated company and associated payments falls within this definition. In addition, dividends or payments on redemption or purchase of shares and payments on a liquidation of an Irish incorporated company would fall within this definition. At present the Financial Transfers Act, 1992 prohibits financial transfers involving Belarus, Al-Qaida, the Taliban of Afghanistan, Democratic Republic of Congo, Democratic People's Republic of Korea (North Korea), Iran, Iraq, Côte d'Ivoire, Lebanon, Liberia, Zimbabwe, Sudan, Somalia, Republic of Guinea, Republic of Guinea-Bissau, Afghanistan, Libya, Syria, Tunisia, certain known terrorists and terrorist groups, countries that harbor certain terrorist groups, Ukraine and persons responsible for human rights violations and the undermining of independence in Ukraine and the misappropriation of Ukrainian State funds without the prior permission of the Central Bank of Ireland.

Any transfer of, or payment in respect of, a share or interest in a share involving the government of any country that is currently the subject of United Nations sanctions, any person or body controlled by any of the foregoing, or by any person acting on behalf of the foregoing, may be subject to restrictions pursuant to such sanctions as implemented into Irish law.

Irish Taxes Applicable to U.S. Holders

Irish Tax on Dividends. While we have no current plans to pay dividends, dividends on our ordinary shares would generally be subject to Irish Dividend Withholding Tax at the standard rate (currently 25%), unless an exemption applies.

Irish Tax on Capital Gains. A shareholder who (i) is neither resident nor ordinarily resident in Ireland for Irish tax purposes and (ii) does not use or hold, and did not acquire, our ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency generally should not be subject to Irish tax on capital gains on a disposal of our ordinary shares.

A shareholder who is an individual and who is temporarily not resident in Ireland may, under Irish anti-avoidance legislation, still be liable for Irish tax on capital gains on any chargeable gain realized upon the disposal of our ordinary shares during the period in which such individual is a non-resident.

Capital Acquisitions Tax. Irish capital acquisitions tax, or CAT, is comprised principally of gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares are regarded as property situated in Ireland as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33% above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (i) the relationship between the donor and the donee and (ii) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same category of relationship for CAT purposes. Gifts and inheritances passing between spouses are exempt from CAT. Our shareholders should consult their own tax advisers as to any tax consequences of holding our ordinary shares, including whether CAT is creditable or deductible in computing any domestic tax liabilities.

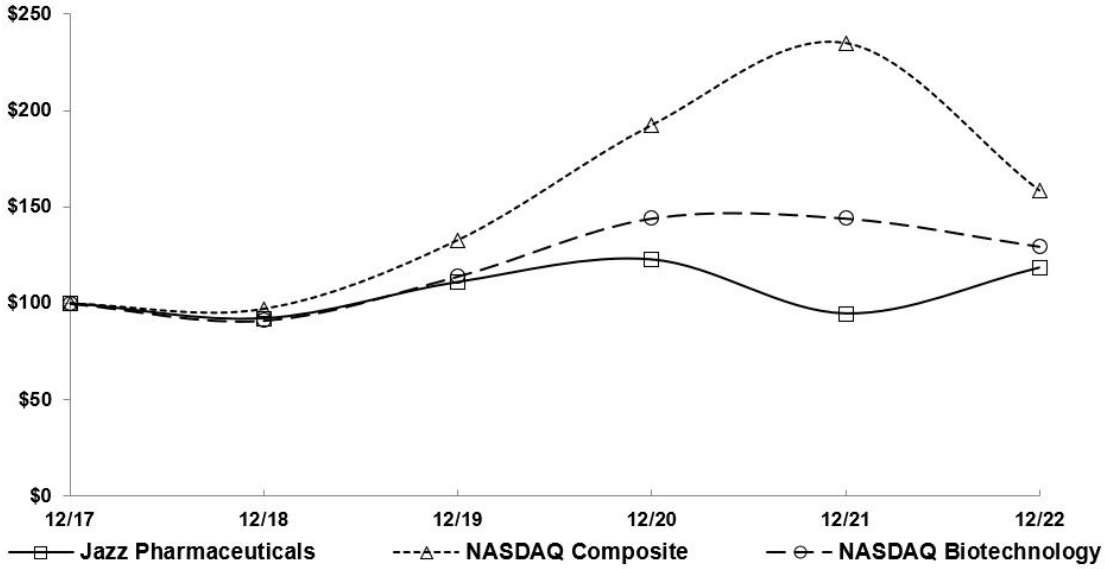
Stamp Duty. Irish stamp duty (if any) may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through Depository Trust Company, or DTC, to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. A transfer of our ordinary shares (i) by a seller who holds ordinary shares outside of DTC to any buyer or (ii) by a seller who holds the ordinary shares through DTC to a buyer who holds the acquired ordinary shares outside of DTC, may be subject to Irish stamp duty (currently at the rate of 1% of the price paid or the market value of the ordinary shares acquired, if greater). The person accountable for payment of stamp duty is the buyer or, in the case of a transfer by way of a gift or for less than market value, all parties to the transfer.

A shareholder who holds ordinary shares outside of DTC may transfer those ordinary shares into DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) as a result of the transfer and at the time of the transfer into DTC there is no sale of those book-entry interests to a third party being contemplated by the shareholder. Similarly, a shareholder who holds ordinary shares through DTC may transfer those ordinary shares out of DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the ordinary shares (and in exactly the same proportions) as a result of the transfer, and at the time of the transfer out of DTC there is no sale of those ordinary shares to a third party being contemplated by the shareholder. In order for the share registrar to be satisfied as to the application of this Irish stamp duty treatment where relevant, the shareholder must confirm to us that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) (or vice-versa) as a result of the transfer and there is no agreement being contemplated for the sale of the related book-entry interest or the ordinary shares or an interest in the ordinary shares, as the case may be, by the shareholder to a third party.

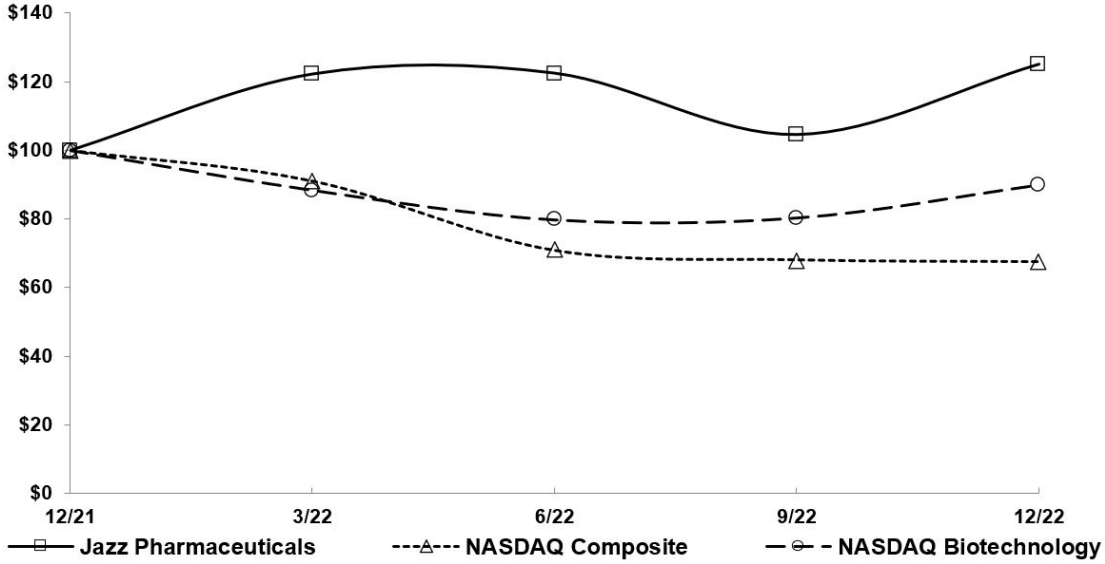
Performance Measurement Comparison (1)

The following graphs show the total shareholder return on the last day of each year of an investment of $100 in cash as if made on December 31, 2017 and on the last day of each quarter of an investment of $100 in cash as if made on December 31, 2021, respectively, in (i) our ordinary shares; (ii) the Nasdaq Composite Index; and (iii) the Nasdaq Biotechnology Index through December 31, 2022. The shareholder return shown in the graphs below are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future shareholder returns.

COMPARISON OF FIVE YEAR CUMULATIVE TOTAL RETURN (2)



COMPARISON OF ONE YEAR CUMULATIVE TOTAL RETURN (2)



(1) This section is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, or Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

(2) Information used in the graph was obtained from Research Data Group, Inc.

Issuer Purchases of Equity Securities

In November 2016, our board of directors authorized a share repurchase program and as of December 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. In 2022, we spent a total of $0.1 million to purchase 338 of our ordinary shares under the share repurchase program at a total purchase price, including commissions, of $160.70 per share. All ordinary shares repurchased were canceled. As of December 31, 2022, the remaining amount authorized under the share repurchase program was $431.2 million.

Under the 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. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The purpose of the Management Discussion and Analysis is to present information that management believes is relevant to promote a understanding of our results of operations and cash flows for the fiscal year ended December 31, 2022 and our financial condition as of December 31, 2022 and should be read in conjunction with the consolidated financial statements and notes to consolidated financial statements included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. When reviewing the discussion below, you should keep in mind the substantial risks and uncertainties that impact our business. In particular, we encourage you to review the risks and uncertainties described in "Risk Factors" in Part I, Item 1A in this Annual Report on Form 10-K. These risks and uncertainties could cause actual results to differ materially from those projected in forward-looking statements contained in this report or implied by past results and trends.

Overview

Jazz Pharmaceuticals plc is a global biopharmaceutical company 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.

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.

Our strategy to deliver sustainable growth and enhanced value is focused on:

- Strong commercial execution to drive diversified revenue growth and address unmet medical needs of our patients across our product portfolio, which focuses on neuroscience and oncology medicines;
- Expanding and advancing our pipeline to achieve a valuable product portfolio of durable, highly differentiated programs;
- Continuing to build a flexible, efficient and productive development engine for targeted therapeutic areas to identify and progress early-, mid- and late-stage assets;
- Identifying and acquiring novel product candidates and approved therapies to complement our existing pipeline and commercial portfolio;

- Investing in an efficient, scalable operating model and differentiated capabilities to enable growth; and
- Unlocking further value through indication expansion and entry into global markets.

In 2022, consistent with our strategy, we continued to focus on research and development activities within our neuroscience and oncology therapeutic areas. For a summary of our ongoing research and development activities, see "Business—Research and Development" in Part I, Item 1 of this Annual Report on Form 10-K.

Our lead marketed products, listed below, are approved in countries around the world to improve patient care.

Product	Indication(s)	Initial Approval Date	Market(s)
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 mark (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.
	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, Israel, Australia and New Zealand
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.	April 2021	EU, Great Britain, Israel
ONCOLOGY			
Zepzelca® (lurbinectedin)	Treatment of adult patients with metastatic small cell lung cancer, or SCLC, with disease progression on or after platinum-based chemotherapy.	June 2020	U.S. (licensed from PharmaMar)**
	Treatment of adults with Stage III or metastatic SCLC who have progressed on or after platinum-containing therapy.	September 2021	Canada (licensed from PharmaMar)***

Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn	A component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia, or ALL, and lymphoblastic lymphoma, or LBL, in adult and pediatric patients 1 month or older who have developed hypersensitivity to *E. coli*-derived asparaginase.	June 2021	U.S.
	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL, in adults and pediatric patients 1 year or older who have developed hypersensitivity to *E. coli*-derived asparaginase.	September 2022	Canada
Vyxeos® (daunorubicin and cytarabine) liposome for injection	Treatment of newly-diagnosed therapy-related acute myeloid leukemia, or t-AML or AML-MRC in adults and pediatric patients one year and older.	August 2017	U.S.
Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion	Treatment of adults with newly-diagnosed t-AML or AML-MRC.	August 2018	EU, Great Britain, Switzerlan Israel, Australia, South Korea
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)	Treatment of severe hepatic VOD, also known as SOS, following HSCT therapy.	October 2013	EU, Great Britain, Switzerlan Israel, Australia, South Korea Saudi Arabia
Defitelio® (defibrotide sodium)	Treatment of adult and pediatric patients with hepatic VOD, also known as SOS, with renal or pulmonary dysfunction following HSCT.	March 2016	U.S., Brazil
Defitelio® (defibrotide sodium)	Treatment of severe hepatic VOD, also known as SOS, following HSCT therapy.	July 2017	Canada
	Treatment of haptic sinusoidal obstruction syndrome (hepatic VOD)	June 2019	Japan
Defitelio® (defibrotide)			

*The Clobazam restriction limited to EU and Great Britain

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

***Conditional approval received from Health Canada

Neuroscience

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

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

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

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

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

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

We have seen strong adoption of Xywav in narcolepsy since its launch in November 2020, and increasing adoption in IH since its launch in November 2021. Exiting the fourth quarter of 2022, there were approximately 10,300 patients taking Xywav, including approximately 8,550 patients with narcolepsy and approximately 1,750 patients with IH. With respect to Xywav and Xyrem in the aggregate, the average number of active oxybate patients on therapy was approximately 18,000 in the fourth quarter of 2022.

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

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

Oncology

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

Rylaze was approved by FDA in June 2021 under the Real-Time Oncology Review, or RTOR, program, and was launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL or LBL in pediatric and adult patients one month and older who have developed hypersensitivity to *E. coli*-derived asparaginase. Rylaze is the only recombinant *erwinia* asparaginase manufactured product that maintains a clinically meaningful level of asparaginase activity throughout the entire course 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 initial approved recommended dosage of Rylaze was for an intramuscular, or IM, administration of 25 mg/m2 every 48 hours. In November 2022, FDA approved a supplemental Biologics License Application, or sBLA, for a Monday/Wednesday/Friday, or M/W/F, IM dosing schedule. In April 2022, we submitted a separate sBLA for intravenous, or IV, administration. In February 2023, we received a complete response letter from FDA requesting additional clinical data on the IV administration of Rylaze. There is no impact on the approved product labeling for Rylaze IM administration. We also completed a Marketing Authorization Application, or MAA, submission to the European Medicines Agency, or EMA, in May 2022 for M/W/F and every 48-hour dosing schedules and IV and IM administration, with potential for approval in 2023. We are also advancing the program for potential submission, approval and launch in Japan, as well as planning additional submissions in other markets.

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

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

Research and Development Progress

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

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

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

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

On June 28, 2022, we announced the nabiximols Phase 3 RELEASE MSS1 trial in multiple sclerosis related, or MS-related, spasticity did not meet the primary endpoint of change in Lower Limb Muscle Tone-6 between baseline and Day 21, as

measured by the Modified Ashworth Scale. The analysis of the MSS1 trial has been completed. We have assessed the nabiximols program's potential to support regulatory approval for MS-related spasticity in the U.S., as well as in the context of our broader pipeline opportunities, and have made the decision to discontinue the program. Sativex (nabiximols) was approved outside the U.S. for the treatment of MS-related spasticity based on a comprehensive clinical trial program, including multiple late-stage randomized, controlled trials completed in Europe. We will continue to support the availability of Sativex in the 29 markets outside the U.S. where it is approved. We remain committed to the GW Cannabinoid Platform and are working to advance multiple early-stage cannabinoid programs with the potential to address critical unmet patient needs.

In 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 JZP441, also known as DSP-0187, a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. In November 2022, the first participant was enrolled in a Phase 1 development program to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of JZP441 in sleep-deprived healthy volunteers. Under the terms of the agreement, we made an upfront payment of $50 million to Sumitomo, and Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to $1.09 billion. If approved, Sumitomo is eligible to receive a tiered, low double-digit royalty on Jazz's net sales of JZP441.

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 either the first-line trial of Zepzelca in combination with Tecentriq or the PharmaMar trial could serve to confirm clinical benefit of Zepzelca and secure full approval in the U.S.

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

For Rylaze, in November 2022, FDA approved an sBLA, with a M/W/F, IM dosing schedule. In April 2022, we submitted a separate sBLA for IV administration. In February 2023, we received a complete response letter from FDA requesting additional clinical data on the IV administration of Rylaze. There is no impact on the approved product labeling for Rylaze IM administration. We completed a MAA submission to the EMA in May 2022 for M/W/F and every 48-hour dosing schedules and IV and IM administration.

In October 2022, we announced an exclusive licensing and collaboration agreement with Zymeworks Inc., or Zymeworks, providing us the right to acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. In December 2022, we exercised the option to continue with the exclusive development and commercialization rights to zanidatamab. Zanidatamab is a bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Under the terms of the agreement, Zymeworks received an upfront payment of $50.0 million, and following the exercise of our option to continue the collaboration, a second, one-time payment of $325 million. Zymeworks is also eligible to receive regulatory and commercial milestone payments of up to $1.4 billion, for total potential payments of $1.76 billion. Pending approval, Zymeworks is eligible to receive tiered royalties between 10% and 20% on our net sales.

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

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

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

Product Candidates	Description
NEUROSCIENCE	
Phase 3	
Epidiolex	EMAS, also known as Doose syndrome (ongoing trial) LGS, TSC and DS (ongoing trial in Japan)
Phase 2b	
Suvecaltamide (JZP385)	ET (ongoing trial)
Phase 2	
Suvecaltamide (JZP385)	Parkinson's disease tremor (ongoing trial)
JZP150	PTSD (ongoing trial)
JZP541	Irritability associated with autism spectrum disorder, or ASD (planned trial)
Additional cannabinoids	ASD (ongoing trial)
Phase 1	
JZP324	Oxybate extended-release formulation (planned trial)
JZP441*	Potent, highly selective oral orexin-2 receptor agonist (ongoing trials in Japan and the U.S.)
Additional cannabinoids	Neonatal hypoxic-ischemic encephalopathy (completed study) Neuropsychiatry targets (ongoing trial)
Preclinical	
Undisclosed targets	Neuroscience Cannabinoids
ONCOLOGY	
Regulatory Review	
Rylaze	ALL/LBL FDA approval in June 2021; approval for M/W/F IM dosing schedule in November 2022; submitted an sBLA for IV administration in April 2022; received complete response letter from FDA requesting additional data on IV administration in February 2023; submitted MA to EMA in May 2022
Phase 3	
Zepzelca	First-line extensive stage SCLC in combination with Tecentriq (collaboration with Roche) (ongoing trial) Confirmatory Study (PharmaMar study) (ongoing trial)
Zanidatamab	HER2-positive gastroesophageal adenocarcinoma, or GEA (ongoing trial)
Vyxeos	AML or high-risk Myelodysplastic Syndrome, or MDS (AML18) (cooperative group studie (ongoing trial) Newly diagnosed adults with standard- and high-risk AML (AML Study Gro cooperative group study) (ongoing trial) Newly diagnosed pediatric patients with AML (Children’s Oncology Group cooperative group study) (ongoing trial)
Pivotal Phase 2	
Zanidatamab	Previously treated, advanced HER2-expressing biliary tract cancer, or BTC (ongoing trial) (pivotal trial)
Phase 2	
Zepzelca	Basket trial including urothelial cancer, PD-NECs, and HRD cancers (ongoing trial)
Vyxeos	High-risk MDS (European Myelodysplastic Syndromes) (cooperative group study) (ongoing trial) Newly diagnosed untreated patients with high-risk AML (cooperative group study) (planned trial)
Vyxeos + venetoclax	De novo or relapsed/refractory, or R/R, AML (MD Anderson collaboration study) (ongoing trial)
Zanidatamab	HER2-expressing GEA, BTC or colorectal cancer in combination with standard first-line chemotherapy (ongoing trial)
Phase 2a	
Zanidatamab	Previously treated HER2+HR+ breast cancer in combination with palbociclib

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

*Also known as DSP-0187

2022 Highlights and Recent Developments

Regulatory Submissions, Approvals and Commercial Launches

Oxybate Franchise

- In January 2022, FDA recognized seven years of ODE for Xywav in IH through August 12, 2028.

Epidiolex/Epidyolex

- In the first quarter of 2022, launched Epidyolex for LGS, DS and TSC in Ireland, for TSC in Scotland and Wales.
- In the third quarter of 2022, launched Epidyolex for TSC in Italy and Switzerland.
- In the fourth quarter of 2022, successfully completed the pricing and reimbursement process and commercial launch of Epidyolex in France. Epidyolex is launched in all five key European markets: United Kingdom, Germany, Italy, Spain and France.

Rylaze

- In January 2022, we submitted an sBLA for Rylaze with additional data in support of a M/W/F IM dosing schedule, and in November 2022, FDA approved the sBLA.
- In April 2022, we submitted an sBLA for IV administration. In February 2023, we received a complete response letter from FDA requesting additional clinical data on the IV administration of Rylaze. There is no impact on the approved product labelling for Rylaze IM administration.
- In May 2022, we completed a MAA submission to the EMA for M/W/F and every 48-hour dosing schedules and IV and IM dosing.

Research & Development

- In January 2022, we initiated a Phase 2 basket trial for Zepzelca in solid tumors.
- In August 2022, we initiated a Phase 3 trial for Epidiolex in EMAS.

- In October 2022, we enrolled the first patient in a Phase 1 trial for JZP815 in patients with advanced or metastatic solid tumors with MAPK pathway alterations, and we enrolled the first patient in a Phase 3 trial of Epidyolex in LGS, DS and TSC in Japan.
- In November 2022, we initiated a Phase 2 trial of suvecaltamide in patients with Parkinson's disease tremor, and we initiated a Phase 1 development program for JZP441 in sleep-deprived healthy volunteers.
- In December 2022, we initiated a trial for JZP341 in solid tumors.

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 maintaining a virtual presence at scientific congresses, when appropriate, designed to ensure we can continue to provide promotional and non-promotional interactions and supporting our field-based teams with virtual customer interaction tools, training and content. These initiatives mark a significant operational evolution that is directly linked to our corporate strategy and are designed to better enable our teams to work collaboratively on an aligned and shared agenda through both virtual and in-person interactions. In most geographies, our teams are increasing the frequency of in-person interactions as medical congresses and healthcare practices begin to resume in-person activities, taking into account applicable public health authority and local government guidelines which are designed to ensure community and employee safety.

Impact to Business Due to COVID-19

The prolonged nature of the pandemic continues to impact the healthcare system and is negatively impacting our business in a varied manner due to the emergence of variants with increased transmissibility, even in vaccinated people, including limited access to health care provider offices and institutions. Workforce trends starting during the pandemic results in staffing shortages in health care organizations and offices, which may impact the ability of patients to seek 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 healthcare 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.

As healthcare systems have adapted to cope with the ongoing situation, we have seen improvements, although in many countries the healthcare system continues to operate under significant strain. We are utilizing technology to continue to engage healthcare professionals and other customers virtually in cases where this is the preferred method of engagement. 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.

Other Challenges, Risks and Trends Related to Our Business

Historically, our business has been substantially dependent on Xyrem and our financial results have been significantly influenced by sales of Xyrem. Our operating plan assumes that Xywav, with 92% lower sodium compared to Xyrem, depending on the dose, absence of a sodium warning and dosing titration option, will remain the treatment of choice for patients who can benefit from oxybate treatment. 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, there is no guarantee that we can maintain oxybate sales at or near historical levels, or that oxybate sales will continue to grow.

Our ability to successfully commercialize Xywav will depend on, among other things, our ability to maintain adequate coverage and reimbursement for Xywav and acceptance of Xywav by payors, physicians and patients, including of Xywav for the treatment of IH in adults. In an effort to support strong adoption of Xywav, we are focused on providing robust patient copay and savings programs and facilitating payor coverage for Xywav. Moreover, we have increasingly experienced pressure from third party payors to agree to discounts, rebates or restrictive pricing terms, and we cannot guarantee we will be able to agree to commercially reasonable terms with PBMs, or similar organizations 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 or similar organizations and payors to ensure patient access has and will likely continue to result in higher gross to net deductions. In addition, beginning in January 2023 our oxybate products face competition from an authorized generic version of sodium oxybate pursuant to a settlement agreement we entered into with an abbreviated new drug application, or ANDA, filer, and, in the future, we expect our oxybate products to face competition from additional authorized generic versions of sodium oxybate and from generic versions of sodium oxybate pursuant to settlement agreements we entered into with multiple ANDA filers. Generic competition can decrease the prices at which Xywav and Xyrem are sold and the number of prescriptions written for

Xywav and Xyrem. Xywav and Xyrem may also face increased competition from new branded products for treatment of cataplexy and/or EDS in narcolepsy in the U.S. market.

Our financial condition, results of operations and growth prospects are also dependent on our ability to maintain or increase sales of Epidiolex/Epidyolex in the U.S. and Europe, which is subject to many risks and there is no guarantee that we will be able to continue to successfully commercialize Epidiolex/Epidyolex for its approved indications. The commercial success of Epidiolex/Epidyolex depends on the extent to which patients and physicians accept and adopt Epidiolex/Epidyolex 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/Epidyolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex/Epidyolex in the market, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex/Epidyolex. Moreover, we expect that Epidiolex will face competition from generic products in the future. For example, in November and December 2022, we received notices from ten ANDA filers that they have each filed with FDA an ANDA for a generic version of Epidiolex. 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. Thus, significant uncertainty remains regarding the commercial potential of Epidiolex/Epidyolex.

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 R&D activities. If we are not successful in the clinical development of these or other product candidates, if we are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, or if sales of an approved product do not reach the levels we expect, our anticipated revenue from our product candidates would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition to continued investment in our R&D pipeline, we intend to continue to grow our business by acquiring or in-licensing, and developing, including with collaboration partners, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. Failure to identify and acquire, in-license or develop additional products or product candidates, successfully manage the risks associated with integrating any products or product candidates into our portfolio or the risks arising from anticipated and unanticipated problems in connection with an acquisition or in-licensing, such as the GW Acquisition, could have a material adverse effect on our business, results of operations and financial condition.

The success of the GW Acquisition will depend, in part, on our ability to realize the anticipated benefits from our and GW's historical businesses. Nonetheless, Epidiolex and the other products and technologies acquired may not be successful or continue to grow at the same rate as if our companies operated independently or they may require significantly greater resources and investments than originally anticipated. For example, in the third quarter of 2022, we recorded a $133.6 million asset impairment charge as a result of the decision to discontinue the nabiximols program. As a result, the anticipated benefits of the GW Acquisition may not be realized at the expected level, within the expected timeframe or at all or may take longer to realize or cost more than expected, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our industry has been, and is expected to continue to be, subject to healthcare cost containment and drug pricing scrutiny by regulatory agencies in the U.S. and internationally. If new healthcare policies or reforms intended to curb healthcare costs are adopted or if we experience negative publicity with respect to pricing of our products or the pricing of pharmaceutical drugs generally, the prices that we charge for our products may be affected, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted. For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 into law, which, among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under the program, that could negatively affect our business and financial condition. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are currently capped at 100 percent of average manufacturer price, but, effective January 1, 2024, this cap will be lifted, which could adversely affect our rebate liability. We are also subject to increasing pricing pressure and restrictions on reimbursement imposed by payors. If we fail to obtain and maintain adequate formulary positions and institutional access for our current

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 such products may be removed from control under the Controlled Substances Act entirely. If any of our product candidates receive FDA approval, the Department of Health and Human Services, or HHS, and the U.S. Drug Enforcement Administration, or DEA, will make a scheduling determination. U.S. or foreign regulatory agencies may request additional information regarding the abuse potential of our products which may require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse potential, which could increase the cost, delay the approval and/or delay the launch of that product.

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. Government investigations 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, could cause use to incur significant monetary charges to resolve these matters and could distract us from the operation of our business and execution of our strategy. For example, in July 2022, we received a subpoena from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to Xyrem and U.S. Patent No. 8,772,306 ("Method of Administration of Gamma Hydroxybutyrate with Monocarboxylate Transporters"), product labeling changes for Xyrem, communications with FDA and the U.S. Patent and Trademark Office, pricing of Xyrem, and other related documents. For more information, see the risk factor under the heading "*We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products*" in Part I, Item 1A. We may also become subject to similar investigations by other state or federal governmental agencies. The investigation by the U.S. Attorney's Office and any additional investigations or litigation related to the subject matter of this investigation may result in damages, fines, penalties, financial charges to resolve the matter or administrative sanctions against us, negative publicity or other negative actions that could harm our reputation, reduce demand for Xyrem and/or reduce coverage of Xyrem, including by federal health care programs and state health care programs. In addition, from June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with certain generic companies violate state and federal antitrust and consumer protection laws. For additional information on these lawsuits and other legal matters, see Note 14, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs were to be successful in their claims against us, they may be entitled to injunctive relief or we may be required to pay significant monetary damages. Moreover, we are, and expect to continue to be, the subject of various claims, legal proceedings, and government investigations apart from those set forth above that have arisen in the ordinary course of business that have not yet been fully resolved and that could adversely affect our business and the execution of our strategy. Any of the foregoing risks and uncertainties could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Results of Operations

The following table presents revenues and expenses for the years ended December 31, 2022, 2021 and 2020 (in thousands except percentages):

	2022	Change	2021[1]	Change	2020
Product sales, net	$ 3,641,429	18 %	$ 3,079,001	31 %	$ 2,346,660
Royalties and contract revenues	17,945	18 %	15,237	(10)%	16,907
Cost of product sales (excluding amortization of acquired developed technologies)	540,517	23 %	440,760	196 %	148,917
Selling, general and administrative	1,416,967	(2 %)	1,451,683	70 %	854,233
Research and development	590,453	17 %	505,748	51 %	335,375
Intangible asset amortization	599,169	14 %	525,769	103 %	259,580
Impairment charge	133,648	N/A(2)	—	N/A(2)	136,139
Acquired in-process research and development	444,148	N/A(2)	—	N/A(2)	251,250
Interest expense, net	288,242	3 %	278,766	180 %	99,707
Foreign exchange loss	19,014	337 %	4,350	33 %	3,271
Income tax expense (benefit)	(158,645)	(173 %)	216,116	545 %	33,517
Equity in loss of investees	9,921	N/A(2)	714	(76)%	2,962

(1) The results of operations of the GW business have been included from the closing of the GW Acquisition on May 5, 2021.
(2) Comparison to prior period is not meaningful.

Revenues

The following table presents product sales, royalties and contract revenues, and total revenues for the years ended December 31, 2022, 2021 and 2020 (in thousands except percentages):

	2022	Change	2021[1]	Change	2020
Xyrem	$ 1,020,453	(19)%	$ 1,265,830	(27)%	$ 1,741,758
Xywav	958,425	79 %	535,297	N/A(3)	15,264
Total Oxybate	1,978,878	10 %	1,801,127	3 %	1,757,022
Epidiolex/Epidyolex	736,398	59 %	463,645	N/A(3)	—
Sativex	16,825	32 %	12,707	N/A(3)	—
Sunosi[2]	28,844	(50)%	57,914	104 %	28,333
Total Neuroscience	2,760,945	18 %	2,335,393	31 %	1,785,355
Zepzelca	269,912	9 %	246,808	173 %	90,380
Rylaze	281,659	229 %	85,629	N/A(3)	—
Vyxeos	127,980	(5)%	134,060	11 %	121,105
Defitelio/defibrotide	194,290	(2)%	197,931	1 %	195,842
Erwinaze/Erwinase	—	N/A(3)	69,382	(53)%	147,136
Total Oncology	873,841	19 %	733,810	32 %	554,463
Other	6,643	(32)%	9,798	43 %	6,842
Product sales, net	3,641,429	18 %	3,079,001	31 %	2,346,660
Royalties and contract revenues	17,945	18 %	15,237	(10)%	16,907
Total revenues	$ 3,659,374	18 %	$ 3,094,238	31 %	$ 2,363,567

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

Product Sales, Net

Total oxybate product sales increased by $177.8 million in 2022 compared to 2021. Total oxybate revenue bottle volume increased by 6% in 2022 compared to 2021. Average active oxybate patients on therapy were approximately 18,000 in the fourth quarter of 2022, an increase of approximately 11% compared to the same period in 2021. Xywav product sales increased in 2022 compared to 2021 primarily due to higher sales volume, with bottle volume increasing 76%. Xywav product sales were positively impacted by the launch of Xywav for IH and continued strong adoption in narcolepsy driven by educational initiatives around the benefit of lowering sodium intake. Xyrem product sales decreased in 2022 compared to 2021 primarily due to a decrease in sales volume, reflecting the continued adoption of Xywav by existing Xyrem patients, partially offset by a higher average selling price. Price increases were instituted in January 2021 and January 2022. Total oxybate product sales increased by $44.1 million in 2021 compared to 2020 primarily due to a higher average net selling price, partially offset by a decrease in sales volume. Total oxybate revenue bottle volume decreased by 1% in 2021 compared to 2020 reflecting our continued investment in patient access programs during the launch of Xywav. Average active oxybate patients on therapy were approximately 16,200 in the fourth quarter of 2021, an increase of approximately 6% compared to the same period in 2020. Xywav product sales were $535.3 million in 2021 compared to $15.3 million in 2020, following its U.S. launch in November 2020. Xyrem product sales decreased in 2021 compared to 2020 primarily due to a decrease in sales volume driven by the strong adoption of Xywav by existing Xyrem patients, partially offset by a higher average selling price. Price increases were instituted in January 2020 and January 2021. In 2020 new patient diagnoses and enrollments were negatively impacted by COVID-19. Epidiolex/Epidyolex product sales increased by 59% in 2022 compared to 2021, which included product sales from the closing of the GW Acquisition on May 5, 2021 to December 31, 2021. On a pro forma basis, Epidiolex/Epidyolex product sales increased by 12% in 2022 compared to 2021, primarily due to an increase in sales volume of 16% and, to a lesser extent, a higher average net selling price, partially offset by higher gross to net deductions. Price increases were instituted in January 2021 and January 2022. Epidiolex/Epidyolex product sales in 2021, from the closing of the GW Acquisition on May 5, 2021 to December 31, 2021 were $463.6 million. On a pro forma basis, Epidiolex/Epidyolex product sales increased by 29% in 2021 compared to 2020, primarily due to an increase in sales volume. Sunosi product sales decreased in 2022 as compared to 2021 as we completed the U.S. divestment of Sunosi in May 2022. Sunosi product sales increased in 2021 compared to 2020 primarily due to higher sales volume partially offset by higher gross to net deductions.

Zepzelca product sales increased by 9% in 2022 compared to 2021 primarily due to a higher average net selling price and higher sales volume. Price increases were instituted in July 2021, January 2022 and July 2022. Zepzelca product sales increased in 2021 compared to 2020 primarily due to higher sales volume following launch in the U.S. in July 2020. Rylaze product sales increased in 2022 compared to 2021 primarily due to higher sales volume following its launch in the U.S. in July 2021. The increase in volumes reflects the significant unmet patient need for a high-quality, reliable supply of Erwinia asparaginase for patients with ALL. Vyxeos product sales decreased by 5% in 2022 compared to 2021 primarily due to higher gross to net deductions, driven by a reduction in the returns provision in 2021 due to lower than estimated actual returns, and the negative impact of foreign exchange rates, partially offset by higher sales volume. Vyxeos product sales increased by 11% in 2021 compared to 2020 primarily due to lower gross to net deductions driven by a reduction in the returns provision. Defitelio/defibrotide product sales in 2022 decreased by 2% compared to 2021 as the impact of a higher average net selling price and increased sales volume were offset by the negative impact of foreign exchange rates. Defitelio/defibrotide product sales increased by 1% in 2021 compared to 2020, primarily due to the positive impact of foreign exchange rates, partially offset by lower average net selling price due to regional mix. Price increases were instituted in July 2021, January 2022 and July 2022. We distributed our final Erwinaze inventory in June 2021 following expiration of our license and supply agreement.

We expect product sales, net will increase in 2023 over 2022, primarily due to an increase in sales of Xywav due to continuing growth in IH and as patients continue to transition to Xywav from Xyrem, expected growth in Epidiolex and our oncology products, primarily Rylaze, offset by a decrease in sales of Xyrem as patients transition to Xywav and the impact of the entry of the authorized generic versions of Xyrem.

Royalties and Contract Revenues

Royalties and contract revenues increased in 2022 compared to 2021 primarily due to higher royalty revenues. Royalties and contract revenues decreased in 2021 compared to 2020 primarily due to lower contract revenues from out-licensing agreements. We expect royalties and contract revenues to increase in 2023 compared to 2022 primarily due to increased royalty revenues arising from the launch of an authorized generic version of Xyrem.

Cost of Product Sales

Cost of product sales increased in 2022 compared to 2021, primarily due to an increase in the acquisition accounting inventory fair value step-up expense, or fair value step-up expense, of $50.3 million, driven by the inclusion of a full year expense in 2022 and an expense for past royalties payable under a settlement agreement reached with Otsuka Pharmaceutical Co., Ltd, or Otsuka. Cost of product sales increased in 2021 compared to 2020, primarily due to the cost of product sales acquired in the acquisition of GW, including fair value step-up expense. Gross margin as a percentage of net product sales was

85.2%, 85.7% and 93.7% in 2022, 2021 and 2020, respectively. The decrease in our gross margin percentage in 2022 compared to 2021 was primarily due to an increase in the fair value step-up expense and the Otsuka royalty expense and the decrease in our gross margin percentage in 2021 compared to 2020 was primarily due to the impact of the fair value step-up expense. We expect our cost of product sales to decrease in 2023 compared to 2022 primarily driven by a reduction in the fair value step-up expense.

Selling, General and Administrative Expenses

Selling, general and administrative expenses decreased in 2022 compared to 2021 primarily due to lower GW related integration expenses of $207.9 million and lower Sunosi related costs, partially offset by restructuring costs of $22.1 million and costs related to program terminations of $42.6 million, the loss on disposal of Sunosi of $40.8 million, an increase in compensation related expenses driven by the inclusion of GW related headcount costs for the full period in 2022, and increased investment in sales and marketing spend relating to Xywav and Epidiolex. Selling, general and administrative expenses increased in 2021 compared to 2020 primarily due to transaction and integration-related expenses of $229.0 million in 2021, an increase in compensation-related expenses driven by higher headcount as a result of the GW Acquisition and increased investment in sales and marketing spend primarily related to Sunosi, Epidiolex and Xywav. We expect selling, general and administrative expenses in 2023 to decrease compared to 2022, primarily due to the removal of costs relating to the Sunosi business following its disposal, together with synergies realized following the GW Acquisition, continued disciplined approach in our capital allocation and our focus on operational efficiencies.

Research and Development Expenses

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

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

	Year Ended December 31,		
	2022	2021	2020
Clinical studies and outside services	$ 270,008	$ 234,462	$ 169,904
Personnel expenses	223,603	193,716	127,794
Restructuring expenses	10,284	—	—
Milestone expense	6,250	15,000	1,000
Other	80,308	62,570	36,677
Total	$ 590,453	$ 505,748	$ 335,375

Research and development expenses increased by $84.7 million in 2022 compared to 2021. Clinical studies and outside services costs increased in 2022 compared to 2021 primarily due to the addition of costs related to clinical programs for zanidatamab, JZP898 and JZP441, and increased costs for JZP150, offset by a reduction in costs related to JZP458 (Rylaze). Personnel expenses increased by $29.9 million in 2022 compared to 2021, primarily due to increased compensation related expenses driven by the inclusion of GW related headcount costs for the full period in 2022. We incurred restructuring costs of $10.3 million in 2022. Milestone expenses of $6.3 million in 2022 primarily related to a milestone expense of $5.0 million made under our asset purchase and collaboration agreements with Redx. Research and development expenses increased by $170.4 million in 2021 compared to 2020. Clinical studies and outside services costs increased in 2021 compared to 2020 primarily due to the addition of costs related to clinical programs for nabiximols, Epidiolex and cannabinoids and an increase in costs related to suvecaltamide (JZP385) and JZP150. Personnel expenses increased by $65.9 million in 2021 compared to 2020, primarily due to increased headcount primarily driven by the GW Acquisition. Milestone expense of $15.0 million in 2021 primarily related to milestones expense of $13.0 million made under our asset purchase and collaboration agreements with Redx.

For 2023, we expect that our research and development expenses will continue to increase from previous levels as we prepare for anticipated data read-outs from clinical trials, initiate and undertake additional clinical trials and related development work primarily relating to zanidatamab and JZP441 and additional spend on new product candidates acquired.

Intangible Asset Amortization

Intangible asset amortization increased by $73.4 million in 2022 compared to 2021 primarily due to the inclusion of the amortization for the full period in 2022, of the intangible assets arising from the acquisition of GW, primarily related to Epidiolex, offset by a decrease relating to the Erwinaze intangible asset that was fully amortized in June 2021. Intangible asset amortization increased in 2021 compared to 2020 primarily due to the commencement of amortization on the intangible assets arising from the GW Acquisition in May 2021, primarily related to Epidiolex.

Impairment Charges

In 2022, we recorded an acquired in-process research and development, or IPR&D, asset impairment charge of $133.6 million as a result of the decision to discontinue our nabiximols program.

In 2020, we recorded an acquired IPR&D asset impairment charge of $136.1 million following the decision to stop enrollment in our Phase 3 clinical study of defibrotide for the prevention of VOD due to a determination that the study was highly unlikely to reach one of its primary endpoints.

Acquired In-Process Research and Development

Acquired IPR&D expense in 2022 primarily related to the upfront payments made in connection with our licensing and collaboration agreements with Zymeworks and Werewolf of $375.0 million and $15.0 million, respectively, and our licensing agreement with Sumitomo of $50.0 million. In 2020, acquired IPR&D expense primarily related to an upfront payment of $200.0 million to PharmaMar in connection with our license agreement for Zepzelca.

Interest Expense, Net

Interest expense, net increased by $9.5 million in 2022 compared to 2021, primarily due to the inclusion of interest expense for the full period in 2022, on the $1.5 billion in aggregate principal amount of 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, which were used, in part, to finance the cash portion of the GW Acquisition, and higher interest rates on the Dollar Term Loan in 2022, offset by a decrease in non-cash interest expense relating to the 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, following the adoption of ASU No. 2020-06, “Debt—Debt with Conversion and Other Options(Subtopic 470-20) and Derivatives and Hedging— Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity”, or ASU 2020-06, on January 1, 2022. Interest expense, net increased by $179.1 million in 2021 compared to 2020, primarily due to increased interest expense incurred on the Dollar Term Loan, the seven-year $625.0 million term loan B facility, or the Euro Term Loan and the Secured Notes and higher non-cash interest expense following the issuance of our 2.00% exchangeable senior notes due 2026, or the 2026 Notes, in June 2020. We expect interest expense, net to increase in 2023 compared to 2022 primarily due to the cash interest expense on the Dollar Term Loan as the interest rate is expected to rise in line with anticipated increases in the US Federal Reserve base rate.

Foreign Exchange Loss

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

Income Tax Expense (Benefit)

Our income tax benefit was $158.6 million in 2022 and our income tax expense was $216.1 million and $33.5 million in 2021 and 2020, respectively, relating to tax arising on income or losses in Ireland, the U.K., the U.S. and certain other foreign jurisdictions, offset by deductions on subsidiary equity, originating tax credits, and, in 2022 and 2021, foreign derived intangible income, or FDII, benefits. Our income tax benefit in 2022 increased primarily due to payments for acquired IPR&D made in the year and the impact of the impairment of our acquired IPR&D asset as a result of the decision to discontinue our nabiximols program. Our income tax expense in 2021 included an expense of $259.9 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory tax rate in the U.K. following enactment of the U.K. Finance Act 2021. Our income tax expense in 2020 included the impact of the disallowance of certain interest deductions and a provision for a proposed settlement reached with the French taxing authorities.

Equity in Loss of Investees

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

Liquidity and Capital Resources

As of December 31, 2022, we had cash and cash equivalents of $881.5 million, borrowing availability under our revolving credit facility of $500.0 million and a long-term debt principal balance of $5.8 billion. Our long-term debt included $2.8 billion aggregate principal amount Dollar Term Loan, $1.5 billion principal amount of the Secured Notes, $575.0 million principal amount of the 2024 Notes, and $1.0 billion principal amount of the 2026 Notes. During 2022, 2021 and 2020, we generated cash flows from operations of $1,272.0 million, $778.5 million and $899.6 million, respectively, and we expect to continue to generate positive cash flow from operations which will enable us to operate our business and de-lever our balance sheet over time.

In 2022, we made voluntary repayments of $300.0 million of the Dollar Term Loan principal outstanding and €208.3 million, or $251.0 million, of the Euro Term Loan, which represented the remaining principal amount. We have made voluntary repayments of €625.0 million, or $753.0 million, relating to Euro Term Loan and voluntary and mandatory repayments of $300.0 million and $46.5 million, respectively, relating to the Dollar Term Loan since the closing of the acquisition of GW in May 2021.

We have a significant amount of debt outstanding on a consolidated basis. For a more detailed description of our debt arrangements, including information relating to our scheduled maturities with respect to our long-term debt see Note 12, Debt, of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. This substantial level of debt could have important consequences to our business, including, but not limited to the factors set forth in in Part I, Item 1A “Risk Factors” of this Annual Report on Form 10-K 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 balance, cash we expect to generate from operations and funds available under our revolving credit facility will be sufficient to fund our operations and to meet our existing obligations for the foreseeable future. The adequacy of our cash resources depends on many assumptions, including primarily our assumptions with respect to product sales and expenses, as well as the other factors set forth in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K under the headings “Risks Related to 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, our ability to raise additional capital may be adversely impacted by worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures or otherwise. Accordingly, we could experience an inability to access additional capital or our liquidity could otherwise be impacted, which could in the future negatively affect our capacity for certain corporate development transactions or our ability to make other important, opportunistic investments. In addition, under Irish law we must have authority from our shareholders to issue any ordinary shares, including ordinary shares that are part of our authorized but unissued share capital, and we currently have such authorization. Moreover, as a matter of Irish law, when an Irish public limited company issues ordinary shares to new shareholders for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders on a pro rata basis, unless this statutory pre-emption obligation is dis-applied, or opted-out of, by approval of its shareholders. At our annual general meeting of shareholders in July 2022, our shareholders voted to approve our proposal to dis-apply the statutory pre-emption obligation on terms that are substantially more limited than our general pre-emption opt-out authority that had been in effect prior to August 4, 2021. This current pre-emption opt-out authority is due to expire in December 2023. If we are unable to obtain further pre-emption authorities from our shareholders in the future, or otherwise continue to be limited by the terms of new pre-emption authorities approved by our shareholders in the future, our ability to use our unissued share capital to fund in-licensing, acquisition or other business opportunities, or to otherwise raise capital could be adversely affected. In any event, an inability to borrow or raise additional capital in a timely manner and on attractive terms could prevent us from expanding our business or taking advantage of acquisition opportunities, and could otherwise have a material adverse effect on our business and growth prospects. In addition, if we use a substantial amount of our funds to acquire or in-license products or product candidates, we may not have sufficient additional funds to conduct all of our operations in the manner we would otherwise choose. 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.

In November 2016, our board of directors authorized a share repurchase program and as of December 31, 2022 had authorized the repurchase 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. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the amended credit agreement, corporate and regulatory requirements and market conditions. The share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2022, we spent a total of $0.1 million to purchase 338 of our ordinary shares at a total purchase price, including brokerage commissions, of $160.70 per share. In 2021, we did not repurchase any of our ordinary shares under the share repurchase program. As of December 31, 2022, the remaining amount authorized under the share repurchase program was $431.2 million.

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

	Year Ended December 31,		
	2022	2021	2020
Net cash provided by operating activities	$ 1,271,977	$ 778,507	$ 899,648
Net cash used in investing activities	(446,230)	(5,212,143)	(1,007,670)
Net cash (used in) provided by financing activities	(529,491)	3,970,522	528,073
Effect of exchange rates on cash and cash equivalents	(6,222)	(3,207)	374
Net increase (decrease) in cash and cash equivalents	$ 290,034	$ (466,321)	$ 420,425

Operating activities

Net cash provided by operating activities increased by $493.5 million in 2022 compared to 2021, primarily due to cash received from increased sales of our products and decreased transaction and integration-related costs associated with the GW Acquisition.

Net cash provided by operating activities decreased by $121.1 million in 2021 compared to 2020, primarily due to the payment of transaction and integration-related costs related to the GW Acquisition.

Investing activities

Net cash used in investing activities decreased by $4,765.9 million in 2022 compared to 2021, primarily due to the following:

- $6,234.8 million outflow in 2021 related to the net cash paid for the GW Acquisition; and
- $53.0 million upfront payment from Axsome in 2022 relating to the Sunosi U.S. disposition; offset by
- $1,069.2 million decrease in net proceeds from maturity of investments, primarily time deposits; and
- $444.1 million in upfront payments in 2022 for acquired IPR&D primarily driven by the $375.0 million, $50.0 million and $15.0 million payments to Zymeworks, Sumitomo and Werewolf, respectively.

Net cash used in investing activities increased by $4,204.5 million in 2021 compared to 2020, primarily due to the following:

- $6,234.8 million outflow in 2021 related to the net cash paid for the GW Acquisition; partially offset by
- $1,710.9 million increase in net proceeds from maturity of investments, primarily time deposits;
- $251.3 million in upfront payments in 2020 for acquired IPR&D primarily driven by the $200.0 million and $35.0 million payments to PharmaMar and SpringWorks Therapeutics, Inc., or SpringWorks, respectively; and
- $95.1 million decrease in acquisition of intangible assets primarily related to our $100.0 million milestone payment to PharmaMar on FDA approval of Zepzelca in 2020.

Financing activities

Net cash (used in) provided by financing activities decreased by $4,500.0 million in 2022 compared to 2021, primarily due to:

- Net proceeds from issuance of borrowings under the Credit Agreement of $3,719.9 million and the Secured Notes of $1,471.5 million in 2021 that were used to fund, in part, the cash consideration payable in connection with the GW Acquisition; offset by
- Repayments of long-term debt of $582.0 million in 2022, compared to $1,320.6 million in 2021.

Net cash provided by financing activities increased by $3,442.4 million in 2021 compared to 2020, primarily due to:

- An increase of $3,279.1 million in debt financing due to:

- Net proceeds from issuance of borrowings under the Credit Agreement of $3,719.9 million and the Secured Notes of $1,471.5 million, partially offset by $1,101.8 million in repayment of long-term debt and payments for repurchase of our 1.875% exchangeable senior notes due 2021, or the 2021 Notes, of $218.8 million in the year ended December 31, 2021; compared to
- Net proceeds from issuance of the 2026 Notes of $981.4 million, partially offset by payments for partial repurchase of the 2021 Notes of $356.2 million and repayment of long-term debt of $33.4 million in the year ended December 31, 2020; and

- The impact of share repurchases of $146.5 million in the year ended December 31, 2020.

Credit Agreement

On May 5, 2021, the Company, Jazz Financing Lux S.à.r.l., or Jazz Lux, and certain of our other subsidiaries, as borrowers, (collectively with the Company and Jazz Lux, the "Borrowers"), entered into the Credit Agreement, that provides for (i) the Dollar Term Loan which was drawn by Jazz Lux on the Closing Date in U.S. dollars (ii) the Euro Term Loan which was drawn by Jazz Lux on the Closing Date in Euros, and, together with the Dollar Term Loan, collectively known as the Term Loan and (iii) the Revolving Credit Facility, which is available to be drawn by any Borrower in U.S. dollars.

We used the proceeds from the Term Loan (i) to repay in full $575.9 million under that certain credit agreement, dated as of June 18, 2015 (as amended) among the Company, and certain of our other subsidiaries as borrowers, the lenders party thereto and Bank of America, N.A., as administrative agent and collateral agent, or the Existing Credit Agreement, (ii) to fund, in part, the cash consideration payable in connection with the GW Acquisition and (iii) to pay related fees and expenses. Upon the repayment in full of loans under the Existing Credit Agreement, it was terminated and all guarantees and liens thereunder were released.

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. The Euro Term Loan bore interest at the Euro Inter-Bank Offered Rate, or EURIBOR, plus an applicable margin. The applicable margin for the Euro Term Loan was 3.50%. During the term of the Euro Term Loan, the interest rate and effective interest rate were 4.43% and 4.93%, respectively.

Loans under the Dollar Term Loan and Revolving Credit Facility bear interest at a rate equal to, at the applicable Borrower's option, either (a) London Inter-Bank Offered Rate, or LIBOR or (b) the prime lending rate. The applicable margin for the Dollar Term Loan is 3.50% (in the case of LIBOR) and 2.50% (in the case of borrowings at the prime lending rate). The applicable margin for the Revolving Credit Facility ranges from 3.25% to 2.75% (in the case of LIBOR borrowings) and 2.25% to 1.75% (in the case of borrowings at the prime lending rate), depending on our first lien secured net leverage ratio level. The Dollar Term Loan is subject to a LIBOR floor of 0.50% and loans under the Revolving Credit Facility are not subject to a EURIBOR or LIBOR (as applicable) floor. The Revolving Credit Facility has a commitment fee payable on the undrawn amount ranging from 0.50% to 0.40% per annum based upon our first lien secured net leverage ratio.

As of December 31, 2022, the interest rate and effective interest rate on the Dollar Term Loan were 7.88% and 4.56%, respectively. As of December 31, 2022, we had an undrawn Revolving Credit Facility totaling $500.0 million.

The Borrowers' obligations under the Credit Agreement and any hedging or cash management obligations entered into with any lender thereunder are guaranteed by the Company, the other borrowers, and each of the Company's other existing or subsequently acquired or organized direct and indirect subsidiaries (subject to certain exceptions), or the Guarantors. We refer to the Borrowers and the Guarantors collectively as the "Loan Parties".

The Loan Parties' obligations under the Credit Agreement are secured, subject to customary permitted liens and other exceptions, by a security interest in (a) all tangible and intangible assets of the Loan Parties, except for certain excluded assets, and (b) all of the equity interests of the subsidiaries of the Loan Parties held by the Loan Parties.

We may make voluntary prepayments at any time without payment of a premium or penalty, subject to certain exceptions, and are required to make certain mandatory prepayments of outstanding indebtedness under the Credit Agreement in certain circumstances.

Principal repayments of the Dollar Term Loan, which are due quarterly, began in September 2021 and are equal to 1.0% per annum of the original principal amount of $3.1 billion with any remaining balance payable on the maturity date. In September 2022, we made a voluntary repayment on the Dollar Term Loan totaling $300.0 million.

The Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants applicable to the Company and its restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. The Credit Agreement contains financial covenants that require the Company and its restricted subsidiaries to (a) not exceed a maximum

first lien secured net leverage ratio and (b) not fall below a minimum interest coverage ratio, provided that such covenants apply only to the Revolving Credit Facility and are applicable only if amounts are drawn (or non-cash collateralized letters of credit in excess of $50 million are outstanding) under the Revolving Credit Facility. The Credit Agreement also contains customary events of default relating to, among other things, failure to make payments, breach of covenants and breach of representations.

2029 Senior Secured Notes

2029 Notes. On April 29, 2021, Jazz Securities Designated Activity Company, or Jazz Securities, our direct wholly owned subsidiary, closed the offering of the Secured Notes in a private placement. We used the proceeds from the Secured Notes to fund, in part, the cash consideration payable in connection with the GW Acquisition.

Interest on the Secured Notes is payable semi-annually in arrears on January 15 and July 15 of each year, beginning on January 15, 2022, at a rate of 4.375% per year. The Secured Notes mature on January 15, 2029.

The Secured Notes are jointly and severally guaranteed by us and each of our restricted subsidiaries, other than Jazz Securities, that is a borrower, or a guarantor, under the Credit Agreement. The Secured Notes and related guarantees are secured by a first priority lien (subject to permitted liens and certain other exceptions), equally and ratably with the Credit Agreement, on the collateral securing the Credit Agreement.

Except as described below, the Secured Notes may not be optionally redeemed before July 15, 2024. Thereafter, some or all of the Secured Notes, may be redeemed at any time and from time to time at a specified redemption prices, plus accrued and unpaid interest, if any, to, but excluding, to the redemption date. Jazz Securities may redeem all but not part of the Secured Notes at its option at any time in connection with certain tax-related events and may redeem some or all of the Secured Notes at any time and from time to time prior to July 15, 2024 at a price equal to 100% of the principal amount of the Secured Notes to be redeemed plus a “make whole” premium, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. In addition, Jazz Securities may redeem up to 40% of the aggregate principal amount of the Secured Notes at any time and from time to time prior to July 15, 2024, with the net proceeds of certain equity offerings at a price of 104.375% of the principal amount of such Secured Notes, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. In addition, during each of the three consecutive twelve-month periods commencing on the issue date of the Secured Notes, Jazz Securities may redeem up to 10% of the original aggregate initial principal amount of the Secured Notes at a redemption price of 103% of the principal amount of such Secured Notes, plus accrued and unpaid interest, if any, to, but excluding, the redemption date.

If we undergo a change of control, Jazz Securities will be required to make an offer to purchase all of the Secured Notes at a purchase price in cash equal to 101% of the principal amount thereof, plus accrued and unpaid interest, if any, to, but excluding, the date of repurchase, subject to certain exceptions.

The indenture governing the Secured Notes contains customary affirmative covenants and negative covenants applicable to us and our restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. If Jazz Securities or our restricted subsidiaries engage in certain asset sales, Jazz Securities will be required under certain circumstances to make an offer to purchase the Secured Notes at 100% of the principal amount, plus accrued and unpaid interest, if any, to, but excluding, the repurchase date.

As of December 31, 2022, the interest rate and effective interest rate on the Secured Notes were 4.375% and 4.64%, respectively.

Exchangeable Senior Notes

2026 Notes. In the second quarter of 2020, Jazz Investments I Limited, our wholly owned subsidiary, completed a private placement of $1.0 billion principal amount of the 2026 Notes. We used a portion of the net proceeds from this offering to repurchase for cash $332.9 million aggregate principal amount of the 1.875% exchangeable senior notes due 2021, or the 2021 Notes, through privately-negotiated transactions concurrently with the offering 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.

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

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

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

Contractual Obligations

Our primary contractual obligations relate to our outstanding indebtedness, as described above. We also have obligations under lease agreements and third-party manufacturing agreements. For information relating to our scheduled maturities with respect to our long-term debt and our lease liabilities see Note 12 Debt and Note 13 Leases, respectively, and for information relating to our noncancelable purchase commitments due within one year see Note 14 Commitments and Contingencies, included in the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Our long-term noncancelable purchase commitments were $36.1 million at December 31, 2022, primarily related to agreements with third party manufactures.

We also have potential future milestone payments or royalty obligations to third parties under asset purchase, product development, license and other agreements as the timing and likelihood of such milestone payments are not known, and, in the case of royalty obligations, as the amount of such obligations are not estimable. Our contingent obligations to third parties, in the form of development, regulatory and sales-based milestone payments, as of December 31, 2022 included $1,387.5 million under our license and collaboration agreement with Zymeworks, $1,260.0 million under our global license and collaboration agreement with Werewolf, $1,090.0 million under our license agreement with Sumitomo, $1,025.0 million with our strategic collaboration agreement with Codiak, $681.0 million under our amended license agreement with PharmaMar, $595.0 million under asset purchase and collaboration agreements with Redx, $375.0 million under the asset purchase and exclusive license agreement with SpringWorks, $260.0 million in connection with our acquisition of Cavion, $155.5 million under our license agreement with Ligand and $345.4 million related to other agreements.

Critical Accounting Policies and Significant Estimates

A critical accounting policy is one that is both important to the portrayal of our financial condition and results of operations and requires management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. While our significant accounting policies are described in more detail in Note 2, Summary of Significant Accounting Policies, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K, we believe the following accounting estimates and policies to be critical.

Revenue Recognition

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

Product Sales, Net

Product sales revenue is recognized when control has transferred to the customer, which occurs at a point in time, which is typically on delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer removes product from our consigned inventory location for shipment directly to a patient.

Items Deducted from Gross Product Sales. Revenues from sales of products are recorded net of government rebates and rebates under managed care plans and commercial payor contracts, estimated allowances for sales returns, government chargebacks, prompt payment discounts, patient coupon programs, and specialty distributor and wholesaler fees. Calculating certain of these items involves estimates and judgments based on sales or invoice data, contractual terms, historical utilization rates, new information regarding changes in applicable regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates and channel inventory data. We review the adequacy of our provisions for sales deductions on a quarterly basis. Amounts accrued for sales deductions are adjusted when trends or significant events indicate that adjustment is appropriate and to reflect actual experience. The most significant items deducted from gross product sales where we exercise judgment are rebates, sales returns and chargebacks.

The following table presents the activity and ending balances for our sales-related accruals and allowances (in thousands):

	Rebates Payable	Sales Returns Reserve	Chargebacks	Discounts and Distributor Fees	Total
Balance at December 31, 2019	$ 82,853	$ 3,462	$ 1,133	$ 14,120	$ 101,568
Provision, net	288,052	18,448	45,550	69,332	421,382
Payments/credits	(260,020)	(3,542)	(41,390)	(66,659)	(371,611)
Balance at December 31, 2020	110,885	18,368	5,293	16,793	151,339
GW Acquisition	53,872	5	1,322	3,260	58,459
Provision, net	440,776	(1,765)	91,425	125,859	656,295
Payments/credits	(409,818)	(794)	(86,651)	(124,104)	(621,367)
Balance at December 31, 2021	195,715	15,814	11,389	21,808	244,726
Provision, net	630,295	13,222	135,854	186,609	965,980
Payments/credits	(528,209)	(2,872)	(132,622)	(190,062)	(853,765)
Balance at December 31, 2022	$ 297,801	$ 26,164	$ 14,621	$ 18,355	$ 356,941

Total items deducted from gross product sales were $966.0 million, $656.3 million and $421.4 million, or 21.0%, 17.6% and 15.2% as a percentage of gross product sales, in 2022, 2021 and 2020, respectively. Included in these amounts are immaterial adjustments related to prior-year sales due to changes in estimates. Such amounts represented approximately 1% of net product sales for each of the years ended December 31, 2022, 2021 and 2020.

Rebates

We are subject to rebates on sales made under governmental and managed-care pricing programs and commercial payor contracts in the U.S. The largest of these rebates is associated with sales covered by Medicaid. We participate in state government-managed Medicaid programs as well as certain other qualifying federal and state government programs under the terms of which discounts and rebates are provided to participating government entities. We offer rebates and discounts to managed health care organizations and commercial payors in the U.S. In estimating our provisions for rebates, we consider relevant statutes with respect to governmental pricing programs and contractual sales terms with managed-care providers, commercial payors and group purchasing organizations. We estimate the rebate provision based on historical utilization rates, historical payment experience, new information regarding changes in regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates and channel inventory data obtained from our major distributors in accordance with our inventory management agreements. Estimating these rebates is complex, in part due to the time delay between the date of sale and the actual settlement of the liability. We believe that the methodology we use to estimate rebates on product sales made under governmental and managed-care pricing programs is reasonable and appropriate given current facts and circumstances. However, estimates may vary from actual experience.

Rebates were $630.3 million, $440.8 million and $288.1 million, or 13.7%, 11.8% and 10.4% as a percentage of gross product sales, in 2022, 2021 and 2020, respectively. Rebates as a percentage of gross product sales increased in 2022 compared to 2021 primarily due to the entry into additional contracts with commercial payors and a full year of Epidiolex in our product portfolio. Rebates as a percentage of gross product sales increased in 2021 compared to 2020 primarily due to the entry into additional contracts with commercial payors and the addition of Epidiolex to our product portfolio. Rebates as a percentage of gross product sales are expected to increase in 2023 compared to 2022, primarily due to rebate rate increases and new government rebates.

Sales returns

For certain products, we allow customers to return product within a specified period before and after the applicable expiration date and issue credits which may be applied against existing or future invoices. We account for sales returns as a reduction in net revenue at the time a sale is recognized by establishing an accrual in an amount equal to the estimated value of products expected to be returned. The sales return accrual is estimated principally based on historical experience, the level and estimated shelf life of inventory in the distribution channel, our return policy and expected market events including generic competition.

Sales returns were $13.2 million, $(1.8) million and $18.4 million, or 0.3%, (0.1)% and 0.7% as a percentage of gross product sales in 2022, 2021 and 2020, respectively. Sales returns as a percentage of gross product sales increased in 2022 compared to 2021 driven by a 2021 reduction in the returns provision due to lower than estimated actual returns. The decrease in sales returns in 2021 compared to 2020 was due to this reduction in the returns provision. Sales returns as a percentage of gross product sales are not expected to change materially in 2023 compared to 2022.

Chargebacks

We participate in chargeback programs with a number of entities, principally Federal Supply Schedule, Group Purchasing Organizations, and other public parties, under which pricing on products below wholesalers' list prices is provided to participating entities. These entities purchase product through wholesalers at the contract price and the wholesalers charge back to us the difference between their acquisition cost and the lower negotiated price. We record the difference as allowances against accounts receivable. We determine our estimate of the chargebacks provision primarily based on historical experience on a product and program basis, current contract prices under the chargeback programs and channel inventory data.

Chargebacks were $135.9 million, $91.4 million and $45.6 million, or 2.9%, 2.4% and 1.6% as a percentage of gross product sales in 2022, 2021 and 2020, respectively. Chargebacks as a percentage of gross product sales increased in 2022 compared to 2021 primarily due to higher chargeback utilization and a full year of Epidiolex in our product portfolio. Chargebacks as a percentage of gross product sales increased in 2021 compared to 2020 primarily due to the addition of Epidiolex to our product portfolio. Chargebacks as a percentage of gross product sales are not expected to change materially in 2023 compared to 2022.

Discounts and distributor fees

Discounts and distributor fees comprise prompt payment discounts, patient coupon programs and specialty distributor and wholesaler fees. We offer customers a cash discount on gross product sales as an incentive for prompt payment. We estimate provisions for prompt pay discounts based on contractual sales terms with customers and historical payment experience. To help patients afford our products, we have various programs to assist them, including patient assistance programs, a free product voucher program and co-pay coupon programs for certain products. We estimate provisions for these programs primarily based on expected program utilization, adjusted as necessary to reflect our actual experience on a product and program basis. Specialty distributor and wholesaler fees comprise fees for distribution of our products. We estimate provisions for distributor and wholesaler fees primarily based on sales volumes and contractual terms with our distributors.

Discounts and distributor fees were $186.6 million, $125.9 million and $69.3 million, or 4.1%, 3.4% and 2.5% as a percentage of gross product sales in 2022, 2021 and 2020, respectively. Discounts and distributor fees as a percentage of gross product sales increased in 2022 compared to 2021, primarily due to a full year of Epidiolex in our product portfolio. Discounts and distributor fees as a percentage of gross product sales increased in 2021 compared to 2020 primarily due to the addition of Epidiolex to our product portfolio. Discounts and distributor fees as a percentage of gross product sales are not expected to change materially in 2023 compared to 2022.

Acquisitions and Valuation of Intangibles

We make certain judgments to determine whether transactions should be accounted for as acquisitions of assets or as business combinations. If it is determined that substantially all of the fair value of gross assets acquired in a transaction is concentrated in a single asset (or a group of similar assets), the transaction is treated as an acquisition of assets. We evaluate the inputs, processes, and outputs associated with the acquired set of activities. If the assets in a transaction include an input and a substantive process that together significantly contribute to the ability to create outputs, the transaction is treated as an acquisition of a business.

We account for business combinations using the acquisition method of accounting, which requires that assets acquired and liabilities assumed generally be recorded at their fair values as of the acquisition date. Goodwill represents the excess of the acquisition consideration over the fair value of assets acquired and liabilities assumed. We test goodwill for impairment annually in October and when events or changes in circumstances indicate that the carrying value may not be recoverable. We have determined that we operate in a single segment and have a single reporting unit associated with the development and commercialization of pharmaceutical products. In performing the annual impairment test, the fair value of the reporting unit is compared to its corresponding carrying value, including goodwill. If the carrying value exceeds the fair value of the reporting unit an impairment loss will be recognized for the amount by which the reporting unit's carrying amount exceeds its fair value, not to exceed the carrying amount of goodwill. We have determined the fair value of our single reporting unit to be equal to our market capitalization, as determined by our traded share price, plus a control premium. The control premium used was based on a review of such premiums identified in recent acquisitions of companies of similar size and in similar industries. We performed our annual goodwill impairment test in October 2022 and concluded that goodwill was not impaired as the fair value of the reporting unit significantly exceeded its carrying amount, including goodwill. As of December 31, 2022, we had $1.7 billion of goodwill resulting from acquisitions accounted for as business combinations.

In transactions accounted for as acquisitions of assets, no goodwill is recorded and contingent consideration such as payments upon achievement of various developmental, regulatory and commercial milestones generally is not recognized at the acquisition date. In an asset acquisition, upfront payments allocated to IPR&D projects at the acquisition date are expensed unless there is an alternative future use. In addition, product development milestones are expensed upon achievement.

Valuation of Intangible Assets

We have acquired, and expect to continue to acquire, intangible assets through asset acquisitions or business combinations. When significant identifiable intangible assets are acquired, we engage an independent third party valuation firm to assist in determining the fair values of these assets as of the acquisition date. Discounted cash flow models are typically used in these valuations, which require the use of significant estimates and assumptions, including but not limited to:

- estimating the timing of and expected costs to complete the in-process projects;
- projecting regulatory approvals;
- estimating future cash flows including revenues and operating profits resulting from completed products and in-process projects; and
- developing appropriate discount rates and probability rates by project.

We believe the fair values that we assign to the intangible assets acquired are based upon reasonable estimates and assumptions given available facts and circumstances as of the acquisition dates. No assurance can be given, however, that the underlying assumptions used to estimate expected cash flows will transpire as estimated. In addition, we are required to estimate the period of time over which to amortize the intangible assets, which requires significant judgment.

Impairment of Intangible Assets

Finite-lived intangible assets consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives, which range from five to eighteen years. The estimated useful lives associated with intangible assets are consistent with the estimated lives of the products and may be modified when circumstances warrant. Intangible assets with finite lives are reviewed for impairment whenever events or circumstances indicate that the carrying value of an asset may not be recoverable. Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. Factors that we consider in deciding when to perform an impairment review include significant under-performance of a product in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in our use of the assets. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Estimating future cash flows related to an intangible asset involves estimates and assumptions. If our assumptions are not correct, there could be an impairment loss or, in the case of a change in the estimated useful life of the asset, a change in amortization expense.

In-process research and development, or IPR&D, is not amortized but is tested for impairment annually or when events or circumstances indicate that the fair value may be below the carrying value of the asset. If the carrying value of the assets is not expected to be recovered, the assets are written down to their estimated fair values.

As of December 31, 2022, we had $5.8 billion of finite-lived intangible assets, of which $3.9 billion related to the Epidiolex intangible asset which we acquired in the GW Acquisition and $1.3 billion related to the Vyxeos intangible asset which we acquired in the Celator Acquisition. As part of our annual impairment assessment, we reviewed these intangible assets as of December 31, 2022 and determined the carrying value is recoverable. Cash flow models used in our assessment are based on our commercial experience to date and require the use of significant estimates, which include, but are not limited to, patient-related assumptions, including patient population and segmentation, patient growth and treatment rates, and long-range pricing expectations.

In 2022, we recorded an acquired IPR&D asset impairment charge of $133.6 million as a result of the decision to discontinue our nabiximols program. We did not recognize an impairment charge related to our intangible assets in 2021. In 2020, we recorded an acquired IPR&D asset impairment charge of $136.1 million following the decision to stop enrollment in our Phase 3 clinical study of defibrotide for the prevention of VOD due to a determination that the study is highly unlikely to reach one of its primary endpoints.

Please refer to Note 10, Goodwill and Intangible Assets, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K, for further information about our intangible assets and the remaining useful lives of our finite-lived intangible assets as of December 31, 2022.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amount and the tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. We provide a valuation allowance when it is more-likely-than-not that deferred tax assets will not be realized.

Our most significant tax jurisdictions are Ireland, the U.K. and the U.S. Certain estimates are required in determining our expense for income taxes. Some of these estimates are based on management's interpretations of jurisdiction-specific tax laws or regulations and the likelihood of settlement related to tax audit issues. Various internal and external factors may have favorable or unfavorable effects on our future effective income tax rate. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, the impact of accounting for share-based compensation, changes in our international organization, likelihood of settlement, and changes in overall levels of income before taxes.

Realization of our deferred tax assets is dependent upon the generation of future taxable income, the amount and timing of which are uncertain. In evaluating our ability to recover our deferred tax assets, we consider all available positive and negative evidence, including cumulative income in recent fiscal years, our forecast of future taxable income exclusive of certain reversing temporary differences and significant risks and uncertainties related to our business. In determining future taxable income, we are responsible for assumptions utilized including the amount of state, federal and international pre-tax operating income, the reversal of certain temporary differences and the implementation of feasible and prudent tax planning strategies. These assumptions require significant judgment about the forecasts of future taxable income in applicable tax jurisdictions, which are based on our commercial experience to date and are consistent with the plans and estimates that we are using to manage our underlying business.

We maintain a valuation allowance against certain other deferred tax assets where realizability is not certain. We periodically evaluate the likelihood of the realization of deferred tax assets and reduce the carrying amount of these deferred tax assets by a valuation allowance to the extent we believe a portion will not be realized. This determination depends on a variety of factors, some of which are subjective, including our recent cumulative earnings experience by taxing jurisdiction, expectations of future taxable income, carryforward periods available to us for tax reporting purposes, various income tax strategies and other relevant factors. If we determine that the deferred tax assets are not realizable in a future period, we would record material changes to income tax expense in that period.

We have also provided for unrecognized tax benefits that we believe are not more-likely-than-not to be sustained upon examination by tax authorities. The evaluation of unrecognized tax benefits is based on factors that include, but are not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate unrecognized tax benefits on a quarterly basis and adjust the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Our liabilities for unrecognized tax benefits can be relieved only if the contingency becomes legally extinguished through either payment to the taxing authority or the expiration of the statute of limitations, the recognition of the benefits associated with the position meet the more-likely-than-not threshold or the liability becomes effectively settled through the examination process. We consider matters to be effectively settled once the taxing authority has completed all of its required or expected examination procedures, including all appeals and administrative reviews. We also accrue for potential interest and penalties related to unrecognized tax benefits in income tax expense (benefit).

Recent Accounting Pronouncements

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

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk. The primary objectives of our investment policy, in order of priority, are as follows: safety and preservation of principal and diversification of risk; liquidity of investments sufficient to meet cash flow requirements; and competitive yield. Although our investments are subject to market risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or certain types of investment. Our investment policy allows us to maintain a portfolio of cash equivalents and short-term investments in a variety of securities, including U.S. federal government and federal agency securities, corporate bonds or commercial paper issued by U.S. corporations, money market instruments, certain qualifying money market mutual funds, certain repurchase agreements, and tax-exempt obligations of states, agencies and municipalities in the U.S. Our cash equivalents as of December 31, 2022 consisted of money market funds and time deposits which are not subject to significant interest rate risk.

We are exposed to risks associated with changes in interest rates in connection with our term loan borrowings. In May 2021 we entered into a credit agreement, or the Credit Agreement, that provides for (i) a seven-year $3.1 billion term loan B facility, or the Dollar Term Loan, (ii) a seven-year €625.0 million term loan B facility, or the Euro Term Loan and, together with the Dollar Term Loan, collectively known as the Term Loan and (iii) a five-year $500.0 million revolving credit facility, or the Revolving Credit Facility. There were no borrowings outstanding under the Revolving Credit Facility or the Euro Term

Loan as of December 31, 2022. Dollar Term Loan borrowings of $2.8 billion were outstanding as of December 31, 2022 and are subject to a London Inter-Bank Offering Rate, or LIBOR, floor of 0.50%. Based on the outstanding borrowings of $2.8 billion as of December 31, 2022, a hypothetical 1% increase or decrease in interest rates, above the LIBOR floor, would increase or decrease net income for 2023 by approximately $27.4 million.

In April 2021, we issued $1.5 billion in aggregate principal amount of 4.375% senior secured notes, due 2029, or the Secured Notes. In 2017, we completed a private placement of $575.0 million aggregate principal amount of 1.50% exchangeable senior notes due 2024, or the 2024 Notes, and in June 2020, we completed a private offering of $1.0 billion aggregate principal amount of 2.00% exchangeable senior notes due 2026, or the 2026 Notes.

The Secured Notes, the 2024 Notes and the 2026 Notes have fixed annual interest rates of 4.375%, 1.50% and 2.00%, respectively, and we therefore do not have economic interest rate exposure on the Secured Notes, the 2024 Notes and the 2026 Notes. However, the fair values of the Secured Notes, the 2024 Notes and the 2026 Notes are exposed to interest rate risk. Generally, the fair values of the Secured Notes, the 2024 Notes and the 2026 Notes will increase as interest rates fall and decrease as interest rates rise. The fair values of the 2024 Notes and the 2026 Notes are also affected by volatility in our ordinary share price. As of December 31, 2022 the fair values of the Secured Notes, the 2024 Notes and the 2026 Notes were estimated to be approximately $1.3 billion, $568.0 million and $1.2 billion, respectively.

Foreign Currency Exchange Rate Risk. We have significant operations in Europe as well as in the U.S. The functional currency of each foreign subsidiary is generally the local currency. We are exposed to foreign currency exchange risk as the functional currency financial statements of foreign subsidiaries are translated to U.S. dollars. The assets and liabilities of our foreign subsidiaries having a functional currency other than the U.S. dollar are translated into U.S. dollars at the exchange rate prevailing at the balance sheet date, and at the average exchange rate for the reporting period for revenue and expense accounts. The cumulative foreign currency translation adjustment is recorded as a component of accumulated other comprehensive loss in shareholders' equity. The reported results of our foreign subsidiaries will be influenced by their translation into U.S. dollars by currency movements against the U.S. dollar. Our primary currency translation exposure is related to our subsidiaries that have functional currencies denominated in sterling and euro. A hypothetical 10% strengthening or weakening in the rates used to translate the results of our foreign subsidiaries that have functional currencies denominated in sterling and euro would have increased or decreased net income for the year ended December 31, 2022 by approximately $63.5 million and $7.4 million, respectively.

Transactional exposure arises where transactions occur in currencies other than the functional currency. Transactions in foreign currencies are recorded at the exchange rate prevailing at the date of the transaction. The resulting monetary assets and liabilities are translated into the appropriate functional currency at exchange rates prevailing at the balance sheet date and the resulting gains and losses are reported in foreign exchange gain (loss) in the consolidated statements of income (loss). As of December 31, 2022, our exposure to transaction risk primarily related to sterling and euro denominated net monetary liabilities, including intercompany loans, held by subsidiaries with a U.S. dollar functional currency. We have entered into foreign exchange forward contracts to manage this currency risk. These foreign exchange forward contracts are not designated as hedges; gains and losses on these derivative instruments are designed to offset gains and losses on the underlying balance sheet exposures. As of December 31, 2022, we held foreign exchange forward contracts with notional amounts totaling $505.0 million. The net asset fair value of outstanding foreign exchange forward contracts was $17.4 million as of December 31, 2022. Based on our foreign currency exchange rate exposures as of December 31, 2022, a hypothetical 10% adverse fluctuation in exchange rates would decrease the fair value of our foreign exchange forward contracts by approximately $8.5 million as of December 31, 2022. The resulting loss on these forward contracts would be offset by a positive impact on the underlying monetary assets and liabilities.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements as listed below are included in this Annual Report on Form 10-K as pages F-1 through F-44.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures. We have carried out an evaluation under the supervision and with the participation of management, including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e) and 15d-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on their evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of December 31, 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 December 31, 2022, there were no changes to our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting. The following report is provided by management in respect of our internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) of the Exchange Act):

1. Our management is responsible for establishing and maintaining adequate internal control over financial reporting.
2. Our management used the Committee of Sponsoring Organizations of the Treadway Commission Internal Control - Integrated Framework (2013), or the COSO framework, to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.
3. Management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 and has concluded that such internal control over financial reporting was effective. There were no material weaknesses in internal control over financial reporting identified by management.
4. KPMG, our independent registered public accounting firm, has audited the consolidated financial statements of Jazz Pharmaceuticals plc as of and for the year ended December 31, 2022, included herein, and has issued an audit report on our internal control over financial reporting, which is included below.

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Jazz Pharmaceuticals plc:

Opinion on Internal Control Over Financial Reporting

We have audited Jazz Pharmaceuticals plc and subsidiaries' (the 'Company') internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of income (loss), comprehensive income (loss), stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2022, and the related notes and financial statement schedule at Item 15(a)2 (collectively, 'the consolidated financial statements'), and our report dated March 1, 2023 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

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

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ KPMG

Dublin, Ireland
March 1, 2023

Item 9B. Other Information

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and incorporated by reference to our definitive proxy statement for our 2023 annual general meeting of shareholders, or our 2023 Proxy Statement, to be filed pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, or Exchange Act. If our 2023 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is to be included in our 2023 Proxy Statement as follows and is incorporated by reference:

- The information relating to our directors and nominees for director is to be included in the section entitled “Proposal 1—Election of Directors;”
- The information relating to our executive officers is to be included in the section entitled “Executive Officers;”
- The information relating to our audit committee, audit committee financial expert and procedures by which shareholders may recommend nominees to our board of directors is to be included in the section entitled “Corporate Governance and Board Matters;” and
- If required, the information regarding compliance with Section 16(a) of the Exchange Act is to be included in the section entitled “Delinquent Section 16(a) Reports.”

Such information is incorporated herein by reference to our 2023 Proxy Statement, provided that if the 2023 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Our Code of Conduct applies to all of our employees, directors and officers, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, and those of our subsidiaries. The Code of Conduct is available on our website at *www.jazzpharmaceuticals.com* under the section entitled “About” under “Corporate Ethics.” We intend to satisfy the disclosure requirements under Item 5.05 of the SEC Form 8-K regarding an amendment to, or waiver from, a provision of our Code of Conduct by posting such information on our website at the website address and location specified above.

Item 11. Executive Compensation

The information required by this item is to be included in our 2023 Proxy Statement under the sections entitled “Executive Compensation,” “Director Compensation,” “Corporate Governance and Board Matters—Compensation Committee Interlocks and Insider Participation” and “Corporate Governance and Board Matters—Compensation Committee Report” and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item with respect to equity compensation plans is to be included in our 2023 Proxy Statement under the section entitled “Equity Compensation Plan Information” and the information required by this item with respect to security ownership of certain beneficial owners and management is to be included in our 2023 Proxy Statement under the section entitled “Security Ownership of Certain Beneficial Owners and Management” and in each case is incorporated herein by reference.

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

The information required by this item is to be included in our 2023 Proxy Statement under the sections entitled "Certain Relationships and Related Party Transactions" and "Corporate Governance and Board Matters—Independence of the Board of Directors" and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item is to be included in our 2023 Proxy Statement under the section entitled "Proposal 2—On a Non-Binding Advisory Basis, Ratify Appointment of Independent Registered Accounting Firm and, On a Binding Basis, Authorize the Board of Directors, Acting Through the Audit Committee, to Determine the Independent Auditors' Remuneration" and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Financial Statements:

See Consolidated Financial Statements in Part II, Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules:

The following financial statement schedule of Jazz Pharmaceuticals plc is filed as part of this Annual Report on Form 10-K on page F-51 and should be read in conjunction with the consolidated financial statements of Jazz Pharmaceuticals plc.

Schedule II: Valuation and Qualifying Accounts

All other schedules are omitted because they are not applicable, not required under the instructions, or the requested information is shown in the consolidated financial statements or related notes thereto.

(b) Exhibits—The following exhibits are included herein or incorporated herein by reference:

Exhibit Number	Description of Document
2.1	Agreement and Plan of Merger and Reorganization, dated as of September 19, 2011, by and among Azur Pharma Limited (now Jazz Pharmaceuticals plc), Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500) filed with the SEC on September 19, 2011).
2.2	Letter Agreement, dated as of January 17, 2012, by and among Jazz Pharmaceuticals plc, Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated herein by reference to Exhibit 2.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
2.3	Agreement and Plan of Merger, dated as of April 26, 2012, by and among Jazz Pharmaceuticals plc, Jewel Merger Sub Inc., EUSA Pharma Inc., and Essex Woodlands Health Ventures, Inc., Mayflower L.P., and Bryan Morton, in their capacity as the representatives of the equity holders of EUSA Pharma Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on April 27, 2012).
2.4	Assignment, dated as of June 11, 2012, by and among Jazz Pharmaceuticals plc and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 2.1B in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 12, 2012).
2.5	Tender Offer Agreement, dated December 19, 2013, by and among Jazz Pharmaceuticals Public Limited Company, Jazz Pharmaceuticals Italy S.r.l. and Gentium S.p.A. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K/A (File No. 001-33500), as filed with the SEC on December 20, 2013).
2.6†	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).

2.7	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).
2.8	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).
2.9‡	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	Investor Rights Agreement, dated July 7, 2009 by and between Jazz Pharmaceuticals, Inc. and the other parties named therein (incorporated herein by reference to Exhibit 10.88 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on July 7, 2009).
4.2B	Assignment, Assumption and Amendment Agreement, dated as of January 18, 2012, by and among Jazz Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and the other parties named therein (incorporated herein by reference to Exhibit 4.7B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
4.3A	Indenture, dated as of August 23, 2017, among Jazz Pharmaceuticals Public Limited Company, Jazz Investments I Limited and U.S. Bank National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 23, 2017).
4.3B	Form of 1.50% Exchangeable Senior Note due 2024 (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 23, 2017).
4.4A	Indenture, dated as of June 11, 2020 among Jazz Pharmaceuticals Public Limited Company, Jazz Investments I Limited and U.S. Bank National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on June 11, 2020).
4.4B	Form of 2.000% Exchangeable Senior Note due 2026 (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 June 11, 2020).
4.5A	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).
4.5B	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).
4.5C	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 (incorporated herein by reference to Exhibit 4.5C in Jazz Pharmaceuticals, plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
4.6	Description of Share Capital.
10.1#	Settlement Agreement, dated as of April 5, 2017, by and between Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited, and Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2022, as filed with the SEC on November 9, 2022).

10.2	Settlement Agreement, dated as of April 4, 2019, by and among United States of America, acting through the United States Department of Justice and on behalf of the Office of Inspector General of the Department of Health and Human Services, Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., and Jazz Pharmaceuticals Ireland Ltd. (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.3	Corporate Integrity Agreement, dated as of April 3, 2019, by and between Jazz Pharmaceuticals plc and the Office of Inspector General of the United States Department of Health and Human Services (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.4†	Supply Agreement, dated as of April 1, 2010, by and between Jazz Pharmaceuticals, Inc. and Siegfried (USA) Inc. (incorporated herein by reference to Exhibit 10.54 in Jazz Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2010, as filed with the SEC on May 6, 2010).
10.5‡	Master Manufacturing Services Agreement, dated as of October 1, 2015, by and between Jazz Pharmaceuticals Ireland Limited and Patheon Pharmaceuticals Inc. (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.6A#	Clinical and Commercial Manufacturing and Supply Agreement, dated as of December 22, 2010, between Celator Pharmaceuticals, Inc. and Baxter Oncology GmbH (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2022, as filed with the SEC on November 9, 2022).
10.6B#	Amendment No. 1 Clinical and Commercial Manufacturing and Supply Agreement, dated as of January 18, 2018, by and between Jazz Pharmaceuticals Ireland Limited and Baxter Oncology GmbH (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2022, as filed with the SEC on November 9, 2022).
10.7‡	Contract Manufacturing Agreement, dated as of January 20, 2020, by and between Jazz Pharmaceuticals Ireland Limited and Siegfried AG (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.8#	Pharmacy Master Services Agreement, dated as of December 1, 2022, by and between Jazz Pharmaceuticals, Inc. and Express Scripts Specialty Distribution Services, Inc.
10.9‡	Amended and Restated License Agreement, dated as of October 14, 2020, between Pharma Mar, S.A. and Jazz Pharmaceuticals Ireland Limited (incorporated herein by reference to Exhibit 10.12 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.10‡	Amendment No. 1, dated as of May 6, 2021, to Amended and Restated License Agreement, dated as of October 14, 2020, between Pharma Mar, S.A. and Jazz Pharmaceuticals Ireland Limited (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals, plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.11#	License and Collaboration Agreement, dated October 18, 2022, between Jazz Pharmaceuticals Ireland Limited and Zymeworks BC Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on December 5, 2022).
10.12	Credit Agreement, dated as of May 5, 2021, by and among Jazz Pharmaceuticals Public Limited Company, the other borrowers from time to time party thereto, the lenders and issuing banks from time to time party thereto, Bank of America, N.A., as administrative agent, and U.S. Bank National Association, as collateral trustee (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on May 5, 2021).
10.13A	Commercial Lease, dated as of June 2, 2004, by and between Jazz Pharmaceuticals, Inc. and The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.52 in Jazz Pharmaceuticals, Inc.'s registration statement on Form S-1, as amended (File No. 333-141164), as filed with the SEC on March 27, 2007).
10.13B	First Amendment of Lease, dated June 1, 2009, by and between Jazz Pharmaceuticals, Inc. and Wheatley-Fields, LLC, successor in interest to The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.86 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on June 4, 2009).

10.13C	Second Amendment of Lease, dated February 28, 2012, by and between Jazz Pharmaceuticals, Inc. and Wheatley-Fields, LLC, successor in interest to The Board of Trustees of the Leland Stanford Junior University (incorporated herein by reference to Exhibit 10.31 in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
10.14	Lease, dated May 8, 2012, by and between John Ronan and Castle Cove Property Developments Limited and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.15A	Commercial Lease, dated as of January 7, 2015, by and between The Board of Trustees of the Leland Stanford Junior University and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2014, as filed with the SEC on February 24, 2015).
10.15B	First Amendment, dated as of January 29, 2018, to Commercial Lease, dated as of January 7, 2015, by and between The Board of Trustees of the Leland Stanford Junior University and Jazz Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.15C	Second Amendment, dated as of July 26, 2018, to Commercial Lease, dated as of January 7, 2015, by and between The Board of Trustees of the Leland Stanford Junior University and Jazz Pharmaceuticals, Inc., as previously amended by the First Amendment to Lease, dated as of January 29, 2018 (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2018, as filed with the SEC on November 6, 2018).
10.16+	Form of Indemnification Agreement between Jazz Pharmaceuticals plc and its officers and directors (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
10.17+	Offer Letter from Jazz Pharmaceuticals, Inc. to Daniel N. Swisher, Jr. (incorporated herein by reference to Exhibit 10.21 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the year ended December 31, 2017, as filed with the SEC on February 27, 2018).
10.18+	Offer Letter from Jazz Pharmaceuticals, Inc. to Robert Iannone dated as of April 11, 2019 (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2019, as filed with the SEC on August 6, 2019).
10.19A+	Employment Agreement, dated as of May 16, 2012 by and between Patricia Carr and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.19B+	Change in Control Severance Terms, dated as of May 15, 2016, by and between Jazz Pharmaceuticals Ireland Ltd. and Patricia Carr (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.19C+	Change in Control Stock Award Acceleration Agreement, dated as of May 15, 2016 by and between Jazz Pharmaceuticals plc and Patricia Carr (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.20+	Offer Letter, dated as of July 5, 2019 by and between Jazz Pharmaceuticals, Inc. and Neena M. Patil (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.21A+	Employment Contract, dated as of February 22, 2013, by and between Jazz Pharmaceuticals Ireland Limited and Finbar Larkin (incorporated herein by reference to Exhibit 10.27 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.21B+	Amendment to Employment Contract, dated as of February 26, 2020, by and between Jazz Pharmaceuticals Ireland Limited and Finbar Larkin ((incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2020, as filed with the SEC on May 5, 2020).

10.22A+	Employment Contract, dated as of December 14, 2019, by and between Jazz Pharmaceuticals UK Limited and Samantha Pearce (incorporated herein by reference to Exhibit 10.28A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.22B+	Amendment to Employment Contract, dated as of April 21, 2020, by and between Jazz Pharmaceuticals UK Limited and Samantha Pearce (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2020, as filed with the SEC on May 5, 2020).
10.22C+	Equity Award Letter, dated as of December 9, 2019, by and between Jazz Pharmaceuticals UK Limited and Samantha Pearce (incorporated herein by reference to Exhibit 10.28B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.23+	Offer Letter, dated as of February 23, 2020, by and between Jazz Pharmaceuticals, Inc. and Renée Galá (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2020, as filed with the SEC on May 5, 2020).
10.24+	Offer Letter, dated as of May 2, 2020, by and between Jazz Pharmaceuticals, Inc. and Kim Sablich (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2020, as filed with the SEC on August 4, 2020).
10.25A+	Service Agreement, dated as of May 5, 2021, by and between Chris Tovey and Jazz Pharmaceuticals UK Limited (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals, plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.25B+	Participation Agreement, dated as of May 5, 2021, by and between Chris Tovey and Jazz Pharmaceuticals UK Limited (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals, plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.26A+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 99.1 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.26B+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan Sub-Plan Governing Awards to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.39B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2012).
10.26C+	Form of Stock Option Grant Notice and Form of Option Agreement (U.S.) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.26D+	Form of Stock Option Grant Notice and Form of Option Agreement (Irish) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.26E+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.28E in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.26F+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.S.) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.26G+	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (Irish) under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.26H+	Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.28H in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).

10.26I+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Option Grant Notice and Form of U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.26J+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.26K+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.26L+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.26M+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2016, as filed with the SEC on May 10, 2016).
10.26N+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Restricted Stock Unit Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2016, as filed with the SEC on May 10, 2016).
10.26O+	Amended and Restated 2011 Equity Incentive Plan (approved August 4, 2016) (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
10.26P+	Amended and Restated 2011 Equity Incentive Plan (approved November 3, 2016) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.26Q+	Amended and Restated 2011 Equity Incentive Plan (approved November 2, 2022).
10.26R+	Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.26S+	Form of U.S. Option Grant Notice and Form of U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.26T+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.26U+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.26V+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).

10.26W+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.26X+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.26Y+	Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.26Z+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.26AA+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2021, as filed with the SEC on November 9, 2021).
10.26BB+	Form of U.S. Performance Restricted Stock Unit Award Grant Notice and Form of U.S. Performance Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.26CC+	Form of Non-U.S. Performance Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Performance Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.27+	Jazz Pharmaceuticals plc Amended and Restated Directors Deferred Compensation Plan (incorporated herein by reference to Exhibit 99.6 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.28A+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 99.4 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.28B+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 10.30B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.28C+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved August 1, 2013) (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.28D+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved August 4, 2016) (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
10.28E+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved November 3, 2016) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.28F+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved July 30, 2020) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2020, as filed with the SEC on August 4, 2020).

10.28G+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.28H+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated Non-Employee Directors 2007 Stock Award Plan (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.28I+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2018, as filed with the SEC on November 6, 2018).
10.28J+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2018, as filed with the SEC on November 6, 2018).
10.28K+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.28L+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.28M+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2020, as filed with the SEC on November 2, 2020).
10.28N+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2020, as filed with the SEC on November 2, 2020).
10.29A+	GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 4.1 in GW's Registration Statement on Form S-8 (file no. 333-238737), filed with the SEC on May 27, 2020).
10.29B+	Form of Restricted Stock Unit Award Agreement under the GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.10B in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.29C+	Form of Replacement Stock Option Award Agreement under the GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.10C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.29D+	Form of Replacement Restricted Stock Unit Award Agreement under the GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.10D in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.30A+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan, as amended and restated (incorporated herein by reference to Exhibit 10.31A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.30B+	Amended and Restated 2007 Employee Stock Purchase Plan (approved November 2, 2022).

10.30C+	Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan Sub-Plan Governing Purchase Rights to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.14C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2012, as filed with the SEC on May 8, 2012).
10.31A+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved October 30, 2019) (incorporated herein by reference to Exhibit 10.34C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.31B+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2020) (incorporated herein by reference to Exhibit 10.34D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.31C+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved October 30, 2020) (incorporated herein by reference to Exhibit 10.33C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.31D+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2021) (incorporated herein by reference to Exhibit 10.33D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.31E+	Jazz Pharmaceuticals plc Global Cash Bonus Plan (approved November, 2021) (incorporated herein by reference to Exhibit 10.34E+ in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2021, as filed with the SEC on March 1, 2022).
10.32+	Amended and Restated Executive Change in Control and Severance Benefit Plan, dated as of July 31, 2019 (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.33A+	Amended and Restated Non-Employee Director Compensation Policy (approved May 3, 2018) (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.33B+	Amended and Restated Non-Employee Director Compensation Policy (approved July 21, 2020) (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2020, as filed with the SEC on November 2, 2020).
10.33C+	Amended and Restated Non-Employee Director Compensation Policy (approved July 29, 2021) (incorporated herein by reference to Exhibit 10.11 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.33D+	Amended and Restated Non-Employee Director Compensation Policy (approved April 28, 2022) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2022, as filed with the SEC on August 3, 2022).
21.1	Subsidiaries of Jazz Pharmaceuticals plc.
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page hereto).
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document - 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)

+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

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

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

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

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 1, 2023

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)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Bruce C. Cozadd, Renée Galá, Neena M. Patil and Patricia Carr, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, the following persons on behalf of the registrant and in the capacities and on the dates indicated have signed this report below:

Signature	Title	Date
/s/ BRUCE C. COZADD **Bruce C. Cozadd**	Chairman, Chief Executive Officer and Director *(Principal Executive Officer)*	March 1, 2023
/s/ RENÉE GALÁ **Renée Galá**	Executive Vice President and Chief Financial Officer *(Principal Financial Officer)*	March 1, 2023
/s/ PATRICIA CARR **Patricia Carr**	Senior Vice President, Chief Accounting Officer *(Principal Accounting Officer)*	March 1, 2023
/s/ JENNIFER E. COOK **Jennifer E. Cook**	Director	March 1, 2023
/s/ PATRICK G. ENRIGHT **Patrick G. Enright**	Director	March 1, 2023
/s/ PETER GRAY **Peter Gray**	Director	March 1, 2023
/s/ HEATHER ANN MCSHARRY **Heather Ann McSharry**	Director	March 1, 2023
/s/ SEAMUS C. MULLIGAN **Seamus C. Mulligan**	Director	March 1, 2023
/s/ KENNETH W. O'KEEFE **Kenneth W. O'Keefe**	Director	March 1, 2023
/s/ ANNE O'RIORDAN **Anne O'Riordan**	Director	March 1, 2023
/s/ NORBERT G. RIEDEL, PH.D. **Norbert G. Riedel, Ph.D.**	Director	March 1, 2023
/s/ MARK D. SMITH, M.D. **Mark D. Smith, M.D.**	Director	March 1, 2023
/s/ CATHERINE A. SOHN, PHARM.D. **Catherine A. Sohn, Pharm.D.**	Director	March 1, 2023
/s/ RICK E WINNINGHAM **Rick E Winningham**	Director	March 1, 2023

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Jazz Pharmaceuticals plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Jazz Pharmaceuticals plc. and subsidiaries (the Company) as of December 31, 2022 and 2021, the related consolidated statements of income (loss), comprehensive income (loss), stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2022, and the related notes and financial statement schedules at Item 15(a)2 (collectively, 'the consolidated financial statements'). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated March 1, 2023 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

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

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

Critical Audit Matter

The critical audit matter communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Valuation of the Vyxeos intangible asset

As discussed in Note 10 to the consolidated financial statements, the finite-lived intangible assets balance as of December 31, 2022 was $5,794,437 thousand, a portion of which related to the finite-lived intangible asset in respect of Vyxeos. As discussed in Note 2, the Company reviews finite-lived intangible assets for impairment when events or circumstances indicate that the carrying value of such assets may not be recoverable.

We identified the assessment of the carrying value of the Vyxeos intangible asset as a critical audit matter. There was a high degree of subjectivity in assessing the carrying value of Vyxeos, specifically revenue forecast assumptions for Vyxeos, which are key inputs to the determination of estimated undiscounted future cash flows.

The following are the primary procedures we performed to address this critical audit matter:

- evaluated the design and tested the operating effectiveness of certain internal controls related to the Vyxeos intangible asset impairment review process, including the Company's control related to the development of the revenue forecast assumptions for Vyxeos;

- evaluated the reasonableness of the Company's revenue forecast assumptions for Vyxeos by comparing certain underlying assumptions against (1) company-specific operational information and management's communication to the Board of Directors and (2) available industry or other third-party reports;
- performed a sensitivity analysis over Vyxeos revenue forecast assumptions to assess the impact of changes to those assumptions on the Company's determination of the carrying value of Vyxeos;
- challenged management's ability to accurately forecast revenue by comparing historical projections to actual results.

/s/ KPMG

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

Dublin, Ireland
March 1, 2023

JAZZ PHARMACEUTICALS PLC

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

	December 31,	
	2022	2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 881,482	$ 591,448
Accounts receivable, net of allowances of $17,843 and $13,813 at December 31, 2022 and 2021, respectively	651,493	563,360
Inventories	714,061	1,072,721
Prepaid expenses	91,912	131,413
Other current assets	267,192	252,392
Total current assets	2,606,140	2,611,334
Property, plant and equipment, net	228,050	256,837
Operating lease assets	73,326	86,586
Intangible assets, net	5,794,437	7,152,328
Goodwill	1,692,662	1,827,609
Deferred tax assets, net	376,247	311,103
Deferred financing costs	9,254	12,029
Other non-current assets	55,139	40,813
Total assets	$ 10,835,255	$ 12,298,639
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 90,758	$ 100,298
Accrued liabilities	803,255	666,304
Current portion of long-term debt	31,000	31,000
Income taxes payable	7,717	9,608
Deferred revenue	463	2,093
Total current liabilities	933,193	809,303
Deferred revenue, non-current	—	463
Long-term debt, less current portion	5,693,341	6,018,943
Operating lease liabilities, less current portion	71,838	87,200
Deferred tax liabilities, net	944,337	1,300,541
Other non-current liabilities	106,812	116,998
Commitments and contingencies (Note 14)		
Shareholders' equity:		
Ordinary shares, nominal value $0.0001 per share; 300,000 shares authorized; 63,214 and 61,633 shares issued and outstanding at December 31, 2022 and 2021, respectively	6	6
Non-voting euro deferred shares, €0.01 par value per share; 4,000 shares authorized, issued and outstanding at both December 31, 2022 and 2021	55	55
Capital redemption reserve	472	472
Additional paid-in capital	3,477,124	3,534,792
Accumulated other comprehensive loss	(1,125,509)	(400,360)
Retained earnings	733,586	830,226
Total shareholders' equity	3,085,734	3,965,191
Total liabilities and shareholders' equity	$ 10,835,255	$ 12,298,639

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

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF INCOME (LOSS)
(In thousands, except per share amounts)

	Year Ended December 31,		
	2022	2021	2020
Revenues:			
Product sales, net	$ 3,641,429	$ 3,079,001	$ 2,346,660
Royalties and contract revenues	17,945	15,237	16,907
Total revenues	3,659,374	3,094,238	2,363,567
Operating expenses:			
Cost of product sales (excluding amortization of acquired developed technologies)	540,517	440,760	148,917
Selling, general and administrative	1,416,967	1,451,683	854,233
Research and development	590,453	505,748	335,375
Intangible asset amortization	599,169	525,769	259,580
Impairment charge	133,648	—	136,139
Acquired in-process research and development	444,148	—	251,250
Total operating expenses	3,724,902	2,923,960	1,985,494
Income (loss) from operations	(65,528)	170,278	378,073
Interest expense, net	(288,242)	(278,766)	(99,707)
Foreign exchange loss	(19,014)	(4,350)	(3,271)
Income (loss) before income tax expense (benefit) and equity in loss of investees	(372,784)	(112,838)	275,095
Income tax expense (benefit)	(158,645)	216,116	33,517
Equity in loss of investees	9,921	714	2,962
Net income (loss)	$ (224,060)	$ (329,668)	$ 238,616
Net income (loss) per ordinary share:			
Basic	$ (3.58)	$ (5.52)	$ 4.28
Diluted	$ (3.58)	$ (5.52)	$ 4.22
Weighted-average ordinary shares used in per share calculations - basic	62,539	59,694	55,712
Weighted-average ordinary shares used in per share calculations - diluted	62,539	59,694	56,517

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

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(In thousands)

	Year Ended December 31,		
	2022	2021	2020
Net income (loss)	$ (224,060)	$ (329,668)	$ 238,616
Other comprehensive income (loss):			
Foreign currency translation adjustments	(725,277)	(268,347)	90,183
Loss on fair value hedging activities reclassified from accumulated other comprehensive income (loss) to foreign exchange loss, net of income tax benefit of $43, $—, and $—, respectively	128	—	—
Unrealized loss on cash flow hedging activities, net of income tax benefit of $—, $2 and $649, respectively	—	(14)	(4,543)
Loss on cash flow hedging activities reclassified from accumulated other comprehensive income (loss) to interest expense, net of income tax expense of $—, $355 and $486	—	2,482	3,401
Unrealized loss on fair value hedging activities, net of income tax benefit of $—, $43 and $—, respectively	—	(129)	—
Other comprehensive income (loss)	(725,149)	(266,008)	89,041
Total comprehensive income (loss)	$ (949,209)	$ (595,676)	$ 327,657

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

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(In thousands)

	Ordinary Shares		Non-voting Euro Deferred		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2019	56,140	$ 6	4,000	$ 55	$ 472	$ 2,266,026	$ (223,393)	$ 1,067,815	$ 3,110,981
Stock issued under directors deferred compensation plan	37	—	—	—	—	—	—	—	—
Issuance of Exchangeable Senior Notes, due 2026	—	—	—	—	—	176,260	—	—	176,260
Partial repurchase of Exchangeable Senior Notes, due 2021	—	—	—	—	—	(12,513)	—	—	(12,513)
Issuance of ordinary shares in conjunction with exercise of share options	780	—	—	—	—	86,984	—	—	86,984
Issuance of ordinary shares under employee stock purchase plan	125	—	—	—	—	12,697	—	—	12,697
Issuance of ordinary shares in conjunction with vesting of restricted stock units	290	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(16,877)	—	—	(16,877)
Share-based compensation	—	—	—	—	—	121,093	—	—	121,093
Shares repurchased	(1,201)	—	—	—	—	—	—	(146,537)	(146,537)
Other comprehensive income	—	—	—	—	—	—	89,041	—	89,041
Net income	—	—	—	—	—	—	—	238,616	238,616
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 connection with the acquisition of GW Pharmaceuticals plc	3,798	—	—	—	—	608,456	—	—	608,456
Share-based payment - precombination service in connection with the acquisition of GW Pharmaceuticals plc	—	—	—	—	—	3,555	—	—	3,555
Issuance of ordinary shares in conjunction with exercise of share options	1,042	—	—	—	—	119,058	—	—	119,058
Issuance of ordinary shares under employee stock purchase plan	157	—	—	—	—	16,203	—	—	16,203
Issuance of ordinary shares in conjunction with vesting of restricted stock units	465	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(35,602)	—	—	(35,602)
Share-based compensation	—	—	—	—	—	189,452	—	—	189,452
Other comprehensive loss	—	—	—	—	—	—	(266,008)	—	(266,008)
Net loss	—	—	—	—	—	—	—	(329,668)	(329,668)
Balance at December 31, 2021	61,633	$ 6	4,000	$ 55	$ 472	$ 3,534,792	$ (400,360)	$ 830,226	$ 3,965,191

JAZZ PHARMACEUTICALS PLC

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

	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	832	—	—	—	—	82,897	—	—	82,897
Issuance of ordinary shares under employee stock purchase plan	139	—	—	—	—	15,123	—	—	15,123
Issuance of ordinary shares in conjunction with vesting of restricted stock units	610	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(45,443)	—	—	(45,443)
Share-based compensation	—	—	—	—	—	223,279	—	—	223,279
Shares repurchased	—	—	—	—	—	—	—	(54)	(54)
Other comprehensive loss	—	—	—	—	—	—	(725,149)	—	(725,149)
Net loss	—	—	—	—	—	—	—	(224,060)	(224,060)
Balance at December 31, 2022	63,214	$ 6	4,000	$ 55	$ 472	$ 3,477,124	$ (1,125,509)	$ 733,586	$ 3,085,734

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

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2022	2021	2020
Operating activities			
Net income (loss)	$ (224,060)	$ (329,668)	$ 238,616
Adjustments to reconcile net income (loss) to net cash provided by operating activities:			
Intangible asset amortization	599,169	525,769	259,580
Acquired in-process research and development	444,148	—	251,250
Acquisition accounting inventory fair value step-up adjustment	273,392	223,085	—
Share-based compensation	221,996	189,006	120,998
Impairment charge	133,648	—	136,139
Non-cash interest expense	37,973	92,655	61,748
Loss on disposal of a business	37,704	—	—
Depreciation	30,302	26,714	18,673
Provision for losses on accounts receivable and inventory	14,537	19,668	15,000
Other non-cash transactions	(14,486)	10,032	14,580
Deferred tax expense (benefit)	(292,251)	69,198	(136,937)
Distributions from equity method investees	—	—	5,438
Changes in assets and liabilities:			
Accounts receivable	(90,135)	(92,735)	(38,647)
Inventories	(49,642)	(48,861)	(30,537)
Prepaid expenses and other current assets	35,788	(83,320)	(98,042)
Operating lease assets	14,769	15,583	12,366
Other non-current assets	(24,038)	817	21,913
Accounts payable	(11,225)	57,021	(18,935)
Accrued liabilities	165,991	142,355	79,477
Income taxes payable	(1,692)	(15,524)	13,038
Deferred revenue	(2,093)	(2,305)	(4,720)
Operating lease liabilities, less current portion	(16,422)	(16,037)	(12,383)
Other non-current liabilities	(11,396)	(4,946)	(8,967)
Net cash provided by operating activities	1,271,977	778,507	899,648
Investing activities			
Proceeds from maturity of investments	60,000	1,095,000	1,755,000
Proceeds from sale of a business	53,000	—	14,259
Acquisition of intangible assets	(25,000)	(17,891)	(113,000)
Purchases of property, plant and equipment	(29,046)	(27,641)	(15,004)
Acquisition of investments	(61,036)	(26,819)	(2,397,675)
Acquired in-process research and development	(444,148)	—	(251,250)
Acquisition of a business, net of cash acquired	—	(6,234,792)	—
Net cash used in investing activities	(446,230)	(5,212,143)	(1,007,670)
Financing activities			
Proceeds from employee equity incentive and purchase plans	98,020	135,261	99,681
Share repurchases	(54)	—	(146,537)
Payment of employee withholding taxes related to share-based awards	(45,443)	(35,602)	(16,877)
Repayments of long-term debt	(582,014)	(1,101,788)	(33,387)
Net proceeds from issuance of borrowings under credit agreement	—	3,719,930	—
Net proceeds from issuance of Senior Secured Notes, due 2029	—	1,471,533	—
Payments for repurchase of Exchangeable Senior Notes, due 2021	—	(218,812)	(356,188)
Net proceeds from issuance of Exchangeable Senior Notes, due 2026	—	—	981,381
Net proceeds from revolving credit facility	—	—	500,000
Repayments under revolving credit facility	—	—	(500,000)
Net cash (used in) provided by financing activities	(529,491)	3,970,522	528,073
Effect of exchange rates on cash and cash equivalents	(6,222)	(3,207)	374
Net increase (decrease) in cash and cash equivalents	290,034	(466,321)	420,425
Cash and cash equivalents, at beginning of period	591,448	1,057,769	637,344
Cash and cash equivalents, at end of period	$ 881,482	$ 591,448	$ 1,057,769

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS—(Continued)
(In thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 270,671	$ 138,271	$ 42,470
Cash paid for income taxes, net of refunds	94,681	271,217	226,823

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

JAZZ PHARMACEUTICALS PLC

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

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 seven years of age and older, and also approved by FDA in August 2021 for the treatment of idiopathic hypersomnia, or IH, in adults and launched in the U.S. in November 2021. Xywav contains 92% less sodium than Xyrem®;
- **Xyrem (sodium oxybate) oral solution**, a product approved by FDA and distributed in the U.S. for the treatment of cataplexy or EDS in patients with narcolepsy seven years of age and older; Jazz also markets Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. Xyrem is also approved and distributed in the European Union, or EU (EU market authorizations include Northern Ireland), Great Britain and other markets through a licensing agreement; and
- **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 and Great Britain (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.

Oncology

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

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP, and include the accounts of Jazz Pharmaceuticals plc and our subsidiaries. Intercompany transactions and balances have been eliminated. Our consolidated financial statements include the results of operations of businesses we have acquired from the date of each acquisition for the applicable reporting periods.

Use of Estimates

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

Adoption of New Accounting Standards

In 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 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 year ended December 31, 2022 the effect of adoption reduced interest expense, net and increased net income by approximately $49 million and increased basic and diluted EPS by approximately $0.78 per share. The Exchangeable Senior Notes were determined to be anti-dilutive for the year ended December 31, 2022. The adoption of ASU 2020-06 did not impact our cash flows or compliance with debt covenants.

Significant Risks and Uncertainties

Historically, 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 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. In this regard, our ability to maintain or increase oxybate product sales and realize the anticipated benefits from our investment in Xywav are subject to a number of risks and uncertainties including, without limitation, those related to the launch of Xywav for the treatment of IH in adults and adoption in that indication; competition from the recent introduction of an authorized generic version of Xyrem and in the future from additional authorized generic versions of sodium oxybate 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; 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 from pending antitrust and intellectual property litigation; and continued acceptance of Xywav and Xyrem by physicians and patients. A significant decline in oxybate product sales could cause us to reduce our operating expenses or seek to raise additional funds, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including on our ability to acquire, in-license or develop new products to grow our business.

In addition to risks related specifically to Xywav and Xyrem, we are subject to other challenges and risks related to successfully commercializing a portfolio of oncology products and other neuroscience products, and other risks specific to our business and our ability to execute on our strategy, as well as risks and uncertainties common to companies in the pharmaceutical industry with development and commercial operations, including, without limitation, risks and uncertainties associated with: ongoing clinical research activity and related outcomes, obtaining regulatory approval of our late-stage product candidates; effectively commercializing our approved or acquired products such as Epidiolex, Zepzelca and Rylaze; obtaining and maintaining adequate coverage and reimbursement for our products; contracting and rebates to pharmacy benefit managers and similar organizations that reduce 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 Agency, 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 our and GW's historical businesses. The anticipated benefits to us of the GW Acquisition may not be realized at the expected levels, 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 December 31, 2022 and 2021, we had foreign exchange forward contracts with notional amounts totaling $505.0 million and $347.2 million, respectively. As of December 31, 2022 and 2021, the outstanding foreign exchange forward contracts had a net asset fair value of $17.4 million and a net liability fair value of $2.6 million, respectively. We had no interest rate swap contracts outstanding as of December 31, 2022 and 2021. As of December 31, 2021, we had a cross-currency interest rate swap outstanding with a notional amount of $251.0 million and a net liability fair value of $15.2 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 December 31, 2022, allowances on receivables were not material. As of December 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, Cardinal Health Inc., or Cardinal, which accounted for 10% of gross accounts receivable and McKesson Corporation and affiliates, or

McKesson, which accounted for 9% of gross accounts receivable. As of December 31, 2021, three customers accounted for 74% of gross accounts receivable, ESSDS, which accounted for 52% of gross accounts receivable, McKesson, which accounted for 12% of gross accounts receivable and Cardinal which accounted for 10% of gross accounts receivable.

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

Business Acquisitions

Our consolidated financial statements include the results of operations of an acquired business from the date of acquisition. We account for acquired businesses using the acquisition method of accounting. The acquisition method of accounting for acquired businesses requires, among other things, that assets acquired, liabilities assumed and any noncontrolling interests in the acquired business be recognized at their estimated fair values as of the acquisition date, with limited exceptions, and that the fair value of acquired in-process research and development, or IPR&D, be recorded on the balance sheet. Also, transaction costs are expensed as incurred. Any excess of the acquisition consideration over the assigned values of the net assets acquired is recorded as goodwill. Contingent consideration is included within the acquisition cost and is recognized at its fair value on the acquisition date. A liability resulting from contingent consideration is remeasured to fair value at each reporting date until the contingency is resolved and changes in fair value are recognized in earnings.

Cash Equivalents

We consider all highly liquid investments, readily convertible to cash, that mature within three months or less from date of purchase to be cash equivalents.

Derivative Instruments and Hedging Activities

We record the fair value of derivative instruments as either assets or liabilities on the consolidated balance sheets. Changes in the fair value of derivative instruments are recorded each period in current earnings or other comprehensive income (loss), depending on whether a derivative instrument is designated as part of a hedging transaction and, if it is, the type of hedging transaction. For a derivative to qualify as a hedge at inception and throughout the hedged period, we formally document the nature and relationships between the hedging instruments and hedged item.

For derivatives formally designated as hedges, we assess both at inception and quarterly thereafter, whether the hedging derivatives are highly effective in offsetting changes in either the fair value or cash flows of the hedged item.

Gains or losses on cash flow hedges are reclassified from other comprehensive income (loss) to earnings when the hedged transaction occurs. If we determine that a forecasted transaction is no longer probable of occurring, we discontinue hedge accounting and any related unrealized gain or loss on the derivative instrument is recognized in current earnings.

We designate cross-currency interest rate swaps as fair value hedges to hedge foreign currency risks related to our borrowings denominated in currencies other than the U.S. dollar. Fair value hedge amounts included in the assessment of hedge effectiveness are recognized in foreign exchange gain (loss) within the consolidated statements of income (loss), along with the offsetting gains and losses of the related hedged item. We have elected to exclude the total forward points or currency basis from the assessment of hedge effectiveness and account for them as excluded components. The initial fair value of the excluded component is amortized to foreign exchange gain (loss) and the difference between changes in fair value of the excluded component and the amount recorded in earnings is recorded in other comprehensive income (loss).

Derivatives that are not designated and do not qualify as hedges are adjusted to fair value through current earnings.

Inventories

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Our policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective and primarily dependent on our estimates of future demand for a particular product. If our estimate of future demand changes, we consider the impact on the reserve for excess inventory and adjust the reserve as required. Increases in the reserve are recorded as charges in cost of product sales.

We capitalize inventory costs associated with our products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The determination to capitalize inventory costs is based on various factors, including status and expectations of the regulatory approval process, any known safety or efficacy concerns,

potential labeling restrictions, and any other impediments to obtaining regulatory approval. We had no pre-approval inventory on our consolidated balance sheet as of December 31, 2022 or 2021.

Our inventory production process for our cannabinoid products includes the cultivation of botanical raw material. Because of the duration of the cultivation process, a portion of our inventory will not be sold within one year. Consistent with the practice in other industries that cultivate botanical raw materials, all inventory is classified as a current asset.

Property, Plant and Equipment

Property, plant and equipment are stated at cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. Estimated useful lives are as follows:

Buildings	40 years
Manufacturing equipment and machinery	4-20 years
Computer software and equipment	3-7 years
Furniture and fixtures	5 years

Leasehold improvements are amortized over the shorter of the noncancelable term of our leases or their economic useful lives. Maintenance and repairs are expensed as incurred.

Leases

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

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

We have elected the short-term lease exemption and, therefore, do not recognize a lease asset or corresponding liability for lease arrangements with an original term of 12 months or less. Rent expense under short-term leases is recognized on a straight-line basis over the lease term.

Goodwill

Goodwill represents the excess of the acquisition consideration over the fair value of assets acquired and liabilities assumed. We have determined that we operate in a single segment and have a single reporting unit associated with the development and commercialization of pharmaceutical products. In performing the annual impairment test, the fair value of the reporting unit is compared to its corresponding carrying value, including goodwill. If the carrying value exceeds the fair value of the reporting unit an impairment loss will be recognized for the amount by which the reporting unit’s carrying amount exceeds its fair value, not to exceed the carrying amount of goodwill. We test goodwill for impairment annually in October and when events or changes in circumstances indicate that the carrying value may not be recoverable.

Acquired In-Process Research and Development

The initial costs of rights to IPR&D projects acquired in an asset acquisition are expensed as IPR&D unless the project has an alternative future use. The fair value of IPR&D projects acquired in a business combination are capitalized and accounted for as indefinite-lived intangible assets until the underlying project receives regulatory approval, at which point the intangible asset will be accounted for as a finite-lived intangible asset, or discontinued, at which point the intangible asset will be written off. Development costs incurred after an acquisition are expensed as incurred.

Intangible Assets

Intangible assets with finite useful lives consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives, which range from five to eighteen years. The estimated useful lives

associated with finite-lived intangible assets are consistent with the estimated lives of the associated products and may be modified when circumstances warrant. Such assets are reviewed for impairment when events or circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset and its eventual disposition are less than its carrying amount. The amount of any impairment is measured as the difference between the carrying amount and the fair value of the impaired asset.

Revenue Recognition

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

Product Sales, Net

Product sales revenue is recognized when control has transferred to the customer, which occurs at a point in time, which is typically on delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer removes product from our consigned inventory location for shipment directly to a patient.

Reserves for Variable Consideration

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

Reserves for returns, specialty distributor fees, wholesaler fees, government rebates, coupon programs and rebates under managed care plans and commercial payor contracts are included within current liabilities in our consolidated balance sheets. Reserves for government chargebacks and prompt payment discounts are shown as a reduction in accounts receivable.

Royalties and Contract Revenues

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

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

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

Cost of Product Sales

Cost of product sales includes manufacturing and distribution costs, the cost of drug substance, royalties due to third parties on product sales, product liability and cargo insurance, FDA user fees, freight, shipping, handling and storage costs and salaries and related costs of employees involved with production. Excluded from cost of product sales shown on the consolidated statements of income (loss) is amortization of acquired developed technology of $599.2 million, $525.8 million and $259.6 million in 2022, 2021 and 2020, respectively.

Research and Development

Research and development expenses consist primarily of costs related to clinical studies and outside services, personnel expenses and other research and development costs, including milestone payments incurred prior to regulatory approval of products. Clinical study and outside services costs relate primarily to services performed by clinical research organizations, clinical studies performed at clinical sites, materials and supplies, and other third party fees. Personnel expenses relate primarily to salaries, benefits and share-based compensation. Other research and development expenses primarily include overhead allocations consisting of various support and facilities-related costs. Research and development costs are expensed as incurred. For product candidates that have not been approved by FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expense. For products that have been approved by FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the trial.

Advertising Expenses

We expense the costs of advertising, including promotional expenses, as incurred. Advertising expenses were $108.8 million, $161.5 million and $99.6 million in 2022, 2021 and 2020, respectively.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amount and the tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more-likely-than-not that some portion or all of a deferred tax asset will not be realized. We recognize the benefits of a tax position if it is “more-likely-than-not” of being sustained. A recognized tax benefit is then measured as the largest amount of tax benefit that is greater than fifty percent likely of being realized upon settlement. Interest and penalties related to an underpayment of income taxes are included in the income tax expense and classified with the related liability on the consolidated balance sheets.

Foreign Currency

Our functional and reporting currency is the U.S. dollar. The assets and liabilities of our subsidiaries that have a functional currency other than the U.S. dollar are translated into U.S. dollars at the exchange rate prevailing at the balance sheet date with the results of operations of subsidiaries translated at the weighted average exchange rate for the reporting period. The cumulative foreign currency translation adjustment is recorded as a component of accumulated other comprehensive income (loss) in shareholders’ equity.

Transactions in foreign currencies are translated into the functional currency of the relevant subsidiary at the weighted average exchange rate for the reporting period. Any monetary assets and liabilities arising from these transactions are translated into the relevant functional currency at exchange rates prevailing at the balance sheet date or on settlement. Resulting gains and losses are recorded in foreign exchange gain (loss) in our consolidated statements of income (loss).

Deferred Financing Costs

Deferred financing costs are reported at cost, less accumulated amortization and are presented in the consolidated balance sheets as a direct deduction from the carrying value of the associated debt, with the exception of deferred financing costs associated with revolving-debt arrangements which are presented as assets. The related amortization expense is included in interest expense, net in our consolidated statements of income (loss).

Contingencies

From time to time, we may become involved in claims and other legal matters arising in the ordinary course of business. We record accruals for loss contingencies to the extent that we conclude that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. Legal fees and other expenses related to litigation are expensed as incurred and included in selling, general and administrative expenses.

Share-Based Compensation

We account for compensation cost for all share-based awards at fair value on the date of grant. The fair value is recognized as expense over the service period, net of estimated forfeitures, using the straight-line method. The estimation of share-based awards that will ultimately vest requires judgment, and, to the extent actual results or updated estimates differ from current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. We primarily consider historical experience when estimating expected forfeitures.

Performance-Based Restricted Stock Unit Awards

Performance-based restricted stock units, or PRSUs, awarded to employees vest upon the achievement of certain performance criteria at the end of a specified performance period, subject to a relative total shareholder return, or TSR, modifier. The estimated fair value of these PRSUs is based on a Monte Carlo simulation model. Compensation expense for PRSUs is recognized from the date the Company determines the performance criteria probable of being achieved to the date the award, or relevant portion of the award, is expected to vest. Cumulative adjustments are recorded on a quarterly basis to reflect subsequent changes to the estimated outcome of the performance criteria until the date results are determined.

Variable Interest Entity

In the year ended December 31, 2021, we invested in a cell of a protected cell company, or the protected cell, as part of our directors' and officers' liability risk financing strategy. Based on our control and the structure of the protected cell, we concluded that Jazz is the primary beneficiary of the protected cell and is required to consolidate the protected cell. The insurance premium payable to the protected cell for the years ended December 31, 2022 and 2021 and the protected cell's assets and liabilities as of December 31, 2022 and 2021 were immaterial.

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.

3. Business Combination, Disposition, Asset Acquisitions and Collaborations

GW Acquisition

On May 5, 2021, or the Closing Date, we acquired the entire issued share capital of GW. As a result, GW became an indirect wholly owned subsidiary of the Company.

We acquired GW with the objective of broadening our neuroscience portfolio, further diversifying our revenue and driving sustainable, long-term value creation opportunities. GW was a global leader in discovering, developing, manufacturing and commercializing novel, regulatory approved therapeutics from its proprietary cannabinoid research platform to address a broad range of diseases.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

The aggregate consideration for the GW Acquisition was $7.2 billion as follows (all amounts in thousands except American Depositary Shares, or ADS, and per GW ADS amounts):

GW ADS outstanding May 5, 2021		31,556,200
Cash consideration per GW ADS	$	200
Total cash consideration to GW ADS holders	$	6,311,240
Cash consideration to GW share option holders (inclusive of payroll taxes)		267,450
Total cash consideration		6,578,690
Equity consideration to GW ADS holders (1)		608,456
Consideration related to replacement share option pre-combination service		3,555
Total equity consideration		612,011
Total purchase consideration	$	7,190,701

(1) 3.8 million ordinary shares were issued to GW ADS holders. The closing price of the ordinary shares on May 4, 2021 ($160.20) was used to determine the fair value of this equity consideration because the closing of the transaction on May 5, 2021 occurred prior to the opening of regular trading.

In April 2021, we closed an offering of $1.5 billion in aggregate principal amount of 4.375% senior secured notes, due 2029, or the Secured Notes. In May 2021, we entered into a credit agreement, or the Credit Agreement, that provides for (i) a seven-year $3.1 billion term loan B facility, or the Dollar Term Loan, (ii) a seven-year €625.0 million term loan B facility, or the Euro Term Loan and, together with the Dollar Term Loan, collectively known as the Term Loan and (iii) a five-year $500.0 million revolving credit facility, or the Revolving Credit Facility. We financed the cash portion of the GW Acquisition consideration through a combination of cash on hand and borrowings under the Term Loan and the Secured Notes. For further information on the Term Loan and the Secured Notes, please see Note 12.

The GW Acquisition was accounted for as a business combination using the acquisition method under which assets and liabilities of GW were recorded at their respective estimated fair values as of the Closing Date and added to the assets and liabilities of the Company, including an amount for goodwill representing the difference between the acquisition consideration and the estimated fair value of the identifiable net assets. The results of operations of GW have been included in our consolidated financial statements since the Closing Date.

In 2021, we incurred $81.9 million in acquisition-related costs related to the GW Acquisition, which primarily consisted of banking, legal, accounting and valuation-related expenses. These expenses were recorded in selling, general and administrative expense in the accompanying consolidated statements of income (loss). In 2021, our consolidated statements of income (loss) included revenues of $476.4 million and a net loss of $704.6 million from the acquired GW business, as measured from the Closing Date.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

The following table summarizes the fair values of assets acquired and liabilities assumed at the Closing Date (in thousands):

	Fair Values of Assets Acquired and Liabilities Assumed
Cash and cash equivalents	$ 343,898
Accounts receivable	76,355
Inventory	1,206,290
Prepaid expenses and other current assets	72,758
Property, plant and equipment	154,407
Acquired developed technologies	5,480,000
In-process research and development	160,000
Total acquired identifiable intangible assets	5,640,000
Goodwill	933,234
Deferred tax liabilities, net	(1,069,076)
Accrued liabilities	(131,971)
Other assets/liabilities	(35,194)
Total purchase consideration	$ 7,190,701

Inventory

Inventories acquired included raw materials, work in progress and finished goods. Inventories were recorded at their estimated fair values. The inventory was valued at estimated selling price less the estimated costs to be incurred to complete (in the case of work in progress) and sell the inventory, the associated margins on these activities and holding costs. A step-up in value of inventory of $1,062.6 million was recorded in connection with the GW Acquisition. The step-up expense will be recorded in cost of product sales on our consolidated statements of income (loss) as the inventory is sold to customers from the Closing Date.

Intangible assets

The fair value of acquired intangible assets was $5,640.0 million. The intangible assets included acquired developed technologies, primarily related to Epidiolex, and IPR&D.

The fair value of the Epidiolex acquired developed technology asset was determined by applying the income approach, which recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs, using a discount rate of 9.4% that reflects the return requirements of the market. This intangible asset is being amortized over an estimated useful life of 12 years.

We acquired a nabiximols IPR&D asset in the acquisition. In the third quarter of 2022, we recorded an impairment charge of $133.6 million to write off the value of this asset as a result of our decision to discontinue the program.

Some of the more significant assumptions inherent in the development of intangible asset fair values include: the amount and timing of projected future cash flows (including revenue, cost of sales, research and development cost and sales and marketing expenses); probability of success; the discount rate selected to measure inherent risk of future cash flows; and the assessment of the asset’s life cycle and the competitive trends impacting the asset, among other factors.

Deferred tax liabilities, net

The net deferred tax liability relates to the difference between the financial statement carrying amount and the tax basis of acquired intangible assets and inventory, partially offset by acquired net operating loss carryforwards and other temporary differences.

Other tangible assets and liabilities

Other tangible assets and liabilities were valued at their respective carrying amounts as management believes that these amounts approximated their acquisition-date fair values.

Goodwill

Goodwill represents the excess of the total purchase consideration over the estimated fair value of net assets acquired and was recorded in the consolidated balance sheet as of the Closing Date. The goodwill was primarily attributable to the establishment of the deferred tax liability for the acquired intangible assets and inventory. We do not expect any portion of this goodwill to be deductible for income tax purposes.

Sunosi Disposition

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

Upon closing, we recognized a loss on disposal of $40.8 million within selling, general and administrative expenses in our consolidated statements of income (loss) in the year ended December 31, 2022. We are accounting for the contingent consideration in the form of the future royalty as it is earned.

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

License Agreements

In October 2022, we entered into a exclusive licensing and collaboration agreement with Zymeworks Inc., or Zymeworks, providing us the right to acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. In December 2022, we exercised the option to continue with the exclusive development and commercialization rights to zanidatamab. Zanidatamab is a bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Under the terms of the agreement, Zymeworks received an upfront payment of $50.0 million, and, following our decision to continue the collaboration after the readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of $325.0 million. We recorded the $375.0 million as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2022. Zymeworks is also eligible to receive regulatory and commercial milestone payments of up to $1.4 billion, for total potential payments of $1.76 billion. Pending approval, Zymeworks is eligible to receive tiered royalties between 10% and 20% on our net sales.

In May 2022, we entered into a licensing agreement with Sumitomo Pharma Co., Ltd, or Sumitomo, to acquire exclusive development and commercialization rights in the U.S., Europe and other territories for DSP-0187, now referred to as JZP441. JZP441 is a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. Under the terms of the agreement, we made an upfront payment of $50.0 million to Sumitomo, which was recorded as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2022. Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to $1.09 billion and, if JZP441 is approved, a tiered, low double-digit royalty on Jazz's net sales of JZP441.

In April 2022, we entered into a licensing and collaboration agreement with Werewolf Therapeutics, Inc., or Werewolf, to acquire exclusive global development and commercialization rights to Werewolf's investigational WTX-613, now referred to as JZP898. JZP898 is a differentiated, conditionally-activated interferon alpha (IFNα) INDUKINE™ molecule. Under the terms of the agreement, we made an upfront payment of $15.0 million to Werewolf, which was recorded as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2022. Werewolf is eligible to receive development, regulatory and commercial milestone payments of up to $1.26 billion and, if JZP898 is approved, a tiered, mid-single-digit percentage royalty on net sales of JZP898.

In December 2019, we entered into an exclusive license agreement, or original license agreement, with Pharma Mar, S.A., or PharmaMar, for development and U.S. commercialization of Zepzelca.

Under the terms of the original license agreement we paid PharmaMar an upfront payment of $200.0 million, which was recorded as acquired IPR&D expense in our consolidated statement of income for the year ended December 31, 2020. In June 2020, we made a milestone payment of $100.0 million to PharmaMar following FDA accelerated approval of Zepzelca, which was capitalized as an intangible asset on our consolidated balance sheet. In October 2021, we reached our first sales milestone triggering a payment of $25.0 million, which was capitalized as an intangible asset on our consolidated balance sheet.

PharmaMar is eligible to receive potential future regulatory milestone payments of up to $150.0 million upon the achievement of continued U.S. regulatory approval of Zepzelca following the successful completion of confirmatory trials

within certain timelines. PharmaMar is also eligible to receive up to $525.0 million in potential U.S. commercial milestone payments, as well as incremental tiered royalties on future net sales of Zepzelca ranging from the high teens up to 30 percent. PharmaMar may receive additional payments on approval of other indications, with any such payments creditable against commercial milestone payment obligations. PharmaMar retains production rights for Zepzelca and will supply the product to us.

In October 2020, we entered into an amendment and restatement of the original license agreement with PharmaMar, or the amended license agreement, which expanded our exclusive license to include rights to develop and commercialize Zepzelca in Canada. To date, we have paid PharmaMar an upfront payment of $1.0 million, which was recorded as acquired IPR&D expense in our consolidated statement of income for the year ended December 31, 2020, and a milestone payment of $1.0 million in September 2021 following the first New Drug Application Approval by Health Canada, which was capitalized as an intangible asset on our consolidated balance sheet. PharmaMar is also eligible to receive up to $6.0 million in potential Canadian regulatory and commercial milestone payments, as well as incremental tiered royalties on future Canadian net sales of Zepzelca ranging from the high teens up to 30 percent.

Asset Acquisition and Exclusive License Agreement

In October 2020, we entered into an asset purchase and exclusive license agreement with SpringWorks Therapeutics, Inc., or SpringWorks, under which we acquired SpringWorks' fatty acid amide hydrolase, or FAAH, inhibitor program. Under the terms of the agreement, SpringWorks has assigned or exclusively licensed all assets relating to its FAAH inhibitor program to us, including assignment of SpringWorks' proprietary FAAH inhibitor PF-04457845, or PF-'845, now named JZP150 and its license agreement with Pfizer, Inc., or Pfizer, under which Pfizer exclusively licensed PF-'845 to SpringWorks in 2017. In addition to assuming all milestone and royalty obligations owed by SpringWorks to Pfizer, we made an upfront payment of $35.0 million to SpringWorks, which was recorded as acquired IPR&D expense in our consolidated statement of income (loss) for the year ended December 31, 2021, and may make potential milestone payments to SpringWorks of up to $375.0 million upon the achievement of certain clinical, regulatory and commercial milestones, and pay incremental tiered royalties to SpringWorks on future net sales of JZP150 in the mid- to high-single digit percentages.

4. Cash and Available-for-Sale Securities

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

	December 31, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents
Cash	$ 334,018	$ —	$ —	$ 334,018	$ 334,018
Time deposits	30,000	—	—	30,000	30,000
Money market funds	517,464	—	—	517,464	517,464
Totals	$ 881,482	$ —	$ —	$ 881,482	$ 881,482

	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 consolidated statements of income (loss). Interest income from available-for-sale securities was $11.5 million, $1.8 million and $11.1 million in 2022, 2021 and 2020, respectively.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

5. Fair Value Measurement

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

	December 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:						
Time deposits	$ —	$ 30,000	$ 30,000	$ —	$ —	$ —
Money market funds	517,464	—	517,464	80,701	—	80,701
Foreign exchange forward contracts	—	17,356	17,356	—	580	580
Totals	$ 517,464	$ 47,356	$ 564,820	$ 80,701	$ 580	$ 81,281
Liabilities:						
Cross-currency interest rate contracts	$ —	$ —	$ —	$ —	$ 15,232	$ 15,232
Foreign exchange forward contracts	—	—	—	—	3,187	3,187
Totals	$ —	$ —	$ —	$ —	$ 18,419	$ 18,419

As of December 31, 2022 our available-for-sale securities included money market funds and time deposits and their carrying values were approximately equal to their fair values. Money market funds were measured using quoted prices in active markets, which represent Level 1 inputs and time deposits were measured at fair value using Level 2 inputs. Level 2 inputs are obtained from various third party data providers and represent quoted prices for similar assets in active markets, or these inputs were derived from observable market data, or if not directly observable, were derived from or corroborated by other observable market data. As of December 31, 2021, our available-for-sale securities were comprised of money market funds.

Our derivative assets and liabilities include cross-currency interest rate and foreign exchange derivatives that are measured at fair value using observable market inputs such as forward rates, interest rates, our own credit risk as well as an evaluation of our counterparties' credit risks. Based on these inputs, the derivative assets and liabilities are classified within Level 2 of the fair value hierarchy. 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 in 2021.

As of December 31, 2022 and 2021, the carrying amount of investments measured using the measurement alternative for equity investments without a readily determinable fair value was $5.5 million and $5.0 million, respectively. The carrying amount, which is recorded within other non-current assets, is based on the latest observable transaction price.

As of December 31, 2022, the estimated fair values of our 2024 Notes and our 2026 Notes, were approximately $568.0 million and $1.2 billion, respectively. As of December 31, 2022, the estimated fair value of the Secured Notes and the Dollar Term Loan were approximately $1.3 billion and $2.7 billion, respectively. The fair values of each of these debt facilities was estimated using quoted market prices obtained from brokers (Level 2).

6. 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, and was de-designated as a fair value hedge. The terms of this contract converted the principal repayments and interest payments on the Euro Term Loan into U.S. dollars. The carrying amount of the Euro Term Loan and the fair value of the cross-currency interest rate swap contract

were remeasured on a monthly basis, with changes in the euro to U.S. dollar foreign exchange rates recognized within foreign exchange loss in the consolidated statements of income (loss).

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

	Year Ended December 31,	
Cross-Currency Interest Rate Contract:	**2022**	**2021**
Loss recognized in accumulated other comprehensive income (loss), net of tax	$ —	$ (375)
Loss reclassified from accumulated other comprehensive income (loss) to foreign exchange loss, net of tax	128	246
Loss recognized in foreign exchange loss	2,646	35,885

We enter into foreign exchange forward contracts, with durations of up to 12 months, designed to limit the exposure to fluctuations in foreign exchange rates related to the translation of certain non-U.S. dollar denominated liabilities, including intercompany balances. Hedge accounting is not applied to these derivative instruments as gains and losses on these hedge transactions are designed to offset gains and losses on underlying balance sheet exposures. As of December 31, 2022 and 2021, the notional amount of foreign exchange contracts where hedge accounting was not applied was $505.0 million and $347.2 million, respectively.

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

	Year Ended December 31,		
Foreign Exchange Forward Contracts:	**2022**	**2021**	**2020**
Gain (loss) recognized in foreign exchange loss	$ (58,755)	$ (19,585)	$ 19,843

The cash flow effects of our derivative contracts are included within net cash provided by operating activities in the consolidated statements of cash flows, except for the settlement of notional amounts of the cross-currency swap, which were included in net cash (used in) provided by 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 was as follows (in thousands):

	Year Ended December 31,		
Interest Rate Contracts:	**2022**	**2021**	**2020**
Loss recognized in accumulated other comprehensive income (loss), net of tax	$ —	$ (14)	$ (4,543)
Gain reclassified from accumulated other comprehensive income (loss) to interest expense, net of tax	—	2,482	3,401

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

	December 31, 2022			
	Asset Derivatives		Liability Derivatives	
	Balance Sheet Location	**Fair Value**	**Balance Sheet Location**	**Fair Value**
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	$ 17,356	Accrued liabilities	$ —
Total fair value of derivative instruments		$ 17,356		$ —

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

	December 31, 2021			
	Asset Derivatives		Liability Derivatives	
	Balance Sheet Location	Fair Value	Balance Sheet Location	Fair Value
Derivatives designated as hedging instruments:				
Cross-currency interest rate contracts	Other current assets	$ —	Accrued liabilities	$ 15,232
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	580	Accrued liabilities	3,187
Total fair value of derivative instruments		$ 580		$ 18,419

Although we do not offset derivative assets and liabilities within our 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. These provisions were not applicable as of December 31, 2022 since all derivatives were in an asset position. The following table summarizes the potential effect on our consolidated balance sheets of offsetting our interest rate contracts and foreign exchange forward contracts subject to such provisions (in thousands) for 2021:

	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)

7. Inventories

Inventories consisted of the following (in thousands):

	December 31,	
	2022	2021
Raw materials	$ 20,786	$ 21,550
Work in process	517,670	886,849
Finished goods	175,605	164,322
Total inventories	$ 714,061	$ 1,072,721

As of December 31, 2022 and 2021, inventories included $457.6 million and $811.3 million, respectively, related to the purchase accounting inventory fair value step-up on inventory acquired in the GW Acquisition.

8. Other Current Assets

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

	December 31,	
	2022	2021
Deferred charge for income taxes on intercompany profit	$ 176,057	$ 203,480
Other	91,135	48,912
Total other current assets	$ 267,192	$ 252,392

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

9. Property, Plant and Equipment

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

	December 31,	
	2022	2021
Manufacturing equipment and machinery	$ 73,580	$ 69,079
Land and buildings	68,935	64,008
Construction-in-progress	67,385	86,511
Leasehold improvements	64,776	66,318
Computer software	34,116	25,646
Computer equipment	16,424	16,234
Furniture and fixtures	10,481	14,412
Subtotal	335,697	342,208
Less accumulated depreciation and amortization	(107,647)	(85,371)
Property, plant and equipment, net	$ 228,050	$ 256,837

Depreciation and amortization expense on property, plant and equipment amounted to $30.3 million, $26.7 million and $18.7 million for the years ended December 31, 2022, 2021 and 2020, respectively.

10. Goodwill and Intangible Assets

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

Balance at December 31, 2021	$ 1,827,609
Goodwill allocated to divestiture of Sunosi [(1)]	(12,927)
Foreign exchange	(122,020)
Balance at December 31, 2022	$ 1,692,662

[(1)] See Note 3 for further information relating to this divestiture.

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

		December 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	10.4	$ 7,491,994	$ (1,697,557)	$ 5,794,437	$ 8,195,675	$ (1,198,333)	$ 6,997,342
Manufacturing contracts	—	11,417	(11,417)	—	12,124	(12,124)	—
Trademarks	—	2,876	(2,876)	—	2,893	(2,893)	—
Total finite-lived intangible assets		7,506,287	(1,711,850)	5,794,437	8,210,692	(1,213,350)	6,997,342
Acquired IPR&D assets		—	—	—	154,986	—	154,986
Total intangible assets		$ 7,506,287	$ (1,711,850)	$ 5,794,437	$ 8,365,678	$ (1,213,350)	$ 7,152,328

The decrease in the gross carrying amount of intangible assets as of December 31, 2022 compared to December 31, 2021 primarily reflects the negative impact of foreign currency translation adjustments due to the weakening of sterling and euro against the U.S. dollar, the impairment of our acquired IPR&D asset of $133.6 million as a result of the decision to discontinue our nabiximols program and the sale of the Sunosi acquired developed technology asset to Axsome.

The assumptions and estimates used to determine future cash flows including revenues and operating profits resulting from completed products and in-process projects, 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 December 31, 2022, and assuming the underlying assets will not be impaired and that we will not change the expected lives of any other assets, future amortization expenses were estimated as follows (in thousands):

Year Ending December 31,	Estimated Amortization Expense
2023	$ 568,969
2024	568,969
2025	568,969
2026	568,969
2027	568,969
Thereafter	2,949,592
Total	$ 5,794,437

11. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2022	2021
Rebates and other sales deductions	$ 313,176	$ 215,397
Employee compensation and benefits	143,243	158,870
Accrued royalties	57,347	20,345
Accrued interest	35,614	48,640
Accrued collaboration expenses	33,205	1,386
Clinical trial accruals	31,338	25,612
Sales return reserve	26,164	15,814
Accrued facilities expenses	25,864	698
Consulting and professional services	22,278	22,507
Selling and marketing accruals	18,553	21,566
Current portion of lease liabilities	15,938	15,763
Inventory-related accruals	8,565	16,166
Accrued construction-in-progress	3,298	2,894
Accrued milestones	—	25,000
Derivative instrument liabilities	—	18,419
Other	68,672	57,227
Total accrued liabilities	$ 803,255	$ 666,304

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

12. Debt

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

	December 31,	
	2022	2021
2024 Notes	$ 575,000	$ 575,000
Unamortized - debt issuance costs	(2,738)	(4,401)
Unamortized discount - equity component	—	(66,836)
2024 Notes, net	572,262	503,763
2026 Notes	1,000,000	1,000,000
Unamortized - debt issuance costs	(8,932)	(11,407)
Unamortized discount - equity component	—	(139,323)
2026 Notes, net	991,068	849,270
Secured Notes	1,476,938	1,473,810
Term Loan	2,684,073	3,223,100
Total debt	5,724,341	6,049,943
Less current portion	31,000	31,000
Total long-term debt	$ 5,693,341	$ 6,018,943

Credit Agreement

On May 5, 2021, the Company, Jazz Financing Lux S.à.r.l., or Jazz Lux, and certain of our other subsidiaries, as borrowers, (collectively with the Company and Jazz Lux, the "Borrowers"), entered into the Credit Agreement, that provides for (i) the Dollar Term Loan which was drawn by Jazz Lux on the Closing Date in U.S. dollars (ii) the Euro Term Loan which was drawn by Jazz Lux on the Closing Date in Euros and (iii) the Revolving Credit Facility, which is available to be drawn by any Borrower in U.S. dollars.

We used the proceeds from the Term Loan (i) to repay in full $575.9 million under that certain credit agreement, dated as of June 18, 2015 (as amended) among the Company, and certain of our other subsidiaries as borrowers, the lenders party thereto and Bank of America, N.A., as administrative agent and collateral agent, or the Existing Credit Agreement, (ii) to fund, in part, the cash consideration payable in connection with the GW Acquisition and (iii) to pay related fees and expenses. Upon the repayment in full of loans under the Existing Credit Agreement, it was terminated and all guarantees and liens thereunder were released.

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. The Euro Term Loan bore interest at the Euro Inter-Bank Offered Rate, or EURIBOR, plus an applicable margin. The applicable margin for the Euro Term Loan was 3.50%. During the term of the Euro Term Loan, the interest rate and effective interest rate were 4.43% and 4.93%, respectively.

Loans under the Dollar Term Loan and Revolving Credit Facility bear interest at a rate equal to, at the applicable Borrower's option, either (a) London Inter-Bank Offered Rate, or LIBOR or (b) the prime lending rate. The applicable margin for the Dollar Term Loan is 3.50% (in the case of LIBOR) and 2.50% (in the case of borrowings at the prime lending rate). The applicable margin for the Revolving Credit Facility ranges from 3.25% to 2.75% (in the case of LIBOR borrowings) and 2.25% to 1.75% (in the case of borrowings at the prime lending rate), depending on our first lien secured net leverage ratio level. The Dollar Term Loan is subject to a LIBOR floor of 0.50% and loans under the Revolving Credit Facility are not subject to a EURIBOR or LIBOR (as applicable) floor. The Revolving Credit Facility has a commitment fee payable on the undrawn amount ranging from 0.50% to 0.40% per annum based upon our first lien secured net leverage ratio.

As of December 31, 2022, the interest rate and effective interest rate on the Dollar Term Loan were 7.88% and 4.56%, respectively. As of December 31, 2022, we had an undrawn Revolving Credit Facility totaling $500.0 million.

The Borrowers' obligations under the Credit Agreement and any hedging or cash management obligations entered into with any lender thereunder are guaranteed by the Company, the other borrowers, and each of the Company's other existing or

subsequently acquired or organized direct and indirect subsidiaries (subject to certain exceptions), or the Guarantors. We refer to the Borrowers and the Guarantors collectively as the "Loan Parties."

The Loan Parties' obligations under the Credit Agreement are secured, subject to customary permitted liens and other exceptions, by a security interest in (a) all tangible and intangible assets of the Loan Parties, except for certain excluded assets, and (b) all of the equity interests of the subsidiaries of the Loan Parties held by the Loan Parties.

We may make voluntary prepayments at any time without payment of a premium or penalty, subject to certain exceptions, and are required to make certain mandatory prepayments of outstanding indebtedness under the Credit Agreement in certain circumstances.

Principal repayments of the Dollar Term Loan, which are due quarterly, began in September 2021 and are equal to 1.0% per annum of the original principal amount of $3.1 billion with any remaining balance payable on the maturity date. In September 2022, we made a voluntary repayment on the Dollar Term Loan totaling $300.0 million.

The Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants applicable to the Company and its restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. The Credit Agreement contains financial covenants that require the Company and its restricted subsidiaries to (a) not exceed a maximum first lien secured net leverage ratio and (b) not fall below a minimum interest coverage ratio, provided that such covenants apply only to the Revolving Credit Facility and are applicable only if amounts are drawn (or non-cash collateralized letters of credit in excess of $50 million are outstanding) under the Revolving Credit Facility. The Credit Agreement also contains customary events of default relating to, among other things, failure to make payments, breach of covenants and breach of representations.

2029 Senior Secured Notes

On April 29, 2021, Jazz Securities Designated Activity Company, or Jazz Securities, a direct wholly owned subsidiary of the Company, closed the offering of the Secured Notes in a private placement. We used the proceeds from the Secured Notes to fund, in part, the cash consideration payable in connection with the GW Acquisition.

Interest on the Secured Notes is payable semi-annually in arrears on January 15 and July 15 of each year, beginning on January 15, 2022, at a rate of 4.375% per year. The Secured Notes mature on January 15, 2029.

The Secured Notes are jointly and severally guaranteed by the Company and each of its restricted subsidiaries, other than Jazz Securities, that is a borrower, or a guarantor, under the Credit Agreement. The Secured Notes and related guarantees are secured by a first priority lien (subject to permitted liens and certain other exceptions), equally and ratably with the Credit Agreement, on the collateral securing the Credit Agreement.

Except as described below, the Secured Notes may not be optionally redeemed before July 15, 2024. Thereafter, some or all of the Secured Notes, may be redeemed at any time and from time to time at a specified redemption prices, plus accrued and unpaid interest, if any, to, but excluding, to the redemption date. Jazz Securities may redeem all but not part of the Secured Notes at its option at any time in connection with certain tax-related events and may redeem some or all of the Secured Notes at any time and from time to time prior to July 15, 2024 at a price equal to 100% of the principal amount of the Secured Notes to be redeemed plus a "make whole" premium, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. In addition, Jazz Securities may redeem up to 40% of the aggregate principal amount of the Secured Notes at any time and from time to time prior to July 15, 2024, with the net proceeds of certain equity offerings at a price of 104.375% of the principal amount of such Secured Notes, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. In addition, during each of the three consecutive twelve-month periods commencing on the issue date of the Secured Notes, Jazz Securities may redeem up to 10% of the original aggregate initial principal amount of the Secured Notes at a redemption price of 103% of the principal amount of such Secured Notes, plus accrued and unpaid interest, if any, to, but excluding, the redemption date.

If Jazz undergoes a change of control, Jazz Securities will be required to make an offer to purchase all of the Secured Notes at a purchase price in cash equal to 101% of the principal amount thereof, plus accrued and unpaid interest, if any, to, but excluding, the date of repurchase, subject to certain exceptions.

The indenture governing the Secured Notes contains customary affirmative covenants and negative covenants applicable to the Company and its restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. If Jazz Securities or the Company's restricted subsidiaries engage in certain asset sales, Jazz Securities will be required under certain circumstances to make an offer to purchase the Secured Notes at 100% of the principal amount, plus accrued and unpaid interest, if any, to, but excluding, the repurchase date.

As of December 31, 2022, the interest rate and effective interest rate on the Secured Notes were 4.375% and 4.64%, respectively.

Exchangeable Senior Notes Due 2026

In 2020 we completed a private placement of $1.0 billion principal amount of the 2026 Notes. We used a portion of the net proceeds from this offering to repurchase for cash $332.9 million aggregate principal amount of the 1.875% exchangeable senior notes due 2021, or 2021 Notes, through privately-negotiated transactions concurrently with the offering 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.

As of December 31, 2022, the “if converted value” of the 2026 Notes exceeded the principal amount by $22.5 million. As of December 31, 2021, the “if converted value” of the 2026 Notes did not exceed the principal amount of the 2026 Notes.

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. We have determined the expected life of the 2026 Notes to be equal to the original 6-year term. The effective interest rate of the 2026 Notes is 2.26%. Please see Note 2 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. We used the net proceeds from this offering to repay $500.0 million in outstanding loans under the revolving credit facility and to pay related fees and expenses. We used the remainder of the net proceeds for general corporate purposes. 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.

As of December 31, 2022 and 2021, the “if-converted value” did not exceed the principal amount of the 2024 Notes.

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. We have determined the expected life of the 2024 Notes to be equal to the original seven-year term. The effective interest rate of the 2024 Notes is 1.79%. Please see Note 2 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.

For the years ended December 31, 2022, 2021 and 2020, we recognized $32.8 million, $89.9 million and $87.6 million, respectively, in interest expense, net related to the contractual coupon rate and the amortization of the debt issuance costs on the Exchangeable Senior Notes, and the years ended December 31, 2021 and 2020, also included the amortization of the debt discount costs.

Scheduled maturities with respect to our long-term debt are as follows (in thousands):

Year Ending December 31,	Scheduled Long-Term Debt Maturities
2023	$ 31,000
2024	606,000
2025	31,000
2026	1,031,000
2027	31,000
Thereafter	4,098,500
Total	$ 5,828,500

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

13. Leases

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

The components of the lease expense for the years ended December 31, 2022, 2021 and 2020 were as follows (in thousands):

	Year Ended December 31,		
Lease Cost	**2022**	**2021**	**2020**
Operating lease cost	$ 19,670	$ 23,869	$ 21,755
Short-term lease cost	5,088	5,540	4,079
Variable lease cost	5	10	3
Sublease income	—	—	(224)
Finance Lease Cost			
Amortization of leased asset	472	324	—
Interest on lease liabilities	429	295	—
Net lease cost	$ 25,664	$ 30,038	$ 25,613

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

		December 31,	
Leases	**Classification**	**2022**	**2021**
Assets			
Operating lease assets	Operating lease assets	$ 73,326	$ 86,586
Finance lease assets	Property, plant and equipment	4,671	5,738
Total lease assets		$ 77,997	$ 92,324
Liabilities			
Current			
Operating lease liabilities	Accrued liabilities	$ 15,557	$ 15,357
Finance lease liabilities	Accrued liabilities	381	406
Non-current			
Operating lease liabilities	Operating lease liabilities, less current portion	71,838	87,200
Finance lease liabilities	Other non-current liabilities	5,210	6,269
Total lease liabilities		$ 92,986	$ 109,232

	December 31,	
Lease Term and Discount Rate	**2022**	**2021**
Weighted-average remaining lease term (years)		
Operating leases	5.8	6.5
Finance leases	12.0	12.9
Weighted-average discount rate		
Operating leases	5.3 %	5.2 %
Finance leases	7.4 %	7.4 %

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

	Year Ended December 31,		
	2022	2021	2020
Cash paid for amounts included in the measurement of lease liabilities:			
Operating cash outflows from operating leases	$ 20,544	$ 24,847	$ 21,678
Operating cash outflows from finance leases	806	625	—
Financing cash outflows from finance leases	429	324	—
Non-cash operating activities:			
Operating lease assets obtained in exchange for new operating lease liabilities	$ 4,312	$ 8,188	$ 1,763
Finance lease assets obtained in exchange for new finance lease liabilities	—	650	—
De-recognition of operating lease asset on lease assignment	—	56,968	—
De-recognition of operating lease liability on lease assignment	—	68,064	—

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

Year Ending December 31,	Operating Leases	Finance Leases
2023	$ 19,144	$ 778
2024	21,497	778
2025	14,707	778
2026	12,721	778
2027	11,944	753
Thereafter	22,701	4,721
Total lease payments	102,714	8,586
Less imputed interest	(15,319)	(2,995)
Present value of lease liabilities	$ 87,395	$ 5,591

14. 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 December 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 December 31, 2022, we had $51.6 million of noncancelable purchase commitments due within one year, primarily related to agreements with third party manufacturers.

Legal Proceedings

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

Xyrem Class Action

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

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

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

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

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

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

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

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

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

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

On March 18, 2021, United Healthcare Services, Inc. filed a lawsuit in the United States District Court for the District of Minnesota against the Company Defendants, Hikma Pharmaceuticals plc, Roxane Laboratories, Inc., Hikma Pharmaceuticals USA Inc., Eurohealth (USA) Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical Inc., Lupin Ltd., and Lupin

Pharmaceuticals, Inc., raising similar allegations, or the UHS Lawsuit. On March 24, 2021, the U.S. Judicial Panel on Multidistrict Litigation conditionally transferred the UHS Lawsuit to the United States District Court for the Northern District of California, where it was consolidated for discovery and pre-trial proceedings with the other cases.

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

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

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

On February 17, 2022, Health Care Service Corporation filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On May 9, 2022, Aetna Inc., or Aetna, filed a lawsuit in the Superior Court of California for the County of Alameda against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations (hereinafter referred to as the Aetna Case). On November 7, 2022, the court in the Aetna Case issued a tentative ruling granting in part and denying in part our motion to dismiss. On December 27, 2022, the Court issued a final order confirming that tentative ruling. As a result of that ruling, the generic defendants have been dismissed from the case, and certain of Aetna’s claims against Jazz have been dismissed. On January 27, Aetna filed an amended complaint against Jazz.

On January 13, 2023, Amneal Pharmaceuticals LLC, Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, notified the court that they had reached a settlement-in-principle with the class action plaintiffs.

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

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

GW Acquisition Litigation

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

Since the filing of the Proxy Statement, Jazz Pharmaceuticals plc has been named in two lawsuits filed in state and federal courts in New York on March 17, 2021 by purported GW shareholders in connection with the GW Acquisition. The first was filed in the United States District Court for the Southern District of New York by James Farrell (hereinafter referred to as the Farrell Lawsuit) and an additional suit was filed in New York state court by Brian Levy (hereinafter referred to as the Levy Lawsuit). In addition to Jazz Pharmaceuticals plc, Jazz Pharmaceuticals U.K. Holdings Ltd., GW Pharmaceuticals plc, and the GW board of directors are named as defendants in the Farrell Lawsuit. In the Levy Lawsuit, GW Pharmaceuticals plc, the GW board of directors, Centerview Partners LLC, and Goldman Sachs & Co. LLC are named as defendants. In addition to the Farrell Lawsuit and the Levy Lawsuit, ten additional suits have been filed in New York, California, and Pennsylvania federal courts by purported GW shareholders against GW Pharmaceuticals plc and its board of directors, but which do not name any Jazz Pharmaceuticals parties (hereinafter referred to as the GW Litigation, and collectively with the Farrell Lawsuit and the

Levy Lawsuit, as the Transaction Litigation). In the Transaction Litigation, the plaintiffs allege that the Proxy Statement omitted material information and contained misrepresentations, and that the individual members of the GW board of directors breached their fiduciary duties, in violation of state and federal laws, including the Securities Exchange Act of 1934. The plaintiffs in the Transaction Litigation sought various remedies, including injunctive relief to prevent the consummation of the GW Acquisition unless certain allegedly material information was disclosed, or in the alternative, rescission or damages.

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

On May 27, 2021, a class action lawsuit was filed in the United States District Court for the Southern District of California by plaintiff Kurt Ziegler against GW and its former Directors asserting claims under Sections 14(a) and 20(a) of the Securities Exchange Act of 1934, referred to as the Ziegler Lawsuit. The allegations in the Ziegler Lawsuit are similar to those in the previously dismissed Transaction Litigation. In December 2022, the parties reached a settlement in principle.

Patent Infringement Litigation

Avadel Patent Litigation

On May 13, 2021, we filed a patent infringement suit against Avadel Pharmaceuticals plc, or Avadel, and several of its corporate affiliates in the United States District Court for the District of Delaware. The suit alleges that Avadel's product candidate FT218 will infringe five of our patents related to controlled release formulations of oxybate and the safe and effective distribution of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe these patents, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents. Avadel filed a motion for partial judgment on the pleadings on its counterclaim that one of our patents should be delisted from the Orange Book. On November 18, 2022 the Court issued an order that we delist the patent from the Orange Book. On November 22, 2022, we filed a notice of appeal to the United States Court of Appeals for the Federal Circuit. The Federal Circuit temporarily stayed the district court's delisting order. Oral argument in the appeal took place on February 14, 2023. On February 24, 2023, the Federal Circuit affirmed the district court's delisting order, lifted the temporary stay, and gave Jazz 14 days to request that FDA delist the patent from the Orange Book. Jazz complied with the Federal Circuit's order and requested delisting on February 28, 2023.

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

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

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

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

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

Canopy Patent Litigation

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

Lupin Patent Litigation

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

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

In April 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On May 11, 2022, we filed an additional lawsuit against Lupin in the United States District Court for the District of New Jersey alleging that by filing its ANDA, Lupin infringed the newly-issued patent related to a method of treatment when Xywav is administered concomitantly with certain other medications. The suit seeks a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patent. On June 22, 2022, the court consolidated the two lawsuits we filed against Lupin.

In November 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On January 19, 2023, we filed an additional lawsuit against Lupin in the United States District Court for the District of New Jersey alleging that by filing its ANDA, Lupin infringed the newly-issued patent referenced in its November 2022 paragraph IV certification, as well as another patent that issued in January 2023. The suit seeks a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe the two patents in suit. On February 15, 2023, the court consolidated the new lawsuit with the two suits we previously filed against Lupin. No trial date has been set in the consolidated case.

Otsuka Patent Litigation

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

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

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

In February 2023, we reached an agreement with Otsuka to settle all outstanding litigation and disputes between the parties related to Epidiolex royalties. Pursuant to that agreement, Otsuka will assign to GW its rights in certain jointly-owned intellectual property, and GW will pay Otsuka royalties on net sales of Epidiolex from product launch through 2032 and, potentially, on certain future cannabidiol products.

Epidiolex Patent Litigation

In November and December 2022, we received notices from Teva Pharmaceuticals, Inc.; Padagis US LLC; Apotex Inc.; API Pharma Tech LLC and InvaGen Pharmaceuticals, Inc.; Lupin Limited; Taro Pharmaceutical Industries Ltd.; Zenara Pharma Private Limited and Biophore Pharma, Inc.; MSN Laboratories Pvt. Ltd. and MSN Pharmaceuticals, Inc.; Alkem Laboratories Ltd.; and Ascent Pharmaceuticals, Inc. (hereinafter referred to as the "Epidiolex ANDA Filers"), that they have each filed with FDA an Abbreviated New Drug Application, or ANDA, for a generic version of Epidiolex (cannabidiol) oral solution. As of the date of this filing, we are not aware of other ANDA filers. The notices from the Epidiolex ANDA Filers each included a "paragraph IV certification" with respect to certain of our patents listed in FDA's Orange Book for Epidiolex on the date of the receipt of the notice. The listed patents relate generally to the composition and method of use of Epidiolex, and methods of treatment using Epidiolex. A paragraph IV certification is a certification by a generic applicant that alleges that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product.

On January 3, 2023, we filed a patent infringement suit against the Epidiolex ANDA Filers in the United States District Court for the District of New Jersey. The complaint alleges that by filing their ANDAs, the Epidiolex ANDA Filers have infringed certain of our Orange Book listed patents, and seeks an order that the effective date of FDA approval of the ANDAs shall be a date no earlier than the expiration of the last to expire of the asserted 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 the Epidiolex ANDA Filers' ANDAs.

Epidiolex also has Orphan Drug Exclusivity for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older through September 28, 2025, and for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients between 1 and 2 years of age and for the treatment of seizures associated with tuberous sclerosis complex through July 31, 2027.

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.

15. Shareholders' Equity

Share Repurchase Program

In November 2016, our board of directors authorized a share repurchase program and as of December 31, 2022, had authorized the repurchase 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. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the amended credit agreement, corporate and regulatory requirements and market conditions. The share repurchase program may be modified, suspended or discontinued at any time without prior notice. In 2022, we spent a total of $0.1 million to repurchase 338 of our ordinary shares at a total purchase price, including brokerage commissions, of $160.70 per share. In 2021, we did not repurchase any of our ordinary shares under the share repurchase program. As of December 31, 2022, the remaining amount authorized under the share repurchase program was $431.2 million.

Authorized But Unissued Ordinary Shares

We had reserved the following shares of authorized but unissued ordinary shares (in thousands):

	December 31,	
	2022	2021
2011 Equity Incentive Plan	23,689	22,195
2007 Employee Stock Purchase Plan	4,069	3,285
GW Incentive Plans	1,707	1,853
Amended and Restated 2007 Non-Employee Directors Stock Award Plan	755	807
Total	30,220	28,140

Dividends

In 2022 and 2021, we did not declare or pay cash dividends on our common equity. Under Irish law, dividends may only be paid, and share repurchases and redemptions must generally be funded only out of, "distributable reserves." In addition, the terms of our credit agreement restrict our ability to make certain restricted payments, including dividends and other distributions by us in respect of our ordinary shares, subject to, among other exceptions, (1) a general exception for dividends and restricted payments up to $30 million in the aggregate and (2) an exception that allows for restricted payments, subject to a cap equal to the sum of (i) $100 million plus (ii) so long as our secured leverage ratio (as defined in our credit agreement) does not exceed 3:1 after giving pro forma effect to the restricted payment, a formula-based amount tied to our consolidated net income; provided that such cap applies only if our total leverage ratio (as defined in our credit agreement) exceeds 2:1 after giving pro forma effect to the restricted payment. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our consolidated financial condition, results of operations, capital requirements, compliance with the terms of our credit agreement or other future borrowing arrangements, and other factors our board of directors deems relevant.

16. Comprehensive Income (Loss)

Comprehensive income (loss) includes net income (loss) and all changes in shareholders' equity during a period, except for those changes resulting from investments by shareholders or distributions to shareholders.

Accumulated Other Comprehensive Loss

The components of accumulated other comprehensive loss as of December 31, 2022 and 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	—	(725,277)	(725,277)
Amounts reclassified from accumulated other comprehensive income (loss)	128	—	128
Other comprehensive income (loss), net	128	(725,277)	(725,149)
Balance at December 31, 2022	$ —	$ (1,125,509)	$ (1,125,509)

In 2022, other comprehensive loss reflects foreign currency translation adjustments, primarily due to the weakening of sterling and the euro against the U.S. dollar.

17. Net Income (Loss) per Ordinary Share

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

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

	Year Ended December 31,		
	2022	2021	2020
Numerator:			
Net income (loss)	$ (224,060)	$ (329,668)	$ 238,616
Denominator:			
Weighted-average ordinary shares used in per share calculations - basic	62,539	59,694	55,712
Dilutive effect of employee equity incentive and purchase plans	—	—	805
Weighted-average ordinary shares used in per share calculations - diluted	62,539	59,694	56,517
Net income (loss) per ordinary share:			
Basic	$ (3.58)	$ (5.52)	$ 4.28
Diluted	$ (3.58)	$ (5.52)	$ 4.22

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 PRSUs, and the assumed issuance of ordinary shares under our employee stock purchase plan, or ESPP.

We adopted ASU 2020-06 on January 1, 2022, on a modified retrospective basis, which eliminates the treasury stock method to calculate diluted earnings per share for convertible instruments and requires the use of the if-converted method. The potential issue of ordinary shares upon exchange of the Exchangeable Senior Notes was anti-dilutive and had no impact on diluted net loss per ordinary share for 2022.

In 2021 and 2020, potentially dilutive ordinary shares from the Exchangeable Senior Notes were determined by applying the treasury stock method to the assumed issuance of ordinary shares upon exchange of the Exchangeable Senior Notes. The average price of our ordinary shares in 2021 exceeded the effective exchange price per ordinary share of the 2026 Notes. However, the potential ordinary shares issuable upon exchange were excluded from the calculation of diluted net loss per ordinary shares because their effect would have been anti-dilutive. The average price of our ordinary shares in 2021 did not exceed the effective exchange price per ordinary share of the 2021 Notes and 2024 Notes. The potential issue of ordinary shares issuable upon exchange of the Exchangeable Senior Notes had no effect on diluted net income per ordinary share for 2020 as the average price of our ordinary shares during 2020 did not exceed the effective exchange prices per ordinary share of the Exchangeable Senior Notes.

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

	Year Ended December 31,		
	2022	2021	2020
Exchangeable Senior Notes	9,044	9,725	8,077
Employee equity incentive and purchase plans	2,751	3,927	4,780

18. Segment and Other Information

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.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

The following table presents total long-lived assets by location (in thousands):

	December 31,	
	2022	2021
Ireland	$ 71,276	$ 65,478
United Kingdom	143,870	176,778
United States	63,559	76,290
Italy	15,768	16,698
Other	6,904	8,179
Total long-lived assets (1)	$ 301,377	$ 343,423

(1) Long-lived assets consist of property, plant and equipment and operating lease assets.

19. Revenues

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

	Year Ended December 31,		
	2022	2021	2020
Xyrem	$ 1,020,453	$ 1,265,830	$ 1,741,758
Xywav	958,425	535,297	15,264
Total Oxybate	1,978,878	1,801,127	1,757,022
Epidiolex/Epidyolex	736,398	463,645	—
Sativex	16,825	12,707	—
Sunosi	28,844	57,914	28,333
Total Neuroscience	2,760,945	2,335,393	1,785,355
Zepzelca	269,912	246,808	90,380
Rylaze	281,659	85,629	—
Vyxeos	127,980	134,060	121,105
Defitelio/defibrotide	194,290	197,931	195,842
Erwinaze/Erwinase	—	69,382	147,136
Total Oncology	873,841	733,810	554,463
Other	6,643	9,798	6,842
Product sales, net	3,641,429	3,079,001	2,346,660
Royalties and contract revenues	17,945	15,237	16,907
Total revenues	$ 3,659,374	$ 3,094,238	$ 2,363,567

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

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

	Year Ended December 31,		
	2022	2021	2020
United States	$ 3,370,379	$ 2,820,242	$ 2,144,541
Europe	239,638	230,158	175,208
All other	49,357	43,838	43,818
Total revenues	$ 3,659,374	$ 3,094,238	$ 2,363,567

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

	Year Ended December 31,		
	2022	2021	2020
ESSDS	56 %	60 %	74 %
McKesson	11 %	12 %	12 %

Financing and payment

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

Contract Liabilities - Deferred Revenue

The deferred revenue balance as of December 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 $2.1 million in 2022 relating to these upfront payments. The deferred revenue balances are being recognized over an average of four years representing the period we expect to perform our research and developments obligations under each agreement.

The following table presents a reconciliation of our beginning and ending balances in contract liabilities from contracts with customers for the year ended December 31, 2022 (in thousands):

	Contract Liabilities
Balance as of December 31, 2021	$ 2,556
Amount recognized within royalties and contract revenues	(2,093)
Balance as of December 31, 2022	$ 463

20. Share-Based Compensation

GW Incentive Plans

On May 5, 2021, Jazz Pharmaceuticals plc acquired the entire issued share capital of GW Pharmaceuticals plc. In connection with the GW Acquisition, we assumed the GW Pharmaceuticals plc 2008 Long-Term Incentive Plan, GW Pharmaceuticals plc 2017 Long-Term Incentive Plan and GW Pharmaceuticals plc 2020 Long-Term Incentive Plan, each as amended from time to time, together referred to as the GW Incentive Plans. The terms of the GW Incentive Plans provide for the grant of stock options, stock appreciation rights, RSUs, other stock awards, and performance awards that may be settled in cash, shares, or other property. Ordinary shares granted to employees in exchange for GW ADS in connection with the GW Acquisition vest ratably over service periods of two years, while all post-acquisition grants vest ratably over service periods of four years and expire no more than 10 years after the date of grant. As of December 31, 2022, a total of 1,864,475 of our ordinary shares had been authorized for issuance under the GW Incentive Plans.

2011 Equity Incentive Plan

On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma were combined in a merger transaction, or the Azur Merger. In connection with the Azur Merger, Jazz Pharmaceuticals, Inc.’s board of directors adopted the 2011 Equity Incentive Plan, or the 2011 Plan, in October 2011 and its stockholders approved the 2011 Plan at the special meeting of the stockholders held in December 2011 in connection with the Azur Merger. The 2011 Plan became effective

immediately before the consummation of the Azur Merger and was assumed and adopted by us upon the consummation of the Azur Merger. The terms of the 2011 Plan provide for the grant of stock options, stock appreciation rights, RSUs, other stock awards, and performance awards that may be settled in cash, shares, or other property. All outstanding grants under the 2011 Plan were granted to employees and vest ratably over service periods of four years and expire no more than 10 years after the date of grant. As of December 31, 2022, a total of 34,836,988 of our ordinary shares had been authorized for issuance under the 2011 Plan.

2007 Employee Stock Purchase Plan

In 2007, Jazz Pharmaceuticals, Inc.'s employees became eligible to participate in the ESPP. The ESPP was amended and restated by Jazz Pharmaceuticals, Inc.'s board of directors in October 2011 and approved by its stockholders in December 2011. The amended and restated ESPP became effective immediately prior to the effective time of the Azur Merger and was assumed by us upon the consummation of the Azur Merger. The amended and restated ESPP allows our eligible employee participants (including employees of any of a parent or subsidiary company if our board of directors designates such company as eligible to participate) to purchase our ordinary shares at a discount of 15% through payroll deductions. The ESPP consists of a fixed offering period of 24 months with four purchase periods within each offering period. The number of shares available for issuance under our ESPP during any six-month purchase period is 175,000 shares. As of December 31, 2022, a total of 7,029,250 of our ordinary shares had been authorized for issuance under the ESPP.

Amended and Restated 2007 Non-Employee Directors Stock Award Plan

The Amended and Restated 2007 Non-Employee Directors Stock Award Plan, or the 2007 Directors Award Plan, which was initially adopted by the Jazz Pharmaceuticals, Inc. board of directors and approved by the Jazz Pharmaceuticals, Inc. stockholders in connection with its initial public offering, was continued and assumed by us upon the consummation of the Azur Merger. Until October 2011, the 2007 Directors Award Plan provided for the automatic grant of stock options to purchase shares of Jazz Pharmaceuticals, Inc.'s common stock to its non-employee directors initially at the time any individual first became a non-employee director, which vest over three years, and then annually over their period of service on its board of directors, which vest over one year. On October 24, 2011, Jazz Pharmaceuticals, Inc.'s board of directors amended the 2007 Directors Award Plan to eliminate all future initial and annual automatic grants so that future automatic grants would not be made that would be subject to the excise tax imposed by Section 4985 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, in connection with the Azur Merger. Accordingly, all future stock option grants under the 2007 Directors Award Plan will be at the discretion of our board of directors. Since the Azur Merger, all of the new grants under the 2007 Directors Award Plan were granted to non-employee directors and vest ratably over service periods of one to three years and expire no more than 10 years after the date of grant. In addition, the 2007 Directors Award Plan provides the source of shares to fund distributions made prior to August 15, 2010 under the Directors Deferred Compensation Plan described below. In August 2016, our shareholders approved our proposal to expand the types of stock awards that may be granted to our non-employee directors under the 2007 Directors Award Plan and eliminate the final automatic share reserve increase under the 2007 Directors Award Plan that was scheduled to occur on January 1, 2017. In July 2020, our shareholders approved our proposal to increase the number of ordinary shares authorized for issuance under the 2007 Directors Award Plan by 500,000 shares. As of December 31, 2022, a total of 1,403,938 of our ordinary shares had been authorized for issuance under the 2007 Directors Award Plan.

Amended and Restated Directors Deferred Compensation Plan

In May 2007, the Jazz Pharmaceuticals, Inc. board of directors adopted the Directors Deferred Compensation Plan, or the Directors Deferred Plan, which was amended in December 2008 and was then amended and restated in August 2010, and which was continued and assumed by us upon consummation of the Azur Merger. The Directors Deferred Plan allows each non-employee director to elect to defer receipt of all or a portion of his or her annual retainer fees to a future date or dates. Amounts deferred under the Directors Deferred Plan are credited as shares of Jazz Pharmaceuticals, Inc.'s common stock (or our ordinary shares following the Azur Merger) to a phantom stock account, the number of which are based on the amount of the retainer fees deferred divided by the market value of Jazz Pharmaceuticals, Inc.'s common stock (or our ordinary shares following the Azur Merger) on the first trading day of the first open window period following the date the retainer fees are deemed earned. On the 10th business day following the day of separation from the board of directors or the occurrence of a change in control, or as soon thereafter as practical once the non-employee director has provided the necessary information for electronic deposit of the deferred shares, each non-employee director will receive (or commence receiving, depending upon whether the director has elected to receive distributions from his or her phantom stock account in a lump sum or in installments over time) a distribution of his or her phantom stock account, in our ordinary shares (i) reserved under the 2007 Directors Option Plan prior to August 15, 2010 and (ii) from a new reserve of 200,000 shares set up under the Directors Deferred Plan on August 15, 2010. Since the consummation of the Azur Merger, we have not permitted non-employee directors to defer any annual retainer fees under the Directors Deferred Plan. On October 31, 2019, our board of directors approved the termination of the Directors

Deferred Plan, and all outstanding phantom stock was distributed to each applicable non-employee director on November 2, 2020. We recorded no expense in 2022, 2021 and 2020 related to retainer fees earned and deferred.

Share-Based Compensation

There were no share options granted in 2022. The table below shows, for market strike price option grants, the weighted-average assumptions used in the Black-Scholes option pricing model and the resulting weighted-average grant date fair value of market strike price option grants granted in 2021 and 2020:

	Year Ended December 31,	
	2021	2020
Grant date fair value	$ 51.39	$ 34.68
Volatility	37 %	33 %
Expected term (years)	4.5	4.6
Range of risk-free rates	0.4-0.8%	0.2-1.6%
Expected dividend yield	— %	— %

We rely on a blend of the historical and implied volatilities of our own ordinary shares to determine expected volatility for share option grants. In addition, we use a single volatility estimate for each share option grant. The weighted-average volatility is determined by calculating the weighted average of volatilities for all share options granted in a given year.

The expected term of share option grants represents the weighted-average period the awards are expected to remain outstanding and our estimates were based on historical exercise data. The risk-free interest rate assumption was based on zero coupon U.S. Treasury instruments whose term was consistent with the expected term of our share option grants. The expected dividend yield assumption was based on our history and expectation of dividend payouts.

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

	Year Ended December 31,		
	2022	2021	2020
Selling, general and administrative	$ 151,986	$ 135,285	$ 84,384
Research and development	57,522	43,758	29,242
Cost of product sales	12,488	9,963	7,372
Total share-based compensation expense, pre-tax	221,996	189,006	120,998
Income tax benefit from share-based compensation expense	(41,058)	(33,958)	(12,838)
Total share-based compensation expense, net of tax	$ 180,938	$ 155,048	$ 108,160

We recognized income tax benefits related to share option exercises of $8.0 million, $9.3 million and $3.9 million in 2022, 2021 and 2020, respectively.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Share Options

The following table summarizes information as of December 31, 2022 and activity during 2022 related to our share option plans:

	Shares Subject to Outstanding Options (In thousands)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2022	4,121	$ 134.48		
Options exercised	(777)	106.76		
Options forfeited	(60)	129.91		
Options expired	(95)	157.03		
Outstanding at December 31, 2022	3,189	$ 140.64	4.8	$ 68,277
Vested and expected to vest at December 31, 2022	3,170	$ 140.70	4.8	$ 67,708
Exercisable at December 31, 2022	2,907	$ 141.78	4.5	$ 59,443

Aggregate intrinsic value shown in the table above is equal to the difference between the exercise price of the underlying share options and the fair value of our ordinary shares for share options that were in the money. The aggregate intrinsic value changes based on the fair market value of our ordinary shares. The aggregate intrinsic value of share options exercised was $34.8 million, $51.8 million and $26.4 million during 2022, 2021 and 2020, respectively. We issued new ordinary shares upon exercise of share options.

As of December 31, 2022, total compensation cost not yet recognized related to unvested share options was $9.6 million, which is expected to be recognized over a weighted-average period of 1.2 years.

As of December 31, 2022, total compensation cost not yet recognized related to grants under the ESPP was $6.3 million, which is expected to be recognized over a weighted-average period of 1.0 year.

Nominal Strike Price Options

During the second quarter of 2021, we issued nominal strike price options to replace certain unvested GW awards in connection with the GW Acquisition with a weighted-average grant date fair value of $170.82. The fair value of nominal strike price options was determined on the date of the grant based on the market price of our ordinary shares as of that date.

The following table summarizes information as of December 31, 2022 and activity during 2022 related to our nominal strike price options:

	Shares Subject to Outstanding Options (In thousands)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2022	116	$ 0.02		
Options exercised	(55)	0.02		
Options forfeited	(5)	0.02		
Outstanding at December 31, 2022	56	$ 0.02	7.2	$ 8,957
Vested and expected to vest at December 31, 2022	56	$ 0.02	7.2	$ 8,865
Exercisable at December 31, 2022	22	$ 0.02	6.3	$ 3,530

The aggregate intrinsic value of nominal strike price options exercised was $8.4 million and $0.2 million during 2022 and 2021, respectively. We issued new ordinary shares upon exercise of nominal strike price options.

As of December 31, 2022, total compensation cost not yet recognized related to unvested nominal strike price options was $0.8 million, which is expected to be recognized over a weighted-average period of 0.2 years.

Restricted Stock Units

In 2022, 2021 and 2020, we granted RSUs covering an equal number of our ordinary shares to employees with a weighted-average grant date fair value of $152.08, $168.10 and $117.23, respectively. The fair value of RSUs is determined on the date of grant based on the market price of our ordinary shares as of that date. The fair value of the RSUs is recognized as an expense ratably over the vesting period of four years. In 2022, 2021 and 2020, 910,000, 692,000 and 423,000 RSUs were

released, respectively, with 610,000, 465,000 and 290,000 ordinary shares issued, respectively, and 300,000, 227,000 and 133,000 ordinary shares withheld for tax purposes, respectively. The total fair value of shares vested was $138.1 million, $109.2 million and $53.5 million during 2022, 2021 and 2020, respectively.

As of December 31, 2022, total compensation cost not yet recognized related to unvested RSUs was $288.8 million, which is expected to be recognized over a weighted-average period of 2.5 years.

The following table summarizes information as of December 31, 2022 and activity during 2022 related to our RSUs:

	Number of RSUs (In thousands)	Weighted-Average Grant-Date Fair Value	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2022	2,631	$ 149.05		
RSUs granted	2,138	152.08		
RSUs released	(910)	146.63		
RSUs forfeited	(650)	152.24		
Outstanding at December 31, 2022	3,209	$ 151.11	1.4	$ 511,185

Performance-Based Restricted Stock Units

The Compensation & Management Development Committee of our board of directors approved awards of PRSUs to certain employees of the Company, subject to vesting on the achievement of certain commercial and pipeline performance criteria to be assessed over a performance period from the date of the grant to December 31, 2023 and December 31, 2024, respectively. Following the determination of the Company's achievement with respect to the performance criteria, the amount of shares awarded will be subject to adjustment based on the application of a relative 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 following table summarizes information as of December 31, 2022 and activity during 2022 related to our PRSUs:

	Number of PRSUs (In thousands)	Weighted-Average Grant-Date Fair Value	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2022	214	$ 190.81		
PRSUs granted	293	178.78		
PRSUs forfeited	(67)	184.99		
Outstanding at December 31, 2022	440	$ 183.68	1.6	$ 70,066

As of December 31, 2022, total compensation cost not yet recognized related to unvested PRSUs was $46.0 million, which is expected to be recognized over a weighted-average period of 1.6 years.

As the PRSUs granted in 2021 and 2022 are subject to a market condition, the grant date fair value for such PRSUs was based on a Monte Carlo simulation model. In 2022 and 2021, we granted PRSUs to employees with a weighted-average grant date fair value of $178.78 and $190.81, respectively. The Company evaluated the performance targets in the context of its current long-range financial plan and its product candidate development pipeline and recognized compensation expense based on the probable number of awards that will ultimately vest.

21. Employee Benefit Plans

We maintain a qualified 401(k) savings plan, in which all U.S. based employees are eligible to participate, provided they meet the requirements of the plan. We match certain employee contributions under the 401(k) savings plan and for the years ended December 31, 2022, 2021 and 2020 we recorded expense of $10.6 million, $9.1 million and $6.3 million, respectively, related to this plan.

We also operate a number of defined contribution retirement plans for certain non-U.S. based employees. Expenses related to contributions to such plans for the years ended December 31, 2022, 2021 and 2020 were $14.6 million, $11.4 million and $4.2 million, respectively.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

22. Income Taxes

The components of income (loss) before income tax expense (benefit) and equity in loss of investees were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Ireland	$ (50,311)	$ 97,557	$ (102,328)
United Kingdom	(963,598)	(681,291)	3,836
United States	224,453	221,185	372,910
Other	416,672	249,711	677
Total	$ (372,784)	$ (112,838)	$ 275,095

The following table sets forth the details of income tax expense (benefit) (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Current			
Ireland	$ 61,550	$ 25,770	$ 19,437
United Kingdom	1,454	(924)	166
United States	37,823	88,850	110,896
Other	32,779	33,222	39,955
Total current tax expense	133,606	146,918	170,454
Deferred, exclusive of other components below			
Ireland	(62,011)	(5,388)	(32,458)
United Kingdom	(193,219)	(111,534)	679
United States	(9,086)	(46,531)	(29,117)
Other	(11,144)	(28,604)	(74,278)
Total deferred, exclusive of other components	(275,460)	(192,057)	(135,174)
Deferred, change in tax rates			
United Kingdom	(16,990)	259,873	(1,155)
United States	201	1,377	(371)
Other	(2)	5	(237)
Total deferred, change in tax rates	(16,791)	261,255	(1,763)
Total deferred tax expense (benefit)	(292,251)	69,198	(136,937)
Total income tax expense (benefit)	$ (158,645)	$ 216,116	$ 33,517

Our income tax benefit was $158.6 million in 2022 and our income tax expense was $216.1 million and $33.5 million in 2021 and 2020, respectively, relating to tax arising on income or losses in Ireland, the U.K., the U.S. and certain other foreign jurisdictions, offset by deductions on subsidiary equity, originating tax credits and FDII benefits. Our income tax benefit in 2022 increased primarily due to payments for acquired IPR&D made in the year and the impact of the impairment of our acquired IPR&D asset as a result of the decision to discontinue our nabiximols program. Our income tax expense in 2021 included an expense of $259.9 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory tax rate in the U.K. following enactment of the U.K. Finance Act 2021. Our income tax expense in 2020 included the impact of the disallowance of certain interest deductions and a provision for a proposed settlement reached with the French taxing authorities.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

The reconciliation between income tax expense (benefit) at the Irish statutory income tax rate of 12.5 percent, the jurisdiction of tax domicile of Jazz Pharmaceuticals, applied to income before the income tax expense (benefit) and equity in loss of investees and our reported income tax expense (benefit) was as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Income tax expense (benefit) at the statutory income tax rate	$ (46,598)	$ (14,105)	$ 34,387
Deduction on subsidiary equity	(158,488)	(116,438)	(25,740)
Change in valuation allowance	95,051	81,280	6,074
Foreign derived intangible income benefit	(29,541)	(3,416)	—
Research and other tax credits	(27,976)	(31,069)	(30,836)
Change in tax rate	(16,790)	261,663	(1,836)
Change in estimates	(14,065)	(2,653)	(3,604)
Non-deductible compensation	13,505	19,914	8,604
Non-deductible facility expense	8,093	—	—
Non-deductible royalty expense	6,274	—	—
Patent box incentive benefit	(6,203)	—	—
Foreign income tax rate differential	5,863	(4,343)	16,126
Change in unrecognized tax benefits	5,029	(6,436)	16,309
Non-deductible financing costs	4,504	14,418	7,132
Tax deficiencies/(excess tax benefits) from share-based compensation	(1,690)	(5,555)	5,274
Non-deductible acquisition-related costs	—	20,929	—
Other	4,387	1,927	1,627
Reported income tax expense (benefit)	$ (158,645)	$ 216,116	$ 33,517

Significant components of our net deferred tax assets (liabilities) were as follows (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Operating loss carryforwards	$ 263,235	$ 265,156
Intangible assets	236,462	176,904
Tax credit carryforwards	189,792	284,155
Deduction on subsidiary equity carryforwards	157,367	78,514
Accrued liabilities	109,257	84,110
Capitalized research and development	88,009	13,453
Indirect effects of unrecognized tax benefits	47,224	46,876
Share-based compensation	42,795	37,289
Lease liabilities	14,081	15,865
Other	11,595	65,224
Total deferred tax assets	1,159,817	1,067,547
Valuation allowance	(234,732)	(154,255)
Deferred tax assets, net of valuation allowance	925,085	913,292
Deferred tax liabilities:		
Intangible assets	(1,367,146)	(1,652,297)
Inventories	(110,927)	(181,742)
Operating lease assets	(10,978)	(12,657)
Other	(4,124)	(56,034)
Total deferred tax liabilities	(1,493,175)	(1,902,730)
Net of deferred tax assets and (liabilities)	$ (568,090)	$ (989,438)

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

The net change in valuation allowance was an increase of $80.5 million, $76.9 million and $11.0 million in 2022, 2021 and 2020, respectively.

The following table summarizes the presentation of deferred tax assets and liabilities (in thousands):

	December 31,	
	2022	2021
Deferred tax assets	$ 376,247	$ 311,103
Deferred tax liabilities	(944,337)	(1,300,541)
Net of deferred tax assets and (liabilities)	$ (568,090)	$ (989,438)

As of December 31, 2022, we had net operating losses, or NOL, carryforwards and tax credit carryforwards for U.S. federal income tax purposes of approximately $21.5 million and $117.2 million, respectively, available to reduce future income subject to income taxes. The U.S. federal NOL carryforwards will expire, if not utilized, in the tax years 2023 to 2033, and the U.S. federal tax credits will expire, if not utilized, in the tax years 2023 to 2042. In addition, we had approximately $28.7 million of NOL carryforwards and $5.9 million of tax credit carryforwards as of December 31, 2022 available to reduce future taxable income for U.S. state income tax purposes. The U.S. state NOL carryforwards will expire, if not utilized, in the tax years 2023 to 2041. As of December 31, 2022, there were NOL and other carryforwards for income tax purposes of approximately $927.1 million, $449.6 million and $188.3 million available to reduce future income subject to income taxes in the United Kingdom, Malta and Ireland respectively. The NOLs and other carryforwards generated in the United Kingdom, Malta and Ireland have no expiration date. We also had foreign tax credit carryforwards in Ireland, as of December 31, 2022, of $66.2 million, which may only be utilized against certain sources of income. The foreign tax credit carryforwards have no expiration date.

Utilization of certain of our NOL and tax credit carryforwards in the U.S. is subject to an annual limitation due to the ownership change limitations provided by Sections 382 and 383 of the Internal Revenue Code and similar state provisions. Such an annual limitation may result in the expiration of certain NOLs and tax credits before future utilization. In addition, as a result of the Azur Merger, until 2022 we were subject to certain limitations under the Internal Revenue Code in relation to the utilization of U.S. NOLs to offset U.S. taxable income resulting from certain transactions.

Valuation allowances require an assessment of both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. Such assessment is required by tax paying component. Our valuation allowance was $234.7 million and $154.3 million as of December 31, 2022 and 2021, respectively, for certain Irish, U.S. (federal and state) and foreign deferred tax assets which we maintain until sufficient positive evidence exists to support reversal. As part of the overall change in valuation allowance, we recognized a net income tax expense of $95.1 million and $81.3 million in 2022 and 2021, respectively, relating primarily to the creation of a valuation allowance against certain deferred tax assets primarily associated with temporary differences related to foreign subsidiaries and foreign tax credit carryforwards. We periodically evaluate the likelihood of the realization of deferred tax assets and will adjust such amounts in light of changing facts and circumstances including, but not limited to, future projections of taxable income, tax legislation, rulings by relevant taxing authorities, the progress of tax examinations and the regulatory approval of products currently under development. Realization of the deferred tax assets is dependent on future taxable income. The Company believes that it is more likely than not to generate sufficient taxable income to realize the deferred tax assets carried as of December 31, 2022 for which no valuation allowance has been recognized.

No provision has been made for income tax on undistributed earnings of the Company’s foreign subsidiaries where such earnings are considered indefinitely reinvested in the foreign operations. Temporary differences related to such earnings totaled approximately $2.7 billion as of December 31, 2022. In the event of the distribution of those earnings in the form of dividends, a sale of the subsidiaries, or certain other transactions, we may be liable for income taxes, subject to an adjustment, if any, for foreign tax credits. The Company estimates that it would incur additional income taxes of up to approximately $135.0 million on repatriation of these unremitted earnings to Ireland.

We only 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.

A reconciliation of our gross unrecognized tax benefits follows (in thousands):

	December 31,		
	2022	2021	2020
Balance at the beginning of the year	$ 137,867	$ 146,557	$ 124,319
Increases related to current year tax positions	25,128	26,675	27,908
Increases related to prior year tax positions	2,794	211	19,712
Decreases related to prior year tax positions	(164)	(182)	(213)
Increases recognized through purchase accounting	—	5,916	—
Decreases related to settlements with taxing authorities	(223)	(14,744)	—
Lapse of the applicable statute of limitations	(21,426)	(26,566)	(25,169)
Balance at the end of the year	$ 143,976	$ 137,867	$ 146,557

The unrecognized tax benefits were included in income taxes payable, other non-current liabilities and deferred tax assets, net, in our consolidated balance sheets. Interest related to our unrecognized tax benefits is recorded in the income tax benefit in our consolidated statements of income (loss). As of December 31, 2022 and 2021, our accrued interest related to income taxes was $5.8 million and $4.6 million, respectively. Interest related to income taxes benefits recognized in the consolidated statements of income (loss) were not significant. Included in the balance of unrecognized tax benefits were potential benefits of $91.7 million and $82.0 million at December 31, 2022 and 2021, respectively, that, if recognized, would affect the effective tax rate on income.

We file income tax returns in multiple tax jurisdictions, the most significant of which are Ireland, the U.K. and the U.S. (both at the federal level and in various state jurisdictions). For Ireland we are no longer subject to income tax examinations by taxing authorities for the years prior to 2018. For the U.K. we are no longer subject to income tax examinations by taxing authorities for the years prior to 2016. 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 2018 and earlier may still be adjusted upon examination by the taxing authorities. Certain of our Luxembourg subsidiaries are currently under examination by the Luxembourg taxing authorities for the years ended December 31, 2017, 2018 and 2019. In October 2022, we received tax assessment notices from the Luxembourg taxing authorities for 2017 and 2018 relating to certain transfer pricing and other adjustments. The notices propose additional Luxembourg income tax of approximately $18.8 million, translated at the foreign exchange rate as December 31, 2022. We disagree with the proposed assessments and are contesting them vigorously.

Schedule II

Valuation and Qualifying Accounts
(In thousands)

		Balance at beginning of period	Additions charged to costs and expenses	Other Additions	Deductions	Balance at end of period
For the year ended December 31, 2022						
Allowance for doubtful accounts	(1)	$ 298	$ —	$ —	$ (56)	$ 242
Allowance for sales discounts	(1)	2,126	20,133	—	(19,279)	2,980
Allowance for chargebacks	(1)	11,389	135,854	—	(132,622)	14,621
Deferred tax asset valuation allowance	(2)(4)	154,255	95,947	—	(15,470)	234,732
For the year ended December 31, 2021						
Allowance for doubtful accounts	(1)	$ 50	$ 127	$ 771	$ (650)	$ 298
Allowance for sales discounts	(1)	144	13,196	1,243	(12,457)	2,126
Allowance for chargebacks	(1)	5,293	91,425	1,322	(86,651)	11,389
Deferred tax asset valuation allowance	(2)(3)(4)	77,342	82,820	9	(5,916)	154,255
For the year ended December 31, 2020						
Allowance for doubtful accounts	(1)	$ 50	$ 5	$ —	$ (5)	$ 50
Allowance for sales discounts	(1)	113	1,432	—	(1,401)	144
Allowance for chargebacks	(1)	1,133	45,550	—	(41,390)	5,293
Deferred tax asset valuation allowance	(2)(3)(4)	66,307	6,576	4,961	(502)	77,342

(1) Shown as a reduction of accounts receivable. Charges related to sales discounts and chargebacks are reflected as a reduction of revenue.

(2) Additions to the deferred tax asset valuation allowance charged to costs and expenses relate to movements on certain Irish, U.S. (federal and state) and other foreign deferred tax assets where we continue to maintain a valuation allowance until sufficient positive evidence exists to support reversal.

(3) Other additions to the deferred tax asset valuation allowance in 2020 and 2021 relate to currency translation adjustments recorded directly in other comprehensive income.

(4) Deductions from the deferred tax asset valuation allowance include movements relating to utilization of NOLs and tax credit carryforwards, release in valuation allowance and other movements including adjustments following finalization of tax returns and currency translation adjustments.

Exhibit 4.6

DESCRIPTION OF SHARE CAPITAL

The following description of the share capital of Jazz Pharmaceuticals plc, or the Company, is a summary. This summary does not purport to be complete and is qualified in its entirety by reference to the Irish Companies Act 2014 (as amended), or the Companies Act, and the complete text of the Company's amended and restated memorandum and articles of association, which amended and restated memorandum and articles of association, or the Company's Constitution, are filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission, or SEC, on August 9, 2016. You should read those laws and documents carefully.

Capital Structure

Authorized Share Capital

The authorized share capital of the Company is €40,000 and $30,000, divided into 4,000,000 non-voting euro deferred shares with nominal value of €0.01 per share and 300,000,000 ordinary shares with nominal value of $0.0001 per share.

The Company may issue shares subject to the maximum authorized share capital contained in the Company's Constitution. The authorized share capital may be increased or reduced (but not below the number of shares then issued and outstanding) by a resolution approved by a simple majority of the votes cast at a general meeting, in person or by proxy, of the Company's shareholders (referred to under Irish law as an "ordinary resolution"). The shares comprising the Company's authorized share capital may be divided into shares of such nominal value as the resolution shall prescribe. As a matter of Irish law, the directors of a company may issue new ordinary or preferred shares for cash without shareholder approval once authorized to do so by the memorandum and articles of association or by an ordinary resolution adopted by the shareholders at a general meeting. The authorization may be granted for a maximum period of five years, at which point it must be renewed by the shareholders by an ordinary resolution.

The Company's board of directors is authorized pursuant to shareholder resolutions passed on July 29, 2021 to issue new ordinary or preferred shares for cash without shareholder approval for a period of five years from the date of the passing of the resolutions.

The rights and restrictions to which ordinary shares are subject are prescribed in the Company's Constitution. The Company's Constitution permits it to issue preferred shares once authorized to do so by ordinary resolution. The Company may, by ordinary resolution and without obtaining any vote or consent of the holders of any class or series of shares, unless expressly provided by the terms of that class or series of shares, provide from time to time for the issuance of other classes or series of shares and to establish the characteristics of each class or series, including the number of shares, designations, relative voting rights, dividend rights, liquidation and other rights, redemption, repurchase or exchange rights and any other preferences and relative, participating, optional or other rights and limitations not inconsistent with applicable law.

Irish law does not recognize fractional shares held of record. Accordingly, the Company's Constitution does not provide for the issuance of fractional shares, and the official Irish register of the Company will not reflect any

fractional shares. Whenever an alteration or reorganization of the Company's share capital would result in any shareholder becoming entitled to fractions of a share, the Company's board of directors may, on behalf of those shareholders that would become entitled to fractions of a share, sell the shares representing the fractions for the best price reasonably obtainable, to any person and distribute the proceeds of the sale in due proportion among those members.

Issued Share Capital

As of December 31, 2022, 63,212,116 ordinary shares were issued and outstanding. In addition, as of December 31, 2022, 4,000,000 non-voting euro deferred shares were issued and outstanding at that time, which shares are held by nominees in order to satisfy an Irish legislative requirement to maintain a minimum level of issued share capital denominated in euro. The euro deferred shares, which are not listed on any stock exchange and are not the subject of any registration, carry no voting rights and are not entitled to receive any dividend or distribution. On a return of assets, whether on liquidation or otherwise, the euro deferred shares will entitle the holder thereof only to the repayment of the amounts paid up on such shares after repayment of the capital paid up on ordinary shares plus the payment of $5,000,000 on each of the ordinary shares and the holders of the euro deferred shares (as such) will not be entitled to any further participation in the assets or profits of the Company.

Preemption Rights, Share Warrants and Share Options

Under Irish law, certain statutory preemption rights apply automatically in favor of shareholders where shares are to be issued for cash. However, the Company has opted out of these preemption rights by way of shareholder resolution as permitted under Irish law. Irish law provides that this opt-out expires every five years unless renewed by a resolution approved by not less than 75% of the votes cast at a general meeting, in person or by proxy, of the Company's shareholders (referred to under Irish law as a "special resolution"). The Company's current opt-out was approved by shareholder resolutions passed at the Company's 2022 annual general meeting on July 28, 2022 (the "**AGM**") and is limited to the allotment of equity securities up to an aggregate nominal value of US$1248.47 (12,484,733 shares) (being equivalent to approximately 20% of the aggregate nominal value of the Company's issued ordinary share capital as at the last practicable date prior to the issue of the notice of the AGM). This opt-out will expire on January 28, 2024 and if it is not renewed before that date, shares issued for cash will need to be offered to existing shareholders on a pro rata basis to their existing shareholding before the shares may be issued to any new shareholders. The statutory preemption rights do not apply (i) where shares are issued for non-cash consideration (such as in a stock-for-stock acquisition), (ii) to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or (iii) where shares are issued pursuant to an employee stock option or similar equity plan.

The Company's Constitution provides that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which it is subject, the Company's board of directors is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as it deems advisable, options to purchase such number of shares of any class or classes or of any series of any class as the Company's board of directors may deem advisable, and to cause warrants or other appropriate instruments evidencing such options to be issued. The Companies Act provides that, save to the extent the constitution of a company provides otherwise, the directors of a company may issue options. The Company is subject to the rules of The NASDAQ Stock Market LLC and the U.S. Internal Revenue Code of 1986, or the Code, which require shareholder approval of certain equity plan and share issuances. The Company's board of directors may issue shares

upon exercise of validly issued warrants or options without shareholder approval or authorization, except as described above (up to the relevant authorized share capital limit).

Dividends

Under Irish law, dividends and distributions may only be made from distributable reserves. Distributable reserves generally means accumulated realized profits less accumulated realized losses and includes reserves created by way of capital reduction. In addition, no distribution or dividend may be made unless the Company's net assets are equal to, or in excess of, the aggregate of its called up share capital plus undistributable reserves and the distribution does not reduce its net assets below such aggregate. Undistributable reserves include the share premium account, the par value of shares acquired by the Company and the amount by which the Company's accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed the Company's accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital.

The determination as to whether or not the Company has sufficient distributable reserves to fund a dividend must be made by reference to its "relevant financial statements." The "relevant financial statements" are either the last set of unconsolidated annual audited financial statements or other financial statements properly prepared in accordance with the Companies Act, which give a "true and fair view" of the Company's unconsolidated financial position and accord with accepted accounting practice. The relevant financial statements must be filed in the Companies Registration Office (the official public registry for companies in Ireland).

The Company's Constitution authorizes the directors to declare dividends without shareholder approval to the extent they appear justified by profits lawfully available for distribution. The Company's board of directors may also recommend a dividend to be approved and declared by the shareholders at a general meeting. The Company's board of directors may direct that the payment be made by distribution of assets, shares or cash, and no dividend issued may exceed the amount recommended by the directors. The dividends declared by the directors or shareholders may be paid in the form of cash or non-cash assets and may be paid in dollars or any other currency.

The Company's board of directors may deduct from any dividend payable to any shareholder any amounts payable by such shareholder to the Company in relation to its shares.

The Company may issue shares with preferred rights to participate in dividends declared by the Company from time to time, as determined by ordinary resolution. The holders of preferred shares may, depending on their terms, rank senior to ordinary shares in terms of dividend rights and/or be entitled to claim arrears of a declared dividend out of subsequently declared dividends in priority to ordinary shareholders.

Share Repurchases, Redemptions and Conversions

Overview

The Company's Constitution provides that, unless the board specifically determines otherwise, any ordinary share that it has agreed to acquire shall be deemed to be a redeemable share. Accordingly, for Irish law purposes, the repurchase of ordinary shares by the Company may technically be effected as a redemption of those shares as described below under "*—Repurchases and Redemptions*." If the Company's Constitution did not contain such provision, repurchases by the Company would be subject to many of the same rules that apply to purchases of its ordinary shares by subsidiaries described below under "*—Purchases by the Company's Subsidiaries*," including the shareholder approval requirements described below, and the requirement that any purchases on market be effected

on a “recognized stock exchange,” which, for purposes of the Companies Act, includes The NASDAQ Global Select Market. Neither Irish law nor any of the Company’s constituent documents places limitations on the right of nonresident or foreign owners to vote or hold its ordinary shares. Except where otherwise noted, references herein to repurchasing or buying back ordinary shares refer to the redemption of ordinary shares by the Company or the purchase of ordinary shares by one of its subsidiaries, in each case in accordance with the Company’s Constitution and Irish law as described below.

Repurchases and Redemptions

Under Irish law, a company may issue redeemable shares and redeem them out of distributable reserves or the proceeds of a new issue of shares for that purpose. Please see also “*—Dividends*.” The Company may not purchase any of its shares if, as a result of such purchase, the nominal value of its issued share capital which is not redeemable would be less than 10% of the nominal value of its total issued share capital. All redeemable shares must also be fully-paid. Redeemable shares may, upon redemption, be cancelled or held in treasury. Based on the provisions of the Company’s Constitution, shareholder approval will not be required to redeem its shares.

The Company may also be given an additional general authority to purchase its ordinary shares on market by way of ordinary resolution, which would take effect on the same terms and be subject to the same conditions as applicable to purchases by the Company’s subsidiaries as described below.

Repurchased and redeemed shares may be cancelled or held as treasury shares. The nominal value of treasury shares held by the Company at any time must not exceed 10% of the aggregate of the par value and share premium received in respect of the allotment of the Company shares together with the par value of any shares acquired by the Company. The Company may not exercise any voting rights in respect of any shares held as treasury shares.

Treasury shares may be cancelled by the Company or re-issued subject to certain conditions.

Purchases by the Company’s Subsidiaries

Under Irish law, an Irish or non-Irish subsidiary of the Company may purchase the Company’s shares either on market or off market. For a subsidiary of the Company to make purchases on market of ordinary shares, the Company’s shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular on market purchase by a subsidiary of ordinary shares is required. For a purchase of ordinary shares by a subsidiary of the Company off market, the proposed purchase contract must be authorized by special resolution of the Company’s shareholders before the contract is entered into. The person whose ordinary shares are to be bought back cannot vote in favor of the special resolution and, from the date of the notice of the meeting at which the resolution approving the contract is proposed, the purchase contract must be on display or must be available for inspection by the Company’s shareholders at the registered office of the Company.

In order for one of the Company’s subsidiaries to make an on market purchase of its shares, such shares must be purchased on a “recognized stock exchange.” The NASDAQ Global Select Market, on which ordinary shares are currently listed, is specified as a recognized stock exchange for this purpose by Irish law.

The number of shares held by the Company’s subsidiaries at any time will count as treasury shares and will be included in any calculation of the permitted treasury share threshold of 10% of the aggregate of the par value and share premium received in respect of the allotment of the Company shares together with the par value of any shares

acquired by the Company. While a subsidiary holds the Company's shares, it cannot exercise any voting rights in respect of those shares and no dividend or other payment (including any payment in a winding up of the Company) shall be payable in respect of those shares. The acquisition of ordinary shares by a subsidiary must be funded out of distributable reserves of the subsidiary.

Lien on Shares, Calls on Shares and Forfeiture of Shares

The Company's Constitution provides that it has a first and paramount lien on every share that is not a fully paid up share for all amounts payable at a fixed time or called in respect of that share. Subject to the terms of their allotment, directors may call for any unpaid amounts in respect of any shares to be paid, and if payment is not made, the shares may be forfeited. These provisions are standard inclusions in the memorandum and articles of association of an Irish public company limited by shares such as the Company's and are only applicable to ordinary shares that have not been fully paid up.

Bonus Shares

Under the Company's Constitution, the Company's board of directors may resolve to capitalize any amount for the time being standing to the credit of any of the Company's reserve accounts or to the credit of the profit and loss account which is not available for distribution through the issuance of fully paid up bonus shares on the same basis of entitlement as would apply in respect of a dividend distribution.

Consolidation and Division; Subdivision

Under the Company's Constitution, the Company may, by ordinary resolution, consolidate and divide all or any of its share capital into shares of larger nominal value than its existing shares or subdivide its shares into smaller amounts than are fixed by the Company's Constitution.

Reduction of Share Capital

The Company may, by ordinary resolution, reduce its authorized share capital in any way. The Company also may, by special resolution and subject to confirmation by the Irish High Court, reduce or cancel its issued share capital (which includes share premium) in any manner permitted by the Companies Act.

Annual Meetings of Shareholders

The Company is required to hold an annual general meeting at intervals of no more than 15 months from the previous annual general meeting, provided that an annual general meeting is held in each calendar year following the first annual general meeting and no more than nine months after the Company's fiscal year-end. The Company's articles of association provide that shareholder meetings may be held outside of Ireland (subject to compliance with the Companies Act). Where a company holds its annual general meeting or extraordinary general meeting outside of Ireland, the Companies Act requires that the company, at its own expense, make all necessary arrangements to ensure that members can by technological means participate in the meeting without leaving Ireland (unless all of the members entitled to attend and vote at the meeting consent in writing to the meeting being held outside of Ireland).

Notice of an annual general meeting must be given to all of the Company's shareholders and to its auditors. The Company's Constitution provides for a minimum notice period of 21 clear days, which is the minimum permitted under Irish law.

The only matters which must, as a matter of Irish law, be transacted at an annual general meeting are the presentation of the annual financial statements and reports of the directors and auditors, a review by the shareholders of the company's affairs, the appointment of new auditors and the fixing of the auditor's remuneration (or delegation of same). If no resolution is made in respect of the reappointment of an existing auditor at an annual general meeting, the existing auditor will be deemed to have continued in office.

Extraordinary General Meetings of Shareholders

Extraordinary general meetings may be convened by (i) the Company's board of directors, (ii) on requisition of the Company's shareholders holding not less than 10% of its paid up share capital carrying voting rights, (iii) on requisition of the Company's auditors or (iv) in exceptional cases, by order of the court. Extraordinary general meetings are generally held for the purpose of approving shareholder resolutions as may be required from time to time. At any extraordinary general meeting only such business shall be conducted as is set forth in the notice thereof.

Notice of an extraordinary general meeting must be given to all of the Company's shareholders and to its auditors. Under Irish law and the Company's Constitution, the minimum notice periods are 21 clear days' notice in writing for an extraordinary general meeting to approve a special resolution and 14 clear days' notice in writing for any other extraordinary general meeting.

In the case of an extraordinary general meeting convened by the Company's shareholders, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of any such valid requisition notice, the Company's board of directors has 21 days to convene a meeting of its shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If the Company's board of directors does not convene the meeting within such 21-day period, the requisitioning shareholders, or any of them representing more than one half of the total voting rights of all of them, may themselves convene a meeting, which meeting must be held within three months of the Company's receipt of the requisition notice.

If the Company's board of directors becomes aware that its net assets are not greater than half of the amount of the Company's called-up share capital, it must convene an extraordinary general meeting of its shareholders not later than 28 days from the date that they learn of this fact to consider how to address the situation.

Quorum for General Meetings

The Company's Constitution provides that no business shall be transacted at any general meeting unless a quorum is present. One or more of the Company's shareholders present in person or by proxy holding not less than a majority of the Company's issued and outstanding shares entitled to vote at the meeting in question constitute a quorum.

Voting

At general meetings of the Company, a resolution put to the vote of the meeting is decided on a poll. The Company's Constitution provides that its board of directors or its chairman may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

Each shareholder is entitled to one vote for each ordinary share that he or she holds as of the record date for the meeting. Voting rights may be exercised by shareholders registered in the Company's share register as of the record date for the meeting or by a duly appointed proxy, which proxy need not be a shareholder. Where interests in shares are held by a nominee trust company, such company may exercise the rights of the beneficial holders on their behalf as their proxy. All proxies must be appointed in the manner prescribed by the Company's Constitution, which permits shareholders to notify the Company of their proxy appointments electronically in such manner as may be approved by the Company's board of directors.

In accordance with the Company's Constitution, it may from time to time be authorized by ordinary resolution to issue preferred shares. These preferred shares may have such voting rights as may be specified in the terms of such preferred shares (e.g., they may carry more votes per share than ordinary shares or may entitle their holders to a class vote on such matters as may be specified in the terms of the preferred shares). Treasury shares or the Company's shares that are held by its subsidiaries are not entitled to be voted at general meetings of shareholders.

Irish law requires special resolutions of the Company's shareholders at a general meeting to approve certain matters. Examples of matters requiring special resolutions include:

- amending the objects or memorandum of association of the Company;
- amending the articles of association of the Company;
- approving a change of name of the Company;
- authorizing the entering into of a guarantee or provision of security in connection with a loan, quasi- loan or credit transaction to a director or a person who is deemed to be "connected" to a director for the purposes of the Companies Act;
- opting out of preemption rights on the issuance of new shares;
- re-registration of the Company from a public limited company to a private company;
- variation of class rights attaching to classes of shares (where the articles of association do not provide otherwise);
- purchase of the Company's shares off market;
- reduction of issued share capital;
- sanctioning a compromise/scheme of arrangement with creditors or shareholders;
- resolving that the Company be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding-up; and
- setting the re-issue price of treasury shares.

Unanimous Shareholder Consent to Action Without Meeting

The Companies Act provides that shareholders may approve an ordinary or special resolution of shareholders without a meeting only if (i) all shareholders sign the written resolution and (ii) the company's articles of association permit written resolutions of shareholders (the Company's articles of association contain the appropriate authorizations for this purpose).

Variation of Rights Attaching to a Class or Series of Shares

Under the Company's Constitution and the Companies Act, any variation of class rights attaching to its issued shares must be approved by a special resolution of the Company's shareholders of the affected class or with the consent in writing of the holders of three-quarters of all the votes of that class of shares.

The provisions of the Company's Constitution relating to general meetings apply to general meetings of the holders of any class of the Company's shares except that the necessary quorum is determined in reference to the shares of the holders of the class. Accordingly, for general meetings of holders of a particular class of the Company's shares, a quorum consists of the holders present in person or by proxy representing at least one half of the issued shares of the class.

Inspection of Books and Records

Under Irish law, shareholders have the right to: (i) receive a copy of the Company's Constitution and any act of the Irish Government which alters its memorandum; (ii) inspect and obtain copies of the minutes of general meetings and the Company's resolutions; (iii) inspect and receive a copy of the register of shareholders, register of directors and secretaries, register of directors' interests and other statutory registers maintained in respect of the ordinary shares; (iv) receive copies of financial statements and directors' and auditors' reports which have previously been sent to shareholders prior to an annual general meeting; and (v) receive financial statements of any of the Company's subsidiaries that have previously been sent to shareholders prior to an annual general meeting for the preceding ten years. The Company's auditors also have the right to inspect all of the Company's books, records and vouchers. The auditors' report must be circulated to the shareholders with the Company's financial statements prepared in accordance with Irish law 21 clear days before the annual general meeting and must be read to the shareholders at the Company's annual general meeting.

Acquisitions

An Irish public limited company may be acquired in a number of ways, including:

- a court-approved scheme of arrangement under the Companies Act. A scheme of arrangement with shareholders requires a court order from the Irish High Court and the approval of a majority in number representing 75% in value of the shareholders present and voting in person or by proxy at a meeting called to approve the scheme;
- through a tender or takeover offer by a third party for all of the Company's shares. Where the holders of 80% or more of the Company's shares have accepted an offer for their shares, the remaining shareholders may also be statutorily required to transfer their shares, and if the bidder does not exercise its "squeeze out" right, then the non-accepting shareholders also have a statutory right to require the bidder to acquire their shares on the same terms. If the Company's shares were to be listed on the main securities market of Euronext Dublin or another main securities market or regulated stock exchange in the European Union, this threshold would be increased to 90%; and
- by way of a merger with an EU-incorporated company under the EU Directive 2017/1132 relating to certain aspects of Company Law (as amended) and the European Communities (Cross-Border Mergers) Regulations 2008 (as amended). Such a merger must be approved by a special resolution.

Irish law does not generally require shareholder approval for a sale, lease or exchange of all or substantially all of a company's property and assets, unless the company is listed on a regulated stock exchange in the European Union.

Appraisal Rights

Generally, under Irish law, shareholders of an Irish company do not have dissenters' or appraisal rights. Under the European Communities (Cross-Border Mergers) Regulations 2008 governing the merger of an Irish company limited by shares such as the Company and a company incorporated in the European Economic Area (the European Economic Area includes all member states of the European Union and Norway, Iceland and Liechtenstein), a shareholder (i) who voted against the special resolution approving the merger or (ii) of a company in which 90% of the shares are held by the other party to the merger, has the right to request that the company acquire its shares for cash at a price determined in accordance with the share exchange ratio set out in the merger agreement.

Disclosure of Interests in Shares

Under the Companies Act, subject to certain limited exceptions, a person must notify the Company (but not the public) if, as a result of a transaction, such person will become interested in three percent or more of the Company's voting shares, or if as a result of a transaction a shareholder who was interested in more than three percent of its voting shares ceases to be so interested. Where any person is interested in more than three percent of the Company's voting shares, such person must notify the Company of any alteration of his or her interest that brings his or her total holding through the nearest whole percentage number, whether an increase or a reduction. The relevant percentage figure is calculated by reference to the aggregate nominal value of the voting shares in which the person is interested as a proportion of the entire nominal value of the Company's issued share capital (or any such class of share capital in issue). Where the percentage level of the person's interest does not amount to a whole percentage, this figure may be rounded down to the next whole number. The Company must be notified within five business days of the transaction or alteration of the person's interests that gave rise to the notification requirement. If a person fails to comply with these notification requirements, such person's rights in respect of any of the Company's shares he or she holds will not be enforceable, either directly or indirectly. However, such person may apply to the court to have the rights attaching to such shares reinstated.

In addition to these disclosure requirements, the Company, under the Companies Act, may, by notice in writing, require a person whom the Company knows or has reasonable cause to believe to be, or at any time during the three years immediately preceding the date on which such notice is issued to have been, interested in shares comprised in the Company's relevant share capital to: (i) indicate whether or not it is the case; and (ii) where such person holds or has during that time held an interest in the Company's shares, to provide additional information, including the person's own past or present interests in the Company's shares. If the recipient of the notice fails to respond within the reasonable time period specified in the notice, the Company may apply to a court for an order directing that the affected shares be subject to certain restrictions, as prescribed by the Companies Act, as follows:

- any transfer of those shares or, in the case of unissued shares, any transfer of the right to be issued with shares and any issue of shares, shall be void;
- no voting rights shall be exercisable in respect of those shares;
- no further shares shall be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and

- no payment shall be made of any sums due from the Company on those shares, whether in respect of capital or otherwise.

The court may also order that shares subject to any of these restrictions be sold with the restrictions terminating upon the completion of the sale.

In the event the Company is in an offer period pursuant to the Irish takeover rules, as defined below, accelerated disclosure provisions apply for persons holding an interest in the Company's securities of one percent or more.

Anti-Takeover Provisions

Irish Takeover Rules and Substantial Acquisition Rules

A transaction in which a third party seeks to acquire 30% or more of the voting rights of the Company and certain other acquisitions of the Company's securities are governed by the Irish Takeover Panel Act 1997 and the Irish Takeover Rules made thereunder, which are referred to herein as the "Irish takeover rules," and are regulated by the Irish Takeover Panel. The "General Principles" of the Irish takeover rules and certain important aspects of the Irish takeover rules are described below.

General Principles

The Irish takeover rules are built on the following General Principles which will apply to any transaction regulated by the Irish Takeover Panel:

- in the event of an offer, all holders of securities of the target company must be afforded equivalent treatment and, if a person acquires control of a company, the other holders of securities must be protected;
- the holders of securities in the target company must have sufficient time and information to enable them to reach a properly informed decision on the offer; where it advises the holders of securities, the board of directors of the target company must give its views on the effects of the implementation of the offer on employment, employment conditions and the locations of the target company's place of business;
- a target company's board of directors must act in the interests of the company as a whole and must not deny the holders of securities the opportunity to decide on the merits of the offer;
- false markets must not be created in the securities of the target company, the bidder or any other company concerned by the offer in such a way that the rise or fall of the prices of the securities becomes artificial and the normal functioning of the markets is distorted;
- a bidder can only announce an offer after ensuring that he or she can pay in full the consideration offered, if such is offered, and after taking all reasonable measures to secure the implementation of any other type of consideration;
- a target company may not be hindered in the conduct of its affairs longer than is reasonable by an offer for its securities (this is a recognition that an offer will disrupt the day-to-day running of a target company, particularly if the offer is hostile and the board of directors of the target company must direct its attention to resisting the offer); and

- an acquisition of securities (whether such acquisition is to be effected by one transaction or a series of transactions) shall take place only at an acceptable speed and shall be subject to adequate and timely disclosure. Specifically, the acquisition of 10% or more of the issued voting shares within a seven day period that would take a shareholder's holding to or above 15% of the issued voting shares (but less than 30%) is prohibited, subject to certain exemptions.

Mandatory Bid

Under certain circumstances, a person who acquires ordinary shares, or other of the Company's voting securities, may be required under the Irish takeover rules to make a mandatory cash offer for the remaining issued and outstanding voting securities at a price not less than the highest price paid for the securities by the acquiror, or any parties acting in concert with the acquiror, during the previous 12 months. This mandatory bid requirement is triggered if an acquisition of securities would increase the aggregate holding of an acquiror, including the holdings of any parties acting in concert with the acquiror, to securities representing 30% or more of the voting rights in the Company, unless the Irish Takeover Panel otherwise consents. An acquisition of securities by a person holding, together with its concert parties, securities representing between 30% and 50% of the voting rights in the Company would also trigger the mandatory bid requirement if, after giving effect to the acquisition, the percentage of the voting rights held by that person (together with its concert parties) would increase by 0.05% within a 12-month period. Any person (excluding any parties acting in concert with the holder) holding securities representing more than 50% of the voting rights of a company is not subject to these mandatory offer requirements in purchasing additional securities.

Voluntary bid; Requirements to Make a Cash Offer and Minimum Price Requirements

If a person makes a voluntary offer to acquire the issued and outstanding ordinary shares of the Company and the bidder acquired ordinary shares in the three-month period prior to the commencement of the offer period, the offer price must not be less than the highest price paid for ordinary shares by the bidder or its concert parties during that period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, taking into account the General Principles, believes it is appropriate to do so.

If the bidder or any of its concert parties has acquired more than 10% of the issued and outstanding ordinary shares (i) during the period of 12 months prior to the commencement of the offer period or (ii) at any time after the commencement of the offer period, the offer must be in cash (or accompanied by a full cash alternative) and the price per ordinary share must not be less than the highest price paid by the bidder or its concert parties during, in the case of (i), the 12-month period prior to the commencement of the offer period or, in the case of (ii), the offer period. The Irish Takeover Panel may apply this rule to a bidder who, together with its concert parties, has acquired less than 10% of the total ordinary shares in the 12-month period prior to the commencement of the offer period if the Irish Takeover Panel, taking into account the General Principles, considers it just and proper to do so.

An offer period will generally commence on the date of the first announcement of the offer or proposed offer.

Substantial Acquisition Rules

The Irish takeover rules also contain rules governing substantial acquisitions of shares and other voting securities which restrict the speed at which a person may increase his or her holding of shares and rights over shares to an aggregate of between 15% and 30% of the voting rights of the Company. Except in certain circumstances, an

acquisition or series of acquisitions of shares or rights over shares representing 10% or more of the voting rights of the Company is prohibited, if such acquisition(s), when aggregated with shares or rights already held, would result in the acquirer holding 15% or more but less than 30% of the voting rights of the Company and such acquisitions are made within a period of seven days. These rules also require accelerated disclosure of acquisitions of shares or rights over shares relating to such holdings.

Frustrating Action

Under the Irish takeover rules, the Company's board of directors is not permitted to take any action that might frustrate an offer for its shares once the Company's board of directors has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which the Company's board of directors has reason to believe an offer is or may be imminent. Exceptions to this prohibition are available where:

- the action is approved by the Company's shareholders at a general meeting; or
- the Irish Takeover Panel has given its consent, where:
- it is satisfied the action would not constitute frustrating action;
- the Company's shareholders holding more than 50% of the voting rights state in writing that they approve the proposed action and would vote in favor of it at a general meeting;
- the action is taken in accordance with a contract entered into prior to the announcement of the offer (or any earlier time at which the Company's board of directors considered the offer to be imminent); or
- the decision to take such action was made before the announcement of the offer and either has been at least partially implemented or is in the ordinary course of business.

Other Provisions

Certain other provisions of Irish law or the Company's Constitution may be considered to have anti-takeover effects, including advance notice requirements for director nominations and other shareholder proposals, as well those described under the following captions: "*—Capital Structure—Authorized Share Capital*" (regarding issuance of preferred shares), "*—Preemption Rights, Share Warrants and Share Options*," "*—Disclosure of Interests in Shares*" and "*—Corporate Governance*."

Corporate Governance

The Company's Constitution delegates the day-to-day management of the Company to the board of directors. The Company's board of directors may then delegate the management of the Company to committees of the board of directors (consisting of one or more members of the board of directors) or executives; regardless, the Company's board of directors remains responsible, as a matter of Irish law, for the proper management of the affairs of the company. Committees may meet and adjourn as they determine proper. A vote at any committee meeting will be determined by a majority of votes of the members present.

The Company's board of directors has a standing audit committee, a compensation committee and a nominating and corporate governance committee, with each committee comprised solely of independent directors, as prescribed by The NASDAQ Global Select Market listing standards and SEC rules and regulations. The Company has adopted corporate governance policies, including a code of conduct and an insider trading policy, as well as an open door reporting policy and a comprehensive compliance program.

The Companies Act require a minimum of two directors. The Company's Constitution provides that the board may determine the size of the board from time to time.

The Company's board of directors is divided into three classes, designated Class I, Class II and Class III. The term of the Class I directors will expire on the date of the 2024 annual general meeting; the term of the Class II directors will expire on the date of the 2025 annual general meeting; and the term of the Class III directors will expire on the date of the 2023 annual general meeting. At each annual general meeting of shareholders, successors to the class of directors whose term expires at that annual general meeting are elected for a three-year term. In no case will any decrease in the number of directors shorten the term of any incumbent director. A director may hold office until the annual general meeting of the year in which his or her term expires and until his or her successor is elected and duly qualified, subject to his or her prior death, resignation, retirement, disqualification or removal from office.

Directors are elected by ordinary resolution at a general meeting. Irish law requires majority voting for the election of directors, which could result in the number of directors falling below the prescribed minimum number of directors due to the failure of nominees to be elected. Accordingly, the Company's Constitution provides that if, at any general meeting of shareholders, the number of directors is reduced below the minimum prescribed by the Constitution due to the failure of any person nominated to be a director to be elected, then, in such circumstances, the nominee or nominees who receive the highest number of votes in favor of election will be elected in order to maintain such prescribed minimum number of directors. Each director elected in this manner will remain a director (subject to the provisions of the Companies Act and the articles of association) only until the conclusion of the next annual general meeting unless he or she is reelected.

Under the Companies Act and notwithstanding anything contained in the Constitution or in any agreement between the Company and a director, the Company's shareholders may, by an ordinary resolution, remove a director from office before the expiration of his or her term at a meeting held on no less than 28 days' notice and at which the director is entitled to be heard. The power of removal is without prejudice to any claim for damages for breach of contract (e.g. employment contract) that the director may have against the Company in respect of his removal.

The Company's Constitution provides that the board of directors may fill any vacancy occurring on the board of directors. If the Company's board of directors fills a vacancy, the director's term expires at the next annual general meeting. A vacancy on the board of directors created by the removal of a director may be filled by the shareholders at the meeting at which such director is removed and, in the absence of such election or appointment, the remaining directors may fill the vacancy.

Legal Name; Formation; Fiscal Year; Registered Office

Jazz Pharmaceuticals Public Limited Company is the Company's current legal and commercial name. The Company was incorporated in Ireland on March 15, 2005 as a private limited company (registration number

399192) under the name Azur Pharma Limited. Azur Pharma Limited was re-registered as a public limited company named Azur Pharma Public Limited Company effective October 20, 2011, and was subsequently renamed Jazz Pharmaceuticals Public Limited Company on January 16, 2012. The Company's fiscal year ends on December 31st and its registered address is Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland D04 E5W7.

Duration; Dissolution; Rights Upon Liquidation

The Company's duration is unlimited. The Company may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding up, a special resolution of shareholders is required. The Company may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure where it has failed to file certain returns.

The Company's Constitution provides that the ordinary shareholders are entitled to participate pro rata in a winding up, but their right to do so may be subject to the rights of any preferred shareholders to participate under the terms of any series or class of preferred shares.

Certificated Shares

Pursuant to the Companies Act, a shareholder is entitled to be issued a share certificate on request and subject to payment of a nominal fee.

No Sinking Fund

Ordinary shares have no sinking fund provisions.

Stock Exchange Listing

Ordinary shares are listed on The NASDAQ Global Select Market under the trading symbol "JAZZ." Ordinary shares are not currently intended to be listed on the Irish Stock Exchange.

Transfer and Registration of Shares

The transfer agent and registrar for ordinary shares is Computershare Trust Company, N.A. Its address is 250 Royall Street, Canton, MA 02021. An affiliate of the transfer agent maintains the share register, registration in which is determinative of ownership of ordinary shares. A shareholder who holds shares beneficially is not the holder of record of such shares. Instead, the depository (for example, Cede & Co., as nominee for DTC) or other nominee is the holder of record of those shares. Accordingly, a transfer of shares from a person who holds such shares beneficially to a person who also holds such shares beneficially through a depository or other nominee will not be registered in the Company's official share register, as the depository or other nominee will remain the record holder of any such shares.

A written instrument of transfer is required under Irish law in order to register on the Company's official share register any transfer of shares (i) from a person who holds such shares directly to any other person, (ii) from a person who holds such shares beneficially but not directly to a person who holds such shares directly, or (iii) from a person who holds such shares beneficially to another person who holds such shares beneficially where the transfer involves a change in the depository or other nominee that is the record owner of the transferred shares. An instrument of transfer is also required for a shareholder who directly holds shares to transfer those shares into his or

her own broker account (or vice versa). Such instruments of transfer may give rise to Irish stamp duty, which must be paid prior to registration of the transfer on the Company's official Irish share register. However, a shareholder who directly holds shares may transfer those shares into his or her own broker account (or vice versa) without giving rise to Irish stamp duty provided there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and the transfer is not made in contemplation of a sale of the shares.

Any transfer of ordinary shares that is subject to Irish stamp duty will not be registered in the name of the buyer unless an instrument of transfer is duly stamped and provided to the transfer agent. The Company, in its absolute discretion and insofar as the Companies Act or any other applicable law permit, may, or may provide that any of its subsidiaries will, pay Irish stamp duty arising on a transfer of ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of ordinary shares which would otherwise be payable by the transferee is paid by the Company or any of its subsidiaries on behalf of the transferee, then in those circumstances, the Company will, on its behalf or on behalf of its subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) to claim a first and permanent lien on ordinary shares on which stamp duty has been paid by the Company or its subsidiary for the amount of stamp duty paid. The Company's lien shall extend to all dividends paid on those ordinary shares. Parties to a share transfer may assume that any stamp duty arising in respect of a transaction in ordinary shares has been paid unless one or both of such parties is otherwise notified.

The Company's Constitution delegates to the secretary or assistant secretary of the Company the authority, on behalf of the Company, to execute an instrument of transfer on behalf of a transferring party. Under the Company's Constitution, the directors can also authorize any person to execute an instrument of transfer on behalf of a transferring party in certain circumstances.

In order to help ensure that the official share register is regularly updated to reflect trading of ordinary shares occurring through normal electronic systems, the Company intends to regularly produce any required instruments of transfer in connection with any transactions for which stamp duty is paid (subject to the reimbursement and set-off rights described above). In the event that the Company notifies one or both of the parties to a share transfer that its believes stamp duty is required to be paid in connection with the transfer and that the Company will not pay the stamp duty, the parties may either themselves arrange for the execution of the required instrument of transfer (and may request a form of instrument of transfer from the Company for this purpose) or request that the Company execute an instrument of transfer on behalf of the transferring party. In either event, if the parties to the share transfer have the instrument of transfer duly stamped (to the extent required) and then provide it to the Company's transfer agent, the buyer will be registered as the legal owner of the relevant shares on the Company's official Irish share register (subject to the suspension right described below).

The directors may suspend registration of transfers from time to time, not exceeding 30 days in aggregate each year.

Irish Restrictions on Import and Export of Capital

Except as indicated below, there are no restrictions on non-residents of Ireland dealing in Irish domestic securities, which includes ordinary shares of Irish companies. Except as indicated below, dividends and redemption proceeds also continue to be freely transferable to non-resident holders of such securities.

The Financial Transfers Act, 1992, provides that the Irish Minister for Finance can make provision for the restriction of financial transfers between Ireland and other countries. For the purposes of this Act, “financial transfers” include all transfers which would be movements of capital or payments within the meaning of the treaties governing the European Communities if they had been made between Member States of the Communities. This Act has been used by the Minister for Finance to implement European Council Directives, which provide for the restriction of financial transfers to certain countries, organizations and people including the Al-Qaeda network and the Taliban, Afghanistan, Belarus, Democratic People’s Republic of Korea, Democratic Republic of Congo, Iran, Iraq, Ivory Coast, Lebanon, Liberia, Libya, Republic of Guinea, Somalia, Sudan, Syria Tunisia, Ukraine and Zimbabwe.

Any transfer of, or payment in respect of, a share or interest in a share involving the government of any country that is currently the subject of United Nations sanctions, any person or body controlled by any of the foregoing, or by any person acting on behalf of the foregoing, may be subject to restrictions pursuant to such sanctions as implemented into Irish law.

CONFIDENTIAL INTERNAL DRAFT

Pharmacy Master Services Agreement

This Pharmacy Master Services Agreement (the "Agreement") is made effective as of December 1, 2022 (the "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"). Jazz Pharmaceuticals and ESSDS may be referred to herein individually as a "Party" and collectively as the "Parties."

RECITALS

WHEREAS, Jazz Pharmaceuticals and ESSDS are parties to that certain Pharmacy Master Services Agreement, dated as of July 1, 2020, as amended, (the "2020 Master Services Agreement") through which ESSDS provides dispensing, distribution, and other services for Xyrem and Xywav;

WHEREAS, the 2020 Master Services Agreement replaced an earlier Pharmacy Master Services Agreement entered into by the Parties, dated as of July 1, 2017, as amended (the "2017 Master Services Agreement") through which ESSDS provided dispensing, distribution, and other services for Xyrem;

WHEREAS, the Parties now desire to terminate the 2020 Master Services Agreement and enter into a new agreement through which ESSDS will continue to provide certain services performed under the 2020 Master Services Agreement, and undertake certain additional services associated herewith; and

WHEREAS, ESSDS has experience in providing the services desired by Jazz Pharmaceuticals and is willing to provide such services under the terms set forth in this Agreement.

NOW THEREFORE, in consideration of the premises and the mutual covenants, representations and warranties set forth in this Agreement, the Parties agree as follows:

ARTICLE I

DEFINITIONS

As used in this Agreement, each of the following terms (and the plural or singular thereof, when appropriate) shall have the meaning set forth herein:

1.1 "Adverse Drug Experience" shall have the meaning assigned to it in 21 CFR 310.305 and 21 CFR 314.80, as such provision may be amended from time to time.

1.2 “Affiliate” of an entity shall mean any person or entity controlling, controlled by, or under common control with such entity for so long as such control exists. As used herein, “control” means ownership, directly or indirectly, of at least fifty percent (50%) of the common stock or voting ownership interests of the entity in question.

1.3 “Applicable Laws” shall mean all federal, state, and local laws and governmental agency regulations and requirements applicable to the Services, including without limitation HIPAA, Medicare and Medicaid laws under Title XVIII and XIX of the Social Security Act, the Controlled Substances Act, and relevant state and federal pharmacy licensure requirements and pharmacy regulations.

1.4 “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.

1.5 “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.

1.6 “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 Xyrem and Xywav (i) for dispensing to VA, and (ii) to Puerto Rico.

1.7 “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, as set forth in any applicable Work Order (as defined below in Section 2.1) and the related Business Rules.

1.8 “Business Rules” shall mean the written documents related to the Enhanced Specialty Pharmacy Services Agreement between the Parties that are mutually agreed upon in writing by ESSDS and Jazz Pharmaceuticals that set forth the way in which the Enhanced Pharmacy Services are to be performed. The Business Rules may be modified with the prior written consent of both Jazz Pharmaceuticals and ESSDS or both the Authorized Generic Partner and ESSDS, but do not require an amendment hereto.

1.9 “Certified Pharmacy” shall mean the facility or facilities licensed and operated by ESSDS in compliance with the REMS Program and utilized by ESSDS in connection with the performance of this Agreement.

1.10 “Confidential Information” shall have the meaning assigned to it in Section 8.2.

1.11 “Coupon Program” shall mean a program that provides co-pay support to eligible Patients, sponsored by either Jazz Pharmaceuticals or an Authorized Generic Partner, as

set forth in any applicable Work Order and the related Business Rules.

1.12 “Data” shall mean the data specified in a Work Order, including but not limited to physician and Patient data, Personal Data and required data elements for the REMS Program Central Database, and such other data as the Parties agree shall be provided by ESSDS to Jazz Pharmaceuticals under this Agreement.

1.13 “DEA” shall mean the United States Drug Enforcement Administration, or any successor thereto.

1.14 “Deliverables” shall mean those items to be delivered to Jazz Pharmaceuticals by ESSDS hereunder and as may be specified in a Work Order.

1.15 “FDA” shall mean the United States Food and Drug Administration or any successor thereto.

1.16 “Full Time Employee” or “FTE” shall mean a full time ESSDS employee working a forty (40) hour week who is dedicated exclusively to performing Pharmacy Services pursuant to the Agreement or any applicable Work Order.

1.17 “HIPAA” means the Health Insurance Portability and Accountability Act of 1996, as amended, and the regulations promulgated pursuant thereto in the United States Code of Federal Regulations (45 CFR Parts 160 and 164).

1.18 “Information Technology” shall have the meaning assigned to it in Section 8.8 herein.

1.19 “Inspection” shall have the meaning assigned to it in Section 5.2 herein.

1.20 “Intellectual Property” means any and all patents, innovations, trade secrets, inventions, know-how, copyrights and works of authorship, trademarks, service marks, trade dress, ideas, improvements, methods, algorithms, designs, software, code, discoveries, enhancements, modifications, data, other registered and/or non-registered intellectual property, and information of every kind and description, applications and issued rights for the same, and registrations and applications for registration or renewals thereof in the United States and all other nations throughout the world, including without limitation all derivative works, renewals, extensions, reversions or restorations associated with such copyrights, now or hereafter provided by Applicable Law, regardless of the medium of fixation or means of expression.

1.21 “Non-PAP Order” shall mean each shipment of Product by ESSDS to any Non-PAP Patient in accordance with this Agreement.

1.22 “Non-PAP Patient” shall mean any Patient other than a PAP Patient.

1.23 “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.

1.24 “PAP Patient” shall mean a Patient receiving Product through the Patient Assistance

Program.

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

1.26 “Patient” shall mean an individual who has been prescribed the Product.

1.27 “Patient Data” shall include data about a Patient including information about a Patient’s health, medical insurance claims, and payment information obtained from the Patient or the Patient’s prescribing physician.

1.28 “Pharmacy Services” shall have the meaning assigned to it in Section 2.1 herein.

1.29 “Physician Confidential Information” shall mean information pertaining to a physician that is protected from use or disclosure pursuant to Applicable Law.

1.30 “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.

1.31 “Product Complaint” shall mean notification relating to quality, purity, identity, potency, packaging, tampering, and/or quality aspect of any Product, or any Products Marketed by Jazz.

1.32 “Products Marketed by Jazz” shall mean any pharmaceutical products other than Product as defined in Section 1.30, which are marketed by Jazz Pharmaceuticals in the U.S., including Epidiolex® (cannabidiol), Defitelio® (defibrotide sodium), Rylaze™ asparaginase erwinia chrysanthemi (recombinant)-rywn, Vyxeos® (daunorubicin and cytarabine), and Zepzelca™ (lurbinectedin). The list of Products Marketed by Jazz may be amended from time to time upon written notice to ESSDS, and any such amendments to the list will be incorporated into the applicable mutually agreed upon SOPs and Work Instructions.

1.33 “Records” shall have the meaning assigned to it in Section 7.1 herein.

1.34 “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.

1.35 “REMS Pharmacy Services” shall have the meaning assigned to it in Section 2.1 herein.

1.36 “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.

1.37 “REMS Program Items” shall mean materials required in connection with the performance of REMS Pharmacy Services by ESSDS hereunder, including, but not limited to, REMS Program enrollment forms and materials to be distributed to

prescribers and Patients. REMS Program Items shall not include any Product.

1.38 "Services" shall mean the Pharmacy Services and REMS Pharmacy Services collectively, as defined in Section 2.1.

1.39 "Service Level Agreements" or "SLAs" shall mean the service levels required for certain Services in order to support Product, and are defined in Exhibit D.

1.40 "SOPs" shall mean the written standard operating procedures of ESSDS, as of the Effective Date of the Agreement, or any others mutually agreed to be the Parties after the Effective Date of the Agreement, which describe the REMS Program-specific operation processes of ESSDS.

1.41 "Territory" shall mean the United States of America, including its territories where ESSDS is allowed to legally distribute and ship Product.

1.42 "Trademarks" shall mean the Jazz Pharmaceuticals trademarks set forth in Exhibit B.

1.43 "Veteran's Administration" or "VA" shall mean the U.S. Department of Veteran's Affairs, which provides a prescription benefit to VA healthcare system enrollees.

1.44 "VA FSS" shall mean the Veteran's Administration Federal Supply Schedule pricing contract provided to Jazz Pharmaceuticals for Xyrem and Xywav.

1.45 "Voucher Program Services" shall mean a program that provides a limited supply of free Product to eligible Patients, sponsored by either Jazz Pharmaceuticals or an Authorized Generic Partner, as set forth in any applicable Work Order and the related Business Rules.

1.46 "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.

1.47 "Work Instructions" or "WIs" shall mean written work instructions of ESSDS, as of the Effective Date of the Agreement, or any others mutually agreed to by the Parties after the Effective Date of the Agreement, 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)).

1.48 "Work Order" shall have the meaning assigned to it in Section 2.1.

ARTICLE II

PHARMACY AND REMS PHARMACY SERVICES

2.1 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 Services and the REMS Pharmacy Services (collectively, the “Services”) to be provided as of the Effective Date of the Agreement 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 2017 Master Services Agreement and the 2020 Master Services Agreement that are ongoing (“Pre-Existing Work Orders) shall henceforth be considered Work Orders under this Agreement. Each of the Pre-Existing 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 the Pre-Existing 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 by the Parties for the calendar year in which the Work Order was executed, [***].

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).

2.2 Modifications in Services. Jazz Pharmaceuticals may propose changes (such as a change in process) to Services through a Work Order by submitting a request in writing setting forth the proposed modifications to such Services (a “Modification Request”). In the event of any Modification Request, or if ESSDS receives a technical direction from Jazz Pharmaceuticals that is reasonably viewed by ESSDS as a Modification Request, ESSDS shall notify Jazz Pharmaceuticals in writing of the anticipated cost impact of such Modification Request. The Parties agree to negotiate in good faith any adjustments to the fees payable under this Agreement that are necessitated by a Modification Request and recognize that ESSDS shall have no obligation to perform modified or additional Services until the Parties have agreed on

the associated fees. A Modification Request must be signed by the Parties.

2.3 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. If, during the term of this Agreement, Jazz Pharmaceuticals no longer utilizes a single pharmacy to dispense Product and Jazz Pharmaceuticals chooses to engage another pharmacy in addition to ESSDS (thus making ESSDS's dispensing hereunder non-exclusive), [***]. Furthermore, in the event that Jazz Pharmaceuticals chooses to engage another pharmacy for commercial, non-clinical trial Product in addition to ESSDS, ESSDS shall maintain the right to continue to provide Services to any Patients enrolled in the REMS Program as of the date that ESSDS no longer maintains its exclusive pharmacy status. 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 Product in the Territory in accordance with the terms and conditions of the Agreement.

2.4 Data and Data Reports. ESSDS will provide to Jazz Pharmaceuticals or third parties authorized by Jazz Pharmaceuticals, the Data and Data Reports as set forth in any data sharing agreement and/or Work Order. Data will be transferred with the content and in the formats defined in the data sharing agreement and/or Work Order, and will be provided in the manner and frequency defined in the data sharing agreement and/or Work Order.

(a) [***]

2.5 Warehousing. All commercial, non-clinical trial Product sold, or made available pursuant to this Agreement in the Territory shall be warehoused at ESSDS at the Certified Pharmacy in accordance with any related Work Orders or SOPs, and Work Instructions, and with due care in accordance with the standards and practices which are generally accepted in the industry and exercised by other persons engaged in performing similar services in the local areas and in accordance with Applicable Law.

2.6 Quality of Services; Compliance with Applicable Law. ESSDS agrees to perform the Services in a professional and timely manner in accordance with the terms and conditions of this Agreement, the applicable Work Orders or any mutually agreed Modification Requests, Work Instructions and SOPs and in compliance with Applicable Laws and currently recognized and accepted industry standards. The SOPs and Work Instructions shall not be modified without notice to Jazz Pharmaceuticals unless required by Applicable Law and Jazz

Pharmaceuticals shall have the right in the event of a change to notify ESSDS of any change it believes will be required to the Work Instructions as a result of the change to such SOPs. In such event, the Parties will work together in good faith to determine whether a Modification Request is required. ESSDS shall provide the Services through personnel, who are appropriately skilled, qualified, properly licensed where applicable, and trained to provide Services. ESSDS shall perform the Services at the designated ESSDS locations listed in Exhibit D, ESSDS Locations. The Certified Pharmacy shall maintain all relevant state and federal licenses required by Applicable Law.

ESSDS shall monitor developments in Applicable Laws and shall promptly notify Jazz Pharmaceuticals of any relevant developments of which it becomes aware, and the Parties shall work together in good faith to determine whether a Modification Request is required.

2.7 Personnel. ESSDS shall provide the REMS Pharmacy Services through personnel who are qualified and appropriately trained to provide the REMS Pharmacy Services (the "Personnel"). ESSDS shall have sole discretion over the management and oversight of its Personnel working on the REMS Pharmacy Services, but will reasonably consult with Jazz Pharmaceuticals with respect to Jazz Pharmaceuticals' personnel recommendations to help to ensure Jazz Pharmaceuticals' satisfaction with the REMS Pharmacy Services. ESSDS shall provide opportunities to review and make recommendation on job descriptions prior to such job descriptions being used in the Personnel recruitment process for open positions. Prior to assigning any individual to work on the REMS Pharmacy Services on a full-time basis, Jazz Pharmaceuticals shall be given an opportunity to confirm that it is satisfied with such person's training and qualifications. ESSDS shall ensure that all employees assigned to support the REMS Pharmacy Services are qualified and competent in their respective roles and responsibilities and have reasonable experience performing the tasks they will perform in connection with the REMS Pharmacy Services, consistent with industry standards. In addition, ESSDS will ensure that its Personnel participate in any instruction and training as required by Jazz Pharmaceuticals, including training directly from Jazz Pharmaceuticals.

[***]

Specific roles are or will be described in more detail in the applicable Work Order(s). In the event that Jazz Pharmaceuticals is dissatisfied with any individual performing REMS Pharmacy Services, it may notify ESSDS of its concerns and ESSDS will take such concerns under advisement and take corrective action as appropriate.

ESSDS will make commercially reasonable efforts to scale its staffing levels up and down to match the forecasted demand for REMS Pharmacy Services that the Parties agree on in

advance of each calendar quarter. ESSDS will provide ad hoc reporting and justification to support FTE change requests.

It is understood that ESSDS and its employees will be serving under this Agreement as an independent contractor, and will not be eligible to participate in any benefits extended by Jazz Pharmaceuticals to its employees.

ESSDS will maintain in full force and effect throughout the term of this Agreement insurance related to Worker's Compensation for its Personnel who perform REMS Pharmacy Services under this Agreement and will provide Jazz Pharmaceuticals a certificate of insurance evidencing such coverage if requested in writing by Jazz Pharmaceuticals.

2.8 Handling of Product. In connection with the provision of Services, ESSDS shall at all times handle, maintain, store, transport and deliver Product in accordance with all Applicable Laws and SOPs. ESSDS will prepare Product under conditions that are consistent with currently accepted standards of care including relevant requirements specified in the applicable SOPs and Work Instructions, the REMS Program, and Product Prescribing Information.

2.9 Subcontracting. ESSDS may not subcontract or otherwise delegate any of its obligations with respect to the Services, except to an Affiliate, without Jazz Pharmaceuticals' prior written consent, which will not be unreasonably withheld, including but not limited to agreeing to a Work Order specifying the subcontractor. Upon receipt of such consent, and before allowing any subcontractor to begin performing Services, ESSDS shall enter into a binding written agreement with such subcontractor that protects Jazz Pharmaceuticals' rights and interests to at least the same degree as this Agreement. ESSDS shall be responsible for any permitted subcontractors' compliance with the terms hereof. Jazz Pharmaceuticals shall have no obligation to pay any subcontractors for any Services.

2.10 Privacy.

(a) Notwithstanding anything to the contrary herein (including the Exhibits hereto), ESSDS shall provide information to Jazz Pharmaceuticals in a manner fully consistent with HIPAA. Accordingly, the Parties agree that ESSDS shall only provide Jazz Pharmaceuticals information that is de-identified in accordance with HIPAA's de-identification provision, 45 C.F.R. § 164.514(b), unless: (i) ESSDS has on file a valid, unrevoked, HIPAA-compliant authorization for each Patient whose protected health information ("PHI") is sought to be disclosed; or (ii) authorization is not required under Applicable Law in order to disclose the PHI. Jazz Pharmaceuticals represents and warrants that it cannot and will not attempt to identify the individual who is the subject of any de- identified information. To the extent that Jazz Pharmaceuticals, or a contractor of Jazz Pharmaceuticals (e.g., a Hub), maintains the relevant HIPAA authorization, Jazz Pharmaceuticals agrees to, or to require its contractor to, appropriately communicate to ESSDS any expiration, revocation, or restriction requested by a Patient related to the HIPAA authorization or the Patient's PHI.

(b) If Jazz Pharmaceuticals seeks PHI from ESSDS for Jazz Pharmaceuticals' public health activities purposes (e.g., REMS Program administration, adverse event reporting), Jazz Pharmaceuticals represents and warrants that the disclosure of such PHI by ESSDS to Jazz

Pharmaceuticals, either directly to Jazz Pharmaceuticals or to Jazz Pharmaceuticals' data collection agent, satisfies the conditions of 45 C.F.R. § 164.512(b) in that: (i) if Jazz Pharmaceuticals uses a third party to collect Data for Jazz Pharmaceuticals, such third party is serving in the capacity as Jazz Pharmaceuticals' agent for the purpose of, among other things, collecting Data on behalf of Jazz Pharmaceuticals; (ii) the Data to be collected is to be used and/or disclosed by Jazz Pharmaceuticals, or its data collection agent, solely for public health activities purposes and for no other purpose; (iii) de-identified data (as described in 45 C.F.R. § 164.514(b)) is not sufficient under the circumstances to enable Jazz Pharmaceuticals to satisfy its public health activities purposes; and (iv) the Data to be collected includes the minimal amount of PHI required in order for Jazz Pharmaceuticals to conduct its public health activities purposes.

2.11 DSCSA Compliance. ESSDS will (a) comply with all applicable requirements of the Drug Supply Chain Security Act ("DSCSA"), including the receipt of electronic and interoperable track and trace information from Jazz Pharmaceuticals, and (b) work in good faith with Jazz Pharmaceuticals as reasonably requested in connection with Jazz Pharmaceuticals' DSCSA-related obligations and requirements.

2.12 Automated Pharmacy Quality Assurance. ESSDS will perform standard periodic frequent checks, calibration, and any required services of equipment and will maintain quality control records of the automated pharmacy equipment and will be able to produce and provide such documentation to Jazz Pharmaceuticals upon request in the event of an audit or as a result of an identified defective distribution of Product.

2.13 Account Management. ESSDS will have a dedicated account management team that is responsible solely for Products.

2.14 REMS Program Items

(a) REMS Program Items. From the Effective Date of this Agreement, Jazz Pharmaceuticals shall provide REMS Program Items to ESSDS of the type and quantities to be reasonably determined by Jazz Pharmaceuticals for performance of REMS Pharmacy Services. ESSDS shall not utilize or distribute REMS Program Items for any purpose other than as set forth in this Agreement and the Work Orders hereunder. ESSDS is strictly prohibited from selling, utilizing, or transferring REMS Program Items to any third-party under any circumstances not contemplated by this Agreement.

(b) Title; Storage. REMS Program Items shall be marked as property of Jazz Pharmaceuticals. ESSDS shall furnish and maintain a suitable place for storage of REMS Program Items. Legal title to all REMS Program Items shall remain with Jazz Pharmaceuticals.

ARTICLE III

COMPENSATION, INVOICING AND PAYMENT

3.1 Services Fees. The full and complete compensation by Jazz Pharmaceuticals for ESSDS' performance of the Services and for assumption of its obligations hereunder shall be as set forth

in the applicable Work Order, which shall be inclusive of all taxes applicable to the performance of Services. The fees for Services may only be modified by written agreement of the Parties via an amendment to the applicable Work Order in accordance with Section 2.1. All expenses, including shipping costs, reimbursed hereunder shall be at cost, without markup.
Unless otherwise set forth in a Work Order, ESSDS shall be responsible for all costs and expenses associated with fulfilling its obligations hereunder. On the first anniversary of the Effective Date of the Agreement, and each anniversary thereafter, [***]. ESSDS shall notify Jazz Pharmaceuticals in writing before the effective time of any such increase in fees.

3.2 Invoices for Services Fees. ESSDS will issue invoices to Jazz Pharmaceuticals for payment and reimbursement of the fees and expenses for the Services as set forth in the applicable Work Order hereunder. ESSDS will provide reasonably detailed invoices, together with adequate supporting documentation. All fees shall be paid in United States dollars and payable in the same. Invoices will be sent to:

Jazz Pharmaceuticals, Inc.
3170 Porter Drive Palo Alto, CA 94304
Attention Accounts Payable
Or via email to: ap@jazzpharma.com

3.3 Payment. Jazz Pharmaceuticals will pay all undisputed amounts invoiced in accordance with the terms hereof within thirty (30) days of receipt. In the event that Jazz Pharmaceuticals disputes any portion of an invoice, Jazz Pharmaceuticals will pay the undisputed portion in the ordinary course and will notify ESSDS within ten (10) business days of the disputed portion and will request information from ESSDS reasonably necessary to substantiate the invoiced amount. ESSDS will provide the requested information within ten (10) business days. If Jazz Pharmaceuticals continues to question the invoiced amounts following such information request and response, it shall promptly notify ESSDS and the Parties shall, within ten (10) business days, meet (in person or by phone) to resolve any dispute. The finally resolved amount shall be payable within thirty (30) days of the original invoice date or within ten (10) business days of the dispute resolution, whichever is later. In the event that Jazz Pharmaceuticals has prepaid any amounts and the actual fees or expenses are less than estimated, then ESSDS will promptly (and in all cases within thirty (30) days) reimburse the amount of any overpayment to Jazz Pharmaceuticals or at Jazz Pharmaceuticals' request credit the amount of such overpayment to other invoices.

3.4 Fair Market Value. ESSDS agrees with Jazz Pharmaceuticals that the compensation payable to ESSDS for the Services to be performed by it (a) are for bona fide services provided by ESSDS to Jazz Pharmaceuticals, (b) have been determined through good faith negotiations at arm's length and as such represent the fair market value for such Services, and (c) does not take into account the volume or value of referrals or business otherwise generated between the Parties or their Affiliates for which payment may be made, in whole or in part, under Medicare, Medicaid or other federal or state health care programs. ESSDS

also confirms to Jazz Pharmaceuticals that it will retain the Services fees provided by Jazz Pharmaceuticals under this Agreement and that such Services fees will not be passed on to any of ESSDS' customers. No provision of this Agreement shall be applied or construed in a manner inconsistent with applicable state or federal laws or regulations.

ARTICLE IV

SUPPLY OF PRODUCT

4.1 Non-PAP Orders

(a) General. Jazz Pharmaceuticals shall deliver to ESSDS at the Certified Pharmacy sufficient quantities of Product to fulfill Non-PAP orders. ESSDS maintains a reasonable quantity of components on-site or nearby to allow Product disbursements to occur in a timely and efficient manner. Product to be shipped pursuant to Non-PAP Orders shall be furnished to, and held by, ESSDS on a consignment basis at a Certified Pharmacy at all times. The consignment of Product hereunder shall at no time be construed as a loan or other debt financing or secured transaction arrangement between the Parties, and title to consigned Product shall remain with Jazz Pharmaceuticals until transferred pursuant to Section 4.1(b).

(b) 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.

For purposes of clarity, if ESSDS fulfills an order for one half bottle of Xyrem or Xywav, ESSDS will purchase the one-half bottle and title for the one-half bottle dispensed will transfer to ESSDS. ESSDS will return the other one-half bottle of Xyrem or Xywav to the storage area for Jazz Pharmaceuticals or Authorized Generic consigned Product, and Jazz Pharmaceuticals or Authorized Generic partner (as applicable) will continue to hold title for such product until such time as ESSDS removes such product for dispensing.

(c) 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.

(d) 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 Pharmaceuticals 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.

4.2 Buy In. ESSDS shall be offered [***] Manufacturer's Product [***].

4.3 PAP, Bridge and Voucher 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, Bridge and Voucher 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, Bridge and Voucher 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, Bridge or Voucher Order in ESSDS' internal order processing system, at which time

title will pass to the Patient. ESSDS will fulfill PAP, Bridge and Voucher Orders as set forth in the applicable Work Orders and Business Rules.

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 Authorized Generic Product to fulfill PAP, Bridge or Voucher 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 Authorized Generic Product shipped pursuant to Bridge or Voucher Orders shall be for the account of Jazz Pharmaceuticals, and title to such Authorized Generic Product shall remain with Jazz Pharmaceuticals until confirmation of the Bridge or Voucher Order in ESSDS' internal order processing system, at which time title will pass to the applicable Authorized Generic Partner and then to the Patient. ESSDS will fulfill Bridge and Voucher Orders as set forth in the applicable Work Orders and Business Rules.

4.4 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.

4.5 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 Work Instructions. 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 an amount equal to the replacement cost of such Xyrem or Xywav.

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 and 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 SOP and Applicable Law. ESSDS will be responsible for covering any shipping costs associated with getting 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.

4.6 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.

4.7 Territory. ESSDS shall use commercially reasonable efforts to obtain and maintain all necessary licenses and approvals to dispense Product in the Territory.

4.8 Recall or Market Withdrawal. Jazz Pharmaceuticals may elect to recall or withdraw Product from the market as a result of (i) a request, instruction, or other action of a government entity; (ii) a determination for reasons associated with safety, quality, technical or other issues directly affecting such Product.

(a) In the event of such recall or withdrawal, Jazz Pharmaceuticals shall provide as much written notice to ESSDS as reasonably possible of such recall or withdrawal (such notice to include the reasons for the recall or withdrawal and any notices or other communication from any government entity in relation thereto). ESSDS shall reasonably cooperate in effecting such recall in accordance with the applicable SOP.

(b) If Jazz Pharmaceuticals is required to recall, or, on its own initiative, recalls or withdraws any Product sold in the Territory, ESSDS shall reasonably assist Jazz Pharmaceuticals in such recall in accordance with the Applicable Laws. For such purposes, ESSDS shall maintain a complete and current list of Patients who ESSDS reasonably believes could have been exposed to Product covered by the recall or withdrawal. Jazz Pharmaceuticals shall pay for all reasonable documented out of pocket costs and expenses of ESSDS solely as a result of any such recall, unless the recall results from ESSDS' negligence, recklessness, or willful misconduct. ESSDS shall provide to Jazz Pharmaceuticals, at Jazz Pharmaceutical's request, any information reasonably requested by Jazz Pharmaceuticals in connection with Jazz Pharmaceuticals' investigations relating to recalled Product, subject to the confidentiality constraints imposed by Applicable Law.

ARTICLE V

UDITS; REGULATORY INQUIRIES; DEBARMENT; OTHER REGULATORY MATTERS

5.1 Audit. During the term of this Agreement and for a period of eighteen (18) months thereafter, ESSDS shall make Records available for Jazz Pharmaceuticals or its designee's
inspection during regular business hours and upon at least forty-eight (48) hours' advance notice. In addition, Jazz Pharmaceuticals shall have the right, during the term of this Agreement, (i) to one time annually inspect (or more frequently and without notice if Jazz Pharmaceuticals has reasonable cause to perform such an inspection) any of ESSDS' facilities from which the Services are performed and equipment used to perform the Services (including computers, call centers,

software programs and any other systems) during normal business hours and upon 30 day prior written notice, accompanied by a detailed audit scope (ii) to be present when Services are being performed by ESSDS or ESSDS' permitted subcontractors, and (iii) to monitor by telephone the performance of any call center or telephone-related Services provided under this Agreement. ESSDS will cooperate in any audits at ESSDS' expense. If any audit results in findings that require follow-up or action, ESSDS will address such findings within a commercially reasonable timeframe at ESSDS' expense. Audits will be excluded during the months of December and January, unless the request is related to an inspection and timing stipulated by a government regulator that impacts the Services performed under this Agreement. If a third party is used to conduct any audit, such third party will sign a confidentiality agreement with ESSDS.

5.2 Regulatory Inquiries and Inspections. To the extent practicable and permitted under Applicable Law, ESSDS shall notify Jazz Pharmaceuticals immediately (with a copy of all associated notices and correspondence) of its receipt of any notice of an inspection, audit or regulatory action relating to Product by any regulatory authority, including without limitation, the United States Department of Health and Human Services, the FDA or any other government agency, any state board of pharmacy, or any national accrediting body (an "Inspection"). Jazz Pharmaceuticals shall have the right to be present at and to participate in any such Inspection or regulatory action with respect to Product or the Services. In the event that ESSDS does not receive prior notice of such regulatory inspection, ESSDS shall notify Jazz Pharmaceuticals as soon as practicable after such inspection begins.

5.3 No Debarment.

(a) ESSDS represents and warrants to Jazz Pharmaceuticals that it (i) is not currently excluded, debarred, suspended or otherwise ineligible to participate in federal health care programs or in federal procurement or nonprocurement programs or proposed for exclusion under such programs, and (ii) has not been convicted of a criminal offense that falls with 42 USC §1320a-7(a) or §1320a-7(b)(1)-(3) but has not yet been excluded, debarred, suspended, or otherwise declared ineligible to participate in federal health care programs or in federal procurement or nonprocurement programs. ESSDS agrees that it will immediately notify Jazz Pharmaceuticals in writing if any of the representations and warranties made by ESSDS in this Section ceases to be true at any time during the term of the Agreement.

(b) Jazz Pharmaceuticals represents and warrants to ESSDS that it (i) is not currently excluded, debarred, suspended or otherwise ineligible to participate in federal health care programs or in federal procurement or nonprocurement programs or proposed for exclusion under such programs, and (ii) has not been convicted of a criminal offense that falls under 42 USC §1320a-7(a) or §1320a-7(b)(1)-(3) but has not yet been excluded, debarred, suspended, or otherwise declared ineligible to participate in federal health care programs or in federal procurement or nonprocurement programs. Jazz Pharmaceuticals agrees that it will immediately notify ESSDS in writing if any of the representations and warranties made by Jazz Pharmaceuticals in this Section cease to be true at any time during the term of the Agreement.

ARTICLE VI

PURCHASE PRICE OF PRODUCTS

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 the foregoing, 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.

6.2 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 typically 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 and 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".

ARTICLE VII

RECORDS AND NOTIFICATIONS

7.1 Records. ESSDS shall at all times keep and maintain complete, timely and accurate written records relating to the performance of the Services as provided for under this Agreement (collectively, the "Records"). ESSDS shall maintain the Records in compliance with Applicable Laws and ESSDS's record retention policies.

7.2 Adverse Event Reporting. ESSDS shall comply with the agreed Potential Adverse Event Reporting SOP and WIs and report any potential Adverse Drug Experiences that it receives to Jazz Pharmaceuticals in compliance with those SOPs and Work Instructions.

7.3 Product Complaints. ESSDS shall comply with the agreed Product Complaint SOP and properly report any technical complaints (e.g., reports about potential production issues such

as packaging irregularities that are not a result of shipping damage) or Product Complaints (e.g. reports regarding contamination, discoloration, improper labeling, adulteration) that it receives to Jazz Pharmaceuticals.

(a) Adverse Event and Product Compliant Reporting for Products Marketed by Jazz. All Adverse Events and Product Complaints for Products Marketed by Jazz that are reported to ESSDS in connection with services provided by ESSDS under the Agreement will be collected and reported to Jazz Pharmaceuticals pursuant to the terms of this Agreement and any relevant Work Order, Work Instructions and/or SOPs;

7.4 Other Notifications. ESSDS shall notify Jazz Pharmaceuticals within one (1) business day if a Product or the REMS Program is within the scope of a FDA or DEA inspection.

ARTICLE VIII

CONFIDENTIALITY

8.1 Confidentiality of Agreement. The Parties agree that the terms and conditions of the Agreement are Confidential Information (as defined in Section 8.2 below) and shall not be disclosed to anyone for any purpose without the prior written consent of the other Party, except as expressly permitted by this Agreement.

8.2 Confidential Information. Each Party acknowledges that in connection with this Agreement, it may receive information, including and without limitation, trade secrets and innovations, information regarding Product and planned products, the REMS Program and the Services and planned Services, contractors, customers, prospective customers, financial data, computer software processes, ideas, marketing information, strategies, forecasts, development programs, Data, know-how, improvements and other valuable business information from or on behalf of the other Party (the "Disclosing Party") which the Disclosing Party considers to be proprietary and confidential and the value of which might be lost if the confidentiality of such information is not maintained (collectively, the "Confidential Information"). The Party receiving such Confidential Information (the "Receiving Party") agrees, at all times during the term of this Agreement, and subject to the limitations set forth herein, (i) to treat as confidential all Confidential Information received from the Disclosing Party with at least the same degree of care with which the Receiving Party treats its own Confidential Information, (ii) to disclose Confidential Information to only those of its employees, agents, consultants, Affiliates and permitted subcontractors who have a need to know such Confidential Information in order to accomplish the purposes of this Agreement and who are subject to obligations of confidentiality at least as restrictive as those obligations of confidentiality in this Section, and (iii) to not use the Disclosing Party's Confidential Information for any purpose except those purposes permitted by this Agreement. Unless otherwise expressly set forth herein to the contrary, each Party hereby acknowledges and agrees that, as between the Parties, the Disclosing Party owns all right, title, and interest in and to the Confidential Information disclosed to the Receiving Party.

8.3. Exceptions. The obligations of confidentiality and nonuse set forth herein shall not apply to information that the Receiving Party can demonstrate by competent written evidence: (i) is or becomes generally available to the public other than as a result of a disclosure by the Receiving Party in breach this Agreement, (ii) was within the Receiving Party's possession prior to the date of the 2017 Agreement and had become known to the Receiving Party from the Receiving Party's own sources without restriction, (iii) becomes available to the Receiving Party on a non-

confidential basis from a third Party not acting on behalf of the Disclosing Party and not under any obligation to keep such information confidential, and (iv)was or is independently developed by the Receiving Party without the use of or access to any Confidential Information. Any combination of features or disclosures will not be deemed to fall within the foregoing exclusions merely because certain individual features fall within such foregoing exclusions unless the combination as a whole falls within any of the above exclusions.

8.4. Authorized Disclosure. The Receiving Party may disclose Confidential Information of the Disclosing Party to the extent such disclosure is required by Applicable Law, a valid order of a court or other governmental body having jurisdiction, or rules of a securities exchange; *provided, however,* that the Receiving Party both: (a) gives prompt notice to the Disclosing Party of the disclosure requirement in order to allow the Disclosing Party to obtain any available limitation on or exemptions from such disclosure requirement, where reasonably practicable, and (b) reasonably cooperates in such efforts by the Disclosing Party, where not prohibited by Applicable Law, court order, or securities exchange rules.

8.5. Permitted Uses and Disclosures. The Receiving Party may use Confidential Information in the performance of its obligations or exercise of its rights under this Agreement or any Work Order.

8.6. 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, and 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 under this Agreement, or the 2020 Master Services Agreement, 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 addresses, 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 Pharmacy Master Services. For purposes of clarity, if Personal Data is disclosed by ESSDS to Jazz Pharmaceuticals pursuant to a valid HIPAA Authorization, Jazz’s further use or ownership of such Personal Data is limited only by applicable law and the HIPAA Authorization, and is independent of ESSDS’s separate rights to said Personal Data. ESSDS agrees that it will not utilize Personal Data outside the scope of this Agreement, other than for compliance with ESSDS’ own obligations under Applicable Law, 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 law, without charge, for research, cost analysis and other internal business 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, or manufacturers of products for the treatment of narcolepsy or idiopathic hypersomnia , or other third party not

specifically authorized in writing by Jazz Pharmaceuticals ,with the exclusion of Data shared for the requirement of Patient benefits investigation and prescription, 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 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.

8.7 Return of Confidential Information. Upon expiration or earlier termination of this Agreement, or upon the Disclosing Party's earlier request, the Receiving Party (a) shall return to the Disclosing Party all documents, papers, and other materials in the Receiving Party's possession or under the Receiving Party's control containing the Disclosing Party's Confidential Information, or (b) shall destroy any or all such documents, papers and other materials items, thereafter sending the Disclosing Party a signed certification of destruction covering the applicable items. Notwithstanding the foregoing, each Party may retain a single archival copy of the other Party's Confidential Information for the sole purpose of facilitating compliance with the surviving provisions of this Agreement.

8.8 Access to Information Technology.

(a) Jazz Pharmaceuticals may provide ESSDS with access to the Jazz Pharmaceuticals network, system, and/or a specific application, as Jazz Pharmaceuticals may decide in its sole discretion (the "Information Technology") for use under this Agreement. This Information Technology will be used solely for purposes of, and in connection with, the Services provided under this Agreement and for no other purpose whatsoever. Access to such Information Technology will be strictly limited to those ESSDS, employees, and permitted subcontractors (the "IT Access Recipients") who are required to use such Information Technology for the performance of the Services. The Information Technology may not be copied, modified or distributed, or provided to or used by any third party. ESSDS will be liable for any unauthorized use of Jazz Pharmaceuticals' Information Technology by any IT Access Recipients.

(b) ESSDS will notify Jazz Pharmaceuticals within forty eight (48) hours in the event that any IT Access Recipient has terminated its relationship with ESSDS, including but not limited to (i) ESSDS employees that have left employment with the ESSDS for any reason whatsoever; and (ii) ESSDS permitted subcontractors that are no longer under contractual obligations with ESSDS relating to the Services provided hereunder.

(c) ESSDS will notify Jazz Pharmaceuticals within forty eight (48) hours in the event that the duties of any IT Access Recipient have been reassigned such that the recipient no longer requires access to Information Technology.

(d) ESSDS will take all reasonable precautions to prevent the unauthorized access to Jazz Pharmaceuticals' Information Technology by ESSDS Personnel. ESSDS will notify Jazz Pharmaceuticals immediately (and in all cases within three days) of becoming aware of any actual or suspected unauthorized access to the Information Technology.

8.9 Injunctive Relief. Each Party acknowledges that the disclosure or use of the other Party's Confidential Information, other than as expressly permitted herein, without such Party's prior written permission, may cause the Disclosing Party irreparable harm and that any material breach or threatened material breach of the obligations of confidentiality and non-use by the Receiving Party will entitle the Disclosing Party to seek injunctive relief, in addition to any other legal remedies available to it, in any court of competent jurisdiction.

ARTICLE IX

REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1 General. Each Party hereby represents, warrants, and covenants to the other that: (i) it has all requisite corporate power and authority to enter into this Agreement and perform and observe all obligations and conditions required to be performed or observed by that Party under this Agreement, neither the execution and delivery of this Agreement nor the performance by that Party of its respective obligations under this Agreement will conflict with or result in a breach of any covenant or agreement between that Party and any third party, (iii) this Agreement represents the legal, valid, and binding obligation of that Party, and (iv) as of the Effective Date, such Party has (or will have at such time as performance of its obligations under this Agreement may require) obtained all of the local, state, and federal permits, licenses, or other regulatory registrations or approvals necessary, if any, for the performance of its obligations under this Agreement.

9.2 ESSDS Representations and Warranties.

(a) ESSDS represents and warrants that, to the best of its knowledge, it owns and possesses all right, title and interest in and to, or has valid licenses to use all the proprietary rights necessary to perform its obligations under this Agreement.

(b) ESSDS warrants that any computer systems used in connection with the Services shall operate substantially in accordance with any descriptions or the specifications set forth in this Agreement or any applicable Work Orders. A business continuity plan, as set forth in the applicable SOP, will be implemented by ESSDS to assure that this warranty will be met.

(c) ESSDS represents, warrants, and covenants that ESSDS's contracted work with pharmaceutical/medical device manufacturers is independent from its parent company's clinical and formulary decisions. There is a firewall between ESSDS's pharmaceutical/ medical device services business and the pharmacy benefit management ("PBM") business. ESSDS will not be influenced by any PBM rebate or other related agreements with pharmaceutical/medical device manufacturers. Similarly, transactions between pharmaceutical/medical device manufacturers and ESSDS will not affect PBM clinical and formulary decisions.

(d) ESSDS shall:

i. provide all Services and Deliverables to Jazz Pharmaceuticals pursuant to this Agreement in compliance with Applicable Laws and in a good, workmanlike, and timely manner, consistent with standards for the industry;

ii. comply with the descriptions, specifications and representations as to the Services and Deliverables (including performance, capabilities, accuracy, completeness, characteristics, specifications, configurations, standards, functions, and requirements) as set forth in this Agreement or in a Work Order, including, without limitation, the Performance Standards and Measures included in the applicable Work Order and the specifications contained within the REMS Documents.

iii. maintain all licenses, certifications, permits and authorizations pertinent to the practice of pharmacy and required by all Applicable Laws, the REMS Documents, rules and regulations and this Agreement.

iv. make no representation, guarantee, or warranty about Product, whether orally or in writing, except as contained in written materials delivered to ESSDS by Jazz Pharmaceuticals for use in connection with the Services; (i) avoid deceptive, misleading or unethical practices that are or might be detrimental to Jazz Pharmaceuticals, Product, or the public; and (ii) make no false or misleading representations with regard to Jazz Pharmaceuticals or Product.

v. use commercially reasonable technical measures to (i) detect and eliminate computer viruses and other destructive code introduced to any computer systems used in connection with the Services, (ii) correct any error reproducible by ESSDS in any computer systems used in connection with the Services, and (iii) ensure that any computer systems used in connection with the Services are available without interruption, except as contemplated by the business continuity plan, included as an Appendix to JPP- 0002 – Inventory Control SOP.

9.3 Jazz Pharmaceuticals Representations and Warranties

(a) Jazz Pharmaceuticals represents and warrants that, to the best of its knowledge, it owns and possesses all right, title and interest in and to, or has valid licenses to use all of the proprietary rights necessary to perform its obligations under this Agreement.

(b) Jazz Pharmaceuticals warrants that, as of the delivery to ESSDS, Product will (i) conform to Jazz Pharmaceuticals' stated Product specifications, (ii) not be adulterated or misbranded within the meaning of the federal Food, Drug and Cosmetic Act of 1938,
Title 21, as amended (the "Act"), and (iii) not be articles which may not, under the provisions of the Act, be introduced into interstate commerce. THE WARRANTY SET FORTH IN THIS SECTION IS THE SOLE AND EXCLUSIVE WARRANTY GIVEN BY JAZZ PHARMACEUTICALS WITH RESPECT TO PRODUCT. JAZZ PHARMACEUTICALS EXPRESSLY DISCLAIMS ALL OTHER WARRANTIES RELATED TO PRODUCT, EXPRESS OR IMPLED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

(c) Jazz Pharmaceuticals represents and warrants that: (i) it is engaging ESSDS to perform bona fide, legitimate, reasonable, and necessary Services; (ii) the Services are not intended to serve, either directly or indirectly, as a means of marketing Product or as remuneration for steering patients or prescribers to Product; (iii) the Services are not intended to diminish the objectivity or professional judgment of ESSDS; (iv) any service requirements imposed by Jazz Pharmaceuticals, including through SOPs, Work Instructions, and Business Rules, are reasonably limited to what is necessary to ensure compliance with Jazz Pharmaceuticals' obligations under Applicable Law, including with respect to the REMS Program; (v) the Services do not involve counseling or promotion of any off-label use of Product; and (vi) the Services do not involve the counseling or promotion of a business arrangement or other activity that violates Applicable Law.

(d) 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 the Xyrem or Xywav or providing Xyrem or Xywav-related or REMS Program-related information.

ARTICLE X

OWNERSHIP AND INTELLECTUAL PROPERTY

10.1 Intellectual Property of Jazz Pharmaceuticals. All Intellectual Property either (a) conceived, generated, made, fixed in a tangible medium of expression or reduced to practice, as the case may be, by ESSDS within the scope and course of providing the Services to Jazz Pharmaceuticals under this Agreement (including Services relating to Authorized Generic Product) ("Work Product") or (b) owned or controlled by Jazz Pharmaceuticals on the Effective Date and/or otherwise independently of ESSDS and this Agreement will be the sole and exclusive property of Jazz Pharmaceuticals (the "Jazz Intellectual Property"). ESSDS will disclose Work Product under subpart (a) of this paragraph promptly to Jazz Pharmaceuticals. For the avoidance of doubt, Jazz Intellectual Property, may include but is not limited to, all, Deliverables, REMS Program Items, and Data. Jazz Pharmaceuticals shall also own all right, title, and interest in any telephone numbers, fax numbers, and web, and email domains established by ESSDS solely in connection with the Services performed hereunder and all such Intellectual Property rights therein, and the Parties will take all actions necessary so that any such numbers and domains will be registered with Jazz Pharmaceuticals following the expiration or termination of this Agreement for any reason, at Jazz Pharmaceuticals' sole cost and expense. ESSDS will execute any documents reasonably required for Jazz Pharmaceuticals to perfect its ownership interest in any Work Product. Any Work Product which constitutes a copyrightable work, whether published or unpublished, created by ESSDS in connection with or during the performance of any Services will be considered a work made for hire to the fullest extent permitted by law. If any such Work Product is not classified as a work made for

hire, then ESSDS assigns all worldwide rights in the work to Jazz Pharmaceuticals without royalty or any other consideration.

10.2 Intellectual Property of ESSDS. Notwithstanding anything to the contrary in Section 10.1 or otherwise, Jazz Intellectual Property does not include, and ESSDS shall retain all right, title and interest in and to, the ESSDS Intellectual Property. "ESSDS Intellectual Property" shall mean (a) all Intellectual Property owned or controlled by ESSDS on the Effective Date and/or otherwise independently of Jazz Pharmaceuticals and this Agreement, including but not limited to, all Intellectual Property developed by ESSDS or its Affiliates in its ordinary course of business whether or not such Intellectual Property is used in providing the Services under this Agreement ("ESSDS Intellectual Property"); and (b) all modifications, improvements, or enhancements to the foregoing made by ESSDS. ESSDS Intellectual Property specifically includes, but is not limited to, (i) computer software, technology, patient-centric services and analytics for pharmaceutical, biotechnology, medical device, vaccine and diagnostic manufacturers ("ESSDS Software"), (ii) pharmacy and specialty pharmacy industry knowledge, (iii) pharmacy and specialty pharmacy distribution, fulfillment, services, technology, and software, and (iv) pharmacy and specialty pharmacy data reporting to payers and manufacturers, subject to any data reporting restrictions set forth elsewhere in this Agreement.

10.3 Licenses to Jazz Pharmaceuticals. To the extent any ESSDS Software, website, portal, or mobile application is necessary for Jazz Pharmaceuticals to receive the Services, ESSDS hereby grants to Jazz Pharmaceuticals a limited, non-transferable, non-exclusive, royalty-free right and license to use such ESSDS Intellectual Property solely as reasonably necessary in Jazz Pharmaceuticals' normal course of receiving and using the Services during the term of this Agreement. In the event any ESSDS Intellectual Property is incorporated into any Work Product, ESSDS hereby grants to Jazz Pharmaceuticals a perpetual, limited, sublicensable to parties performing services to Jazz, non-exclusive, royalty-free right and license to use such ESSDS Intellectual Property solely in connection with such Work Product and provided that such ESSDS Intellectual Property shall not be used separate or apart from the Work Product.

ARTICLE XI

TERM AND TERMINATION

11.1 Term; Renewal. Unless otherwise terminated in accordance with the terms hereof, this Agreement will remain in effect for a period of two (2) years from the Effective Date. If no such notice of termination is given, this Agreement can be renewed for one (1) additional one (1) year term at the discretion of Jazz Pharmaceuticals by a written amendment hereto, subject to the right of termination as otherwise provided herein.

11.2 Termination Without Cause. Either Party may terminate this Agreement or any Work Order at any time without cause on one hundred eighty (180) days' prior written notice to the other Party.

11.3 Termination for Cause. Either Party may terminate this Agreement immediately upon written notice to the other Party if such other Party materially breaches this Agreement and, after receiving written notice identifying such breach, fails to cure such material breach within thirty (30) days after receipt of such notice. Such notice will include the effective date of termination.

11.4 Termination for Legal Necessity. Either Party may terminate this Agreement immediately upon written notice to the other Party in the event that (1) any Applicable Law, court decision, or the like is enacted, promulgated, published, or otherwise made effective, which would make ESSDS' performance of the Pharmacy Services illegal or otherwise commercially impracticable or Jazz Pharmaceuticals' development or commercialization of Product commercially, medically, or technically impracticable or (2) Jazz Pharmaceuticals receives notice of regulatory action by the FDA that results in the termination or suspension of its rights to manufacture or distribute Product in the United States.

11.5 Bankruptcy or Insolvency. Either Party may terminate this Agreement immediately upon written notice to the other Party, if such other Party makes an assignment for the benefit of creditors, files a petition in bankruptcy, is adjudicated insolvent or bankrupt, a receiver or trustee is appointed with respect to a substantial part of such other Party's property, or a proceeding is commenced against it which will substantially impair its ability to perform hereunder.

11.6 Partial Termination. A Party shall have the option and right to terminate (i) all of the Services or (ii) one or more specific services that may be part of the Services (collectively or individually referred to as "Specified Service") as provided for in this Article XI with one hundred eighty (180) days' prior written notice to the other Party.

11.7 Effect of Termination. Upon expiration or earlier termination of this Agreement:

(a) ESSDS shall deliver to Jazz Pharmaceutical, at Jazz Pharmaceuticals' expense, all tangible materials in ESSDS' possession or control belonging to Jazz Pharmaceuticals.

(b) ESSDS shall notify any person or entity who contacts ESSDS in connection with any matter related to the Services that ESSDS is no longer providing those Services and direct them as requested by Jazz Pharmaceuticals.

(c) S shall invoice Jazz Pharmaceuticals for any payments due for the applicable Services through the date of termination, pursuant to Section 3.2 and Jazz Pharmaceuticals shall pay such invoice(s) in accordance with Section 3.3.

(d) ESSDS shall otherwise provide all other cooperation reasonably requested by Jazz Pharmaceuticals to ensure a smooth transition and the uninterrupted operation of the Specified Service.

11.8 Transition of Services. Upon termination or expiration of this Agreement or any Specified Service, the Parties shall mutually agree on an expeditious schedule of transition of the applicable Services.

11.9 Transition of Patient Information. In connection with any of the Services, Jazz Pharmaceuticals may request that ESSDS transfer all prescriptions, all patient and prescriber data required to administer and maintain compliance with the REMS Program, SOPs and Business Rules at Jazz Pharmaceutical's request to a pharmacy assuming responsibility for such services for the purpose of continuing "treatment" (as that term is defined by HIPAA) of affected Patients, and ESSDS shall expeditiously honor that request to the extent disclosure of such Patient Data by ESSDS is permitted under Applicable Law, including, but not limited to,

HIPAA. All such Patient Data shall be transferred in standard NCPDP format. The purpose of any transfer of Patient Data is to assure, to the extent possible, a smooth transition for Patients.

11.10 Survival. Termination or expiration of the Agreement for any reason shall not affect the continuing rights and obligations of the Parties under Articles III; VII; VIII; X; XII; and XIV; and Sections 2.3; 2.4.1; 5.1; 5.2; 9.1; 11.7; 11.8; 11.9; 11.10; and 13.4 of this Agreement.

ARTICLE XII

INDEMNIFICATION; LIMITATION OF LIABILITY; INSURANCE

12.1 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 attorneys' 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 Product; (b) the negligence, recklessness, or willful misconduct of Jazz Pharmaceuticals or any of its employees, or (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 and Claims are caused by ESSDS' breach hereof, negligence, recklessness, or willful misconduct.

12.2 Indemnification by ESSDS. Subject to the terms hereof, ESSDS shall indemnify and defend Jazz Pharmaceuticals, its Affiliates, and their respective directors, officers, employees, agents, successors and permitted assigns, from and against any Losses as a result of any third- party Claims, to the extent arising from (a) the negligence, recklessness or willful misconduct of ESSDS or any of its employees, Affiliates or permitted subcontractors or (b) ESSDS' breach of any representation, warranty, or obligation under this Agreement. Such obligation to indemnify, defend, and hold harmless shall not apply to the extent Losses and Claims are caused by Jazz Pharmaceuticals' breach hereof, negligence, recklessness or willful misconduct.

12.3 Indemnification Conditions and Procedures. The Party seeking indemnification (the "Requesting Party") shall (a) promptly notify the other Party (the "Indemnifying Party") in writing upon receipt of oral or written notice of any actual or alleged Claim, (b) allow the Indemnifying Party, at its discretion and cost, to undertake and control the defense of such Claim, (c) diligently assist the Indemnifying Party and cooperate in defending against such Claim; and (d) not, except at its own cost, voluntarily make or agree to make any payment or incur any expense in connection with any such Claim without the prior written consent of the Indemnifying Party.

12.4 Limitation of Liability. EXCEPT WITH RESPECT TO BREACHES OF CONFIDENTIALITY OBLIGATIONS UNDER ARTICLE VIII, INTELLECTUAL

PROPERTY INFRINGEMENT CLAIMS, AND THE PARTIES' INDEMNIFICATION OBLIGATIONS UNDER SECTIONS 12.1 AND 12.2, OR A PARTY'S (OR ITS AFFILIATES OR PERMITTED SUBCONTRACTORS) GROSS NEGLIGENCE, RECKLESSNESS OR WILLFUL MISCONDUCT IN NO EVENT SHALL EITHER PARTY BE LIABLE FOR LOST PROFITS OR ANY INDIRECT, SPECIAL, INCIDENTAL, CONSEQUENTIAL, PUNITIVE OR SIMILAR DAMAGES, HOWEVER CAUSED AND ONANY LEGAL THEORY, EVEN IF SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

12.5 Insurance.

Each Party shall maintain such policies of general liability in an amount [*], and other insurance of the types and in amounts [***]. ESSDS will maintain professional liability insurance in an amount [***]. Notwithstanding the foregoing, Jazz Pharmaceuticals shall maintain throughout the term of this Agreement commercial products liability coverage through commercial insurance in an amount [***]. Jazz Pharmaceuticals shall name ESSDS as an additional insured under said commercial products liability policy. Jazz Pharmaceuticals commercial products liability insurance coverage shall be primary and non-contributory with respect to all other available sources of insurance.

If confidential information including but not limited to Protected Health Information ("PHI") or Personal Identifying Information ("PII") will be shared between the Parties, ESSDS shall maintain a cyber-risks or similar data breach or privacy liability insurance program to cover liability arising out of ESSDS's failure to protect any information deemed confidential by any Applicable or governing law, statute, or regulation with a limit of no less than ten million dollars ($10,000,000) per claim or policy aggregate.

Jazz Pharmaceuticals, as of the Effective Date, utilizes the following cyber-security measures: (i) appointed Chief Information Security Officer (CISO) and dedicated security team, (ii) information security risks and program progress are presented to an audit committee quarterly,
(iii) International Organization for Standardization (ISO) 27001 compliant and annually assessed, (iv) conduct independent Red Team and Blue Team penetration tests annually, (v) independent information security maturity assessments conducted every two (2) years measured against National Institute Standards and Technology (NIST) cybersecurity framework (CSF),
(vi) security operations center team in place monitoring and responding to events twenty-four
(24) hours a day and seven (7) days a week, (vii) centralized identity management with multi- factor identification in place for all team members, and (viii) incident response plan in place and tested annually.

In the event that any of the above-described insurance policies are written on a claims-made basis, then such policy or policies shall be maintained during the entire period of the Agreement and for a period of no less than three (3) years following the termination or expiration of the Agreement. Each Party represents and warrants that any retroactive date under such policies shall precede the Effective date of this Agreement. Each Party shall provide the other Party a 30-day notice of cancellation of any of the required insurance programs if any insurance policy(ies) is(are) cancelled or not renewed and not immediately replaced by a substantially similar insurance program without a disruption in coverage while continuing to meet the requirements herein. The above-described insurance policies will be issued by insurance carriers with a minimum A.M. Best rating of A- VIII (or the substantial equivalent rating

provided by Fitch, Standard & Poor's or Moody's) at the time of each policy inception and such insurance carriers shall be lawfully authorized to do business in the jurisdiction(s) in which the Services are rendered.

In no event will the coverage or limits of any insurance maintained under this Agreement, or the lack or unavailability of any other insurance, limit or diminish in any way either Parties obligations or liability under this Agreement. Upon request, each Party shall furnish the other with Certificates of Insurance relevant to this Agreement. Any acceptance of insurance certificates by either Party shall not limit or relieve their duties and responsibilities assumed under this Agreement.

ARTICLE XIII

COLLABORATION

13.1 Annual Review. No less than one hundred-eighty (180) days prior to each anniversary of the Effective Date of this Agreement, ESSDS and Jazz Pharmaceuticals will meet to review the Services to be performed during the next twelve (12) months (each such meeting, an "Annual Review"). The purpose of each Annual Review is to assess the operational program(s), identify any areas of improvement, and discuss any additional or revised services. The Annual Review is not intended to take the place of regular and ongoing communications between the Parties pursuant to Section 13.2. The Annual Review will take place at a time, location, and method (i.e., in-person or teleconference) mutually determined by the Parties.

13.2 Regular Meetings and Communication. Jazz Pharmaceuticals and ESSDS agree to meet (whether in-person or by teleconference) as necessary, for ESSDS to effectively perform the Services specified in each Work Order hereunder. Jazz Pharmaceuticals and ESSDS agree to meet formally on at least a quarterly basis during the term of this Agreement to, among other things, discuss performance under the Agreement, strategic planning, and to evaluate the progress being made against objectives established in this Agreement or Work Orders and any enhancements that might be made to the processes set forth herein.

13.3 Non-Disparagement; No Disadvantaging. Neither Party will disparage the other Party or any Product or Services. Notwithstanding the foregoing, the following actions shall not be considered disparaging: (i) the action taken is related to drug interactions with other prescription or over-the-counter drug products, (ii) the action taken is related to contraindications for such Product; the action taken involves displaying or communicating relative Patient costs or coverage, (iv) or as otherwise may be consistent with ESSDS's independent exercise of the practice of pharmacy in accordance with all Applicable Law.

13.4 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 of the this Agreement 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 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 of the this Agreement 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 in narcolepsy or excessive daytime sleepiness in narcolepsy or idiopathic hypersomnia.

ARTICLE XIV

GENERAL PROVISIONS

14.1 Amendment. This Agreement may not be amended or modified except by a written instrument signed by both Parties.

14.2 Waiver. A failure by either Party to insist upon strict compliance with any term of this Agreement, to exercise any option, to enforce any right, or to seek any remedy upon any default of the other Party shall not affect, or constitute a waiver of, such Party's right to insist upon strict compliance with that term, to exercise that option, to enforce that right, or to seek that remedy with respect to that default or any prior, contemporaneous, or subsequent default. No custom or practice of the Parties at variance with any provision of this Agreement shall affect, or constitute a waiver of, a Party's right to demand strict compliance with all provisions of this Agreement.

14.3 Assignment. Jazz Pharmaceuticals may assign this Agreement, in whole or in part, to any Affiliate or to a third-party successor to substantially all of the business to which this Agreement relates, whether in a merger, sale of stock, sale of assets or other transaction. ESSDS may assign this Agreement, in whole or in part, upon consent of Jazz Pharmaceuticals, such consent not to be unreasonably withheld.

14.4 No Implied Licenses. Except as expressly provided in this Agreement, nothing contained herein shall be deemed to grant either Party any rights or licenses under any Intellectual Property rights of the other Party.

14.5 Entire Agreement. This Agreement (together with all Exhibits and Work Orders hereto incorporated by reference) constitutes the entire agreement between the Parties with respect to the Services and supersedes all prior negotiations, representations or agreements, written or oral, regarding the subject matter hereof, which will remain in full force and effect in accordance with its terms with respect to disclosures made prior to the date hereof. Jazz Pharmaceuticals specifically rejects and will not be bound by any other terms and conditions.

14.6 Tax Liability. ESSDS will be solely responsible for meeting its corporation tax and any applicable social security (or equivalent in any other country, e.g., national insurance obligations) and for enabling that its employees meet their respective income tax and applicable social security obligations (or equivalent in any other country) and all other applicable social insurances. ESSDS shall indemnify and hold harmless Jazz Pharmaceuticals for all taxes, social security or its equivalent and other contributions, costs, claims, penalties, interest, expenses or proceedings which Jazz Pharmaceuticals may incur arising from or in connection with the failure of ESSDS or its employees to meet their respective responsibilities under this Section.

14.7 Relationship of the Parties. ESSDS will be an independent contractor of Jazz Pharmaceuticals, and nothing in this Agreement will be construed to create any partnership, joint venture, agency, or employment relationship between the Parties or between Jazz Pharmaceuticals and the Personnel of ESSDS. ESSDS is and will remain responsible for its

respective Personnel and will make no claim against Jazz Pharmaceuticals or its Affiliates for eligibility to participate in any benefits extended by Jazz Pharmaceuticals to its employees. ESSDS will have no authority to act for, bind or commit Jazz Pharmaceuticals or its Affiliates in any way.

14.8 Force Majeure. If the performance of any part of this Agreement by either Party shall be affected for any length of time by fire or other casualty, government restrictions, war, riots, strikes, or labor disputes, lock outs, transportation delays, and acts of God, or any such similar causes which are beyond the reasonable control of such Party, such Party shall not be responsible for delay or failure of the performance of this Agreement for such length of time; provided, however, that the obligation of the Parties to pay amounts then due shall not be suspended or delayed; and provided, further, that if ESSDS is precluded from rendering Services for a continuous period in excess of ten (10) business days, Jazz Pharmaceuticals shall be entitled to terminate this Agreement upon five (5) days' notice.

14.9 Severability. If any of the provisions or any portion of any provision of this Agreement is held to be unenforceable or invalid by a court or arbitration panel of competent jurisdiction, the validity and enforceability of the enforceable portion of any such provision and/or the remaining provisions will not be affected.

14.10 Governing Law. This Agreement, 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.

14.11 Notices. Any notice delivered to a Party pursuant to this Agreement must be in writing and may be delivered: personally (effective upon receipt); by depositing with a nationally- recognized overnight courier (effective one business day after deposit); or by depositing in the United States Mail, postage prepaid, registered or certified mail, return receipt requested (effective five (5) days after deposit). All notices hereunder will be addressed to the Party at the address indicated below, or at such other address that may have been specified by written notice delivered in accordance with this Section:

If to ESSDS:

Express Scripts, Inc.
c/o Express Scripts Specialty Distribution Services,
Inc. One Express Way,
St. Louis, MO 63121
Attn: Legal
Department

with a copy to:

Express Scripts Specialty Distribution Services, Inc.
One Express Way,
St. Louis, MO
63121

Attn: General Manager

If to Jazz Pharmaceuticals:

Jazz Pharmaceuticals, Inc.
Attention: Legal Department
3170 Porter Drive
Palo Alto, CA 94304
Email: Jazz_Notices@jazzpharma.com

14.12 Counterparts. This Agreement, any Work Order, and any amendments hereto or thereto, 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.

14.13 Compliance with Laws. Each Party shall, in its respective performance of this Agreement, take all actions necessary and appropriate to assure that it complies with all applicable federal, state, and local laws and regulations, including, without limitation, the Anti-Kickback Statute (42 U.S.C. § 1320a-7b(b)), the Public Contracts Anti-Kickback Act (41 U.S.C. § 51 et seq.) and the Stark Law (42 U.S.C. § 1395nn).

14.14 Publicity. Neither Party shall cause or permit the oral or written release of any statement, advertisement, information or publicity referring to the other Party or any of its personnel without such Party's prior written consent.

(Signature Page to Follow)

Intending to be bound by the provisions hereof, each of the Parties hereto have caused this Agreement to be executed personally or by its duly authorized representative, to be effective as of the Effective Date.

AGREED TO:

Jazz Pharmaceuticals, Inc.

By: /s/ Barrett Land
Name: Barrett Land
Title: VP, Pricing, Contracting, & Reimbursement
Date: 29 November 2022

AGREED TO:

Express Scripts Specialty Distribution Services, Inc.

By: /s/ Joshua B. Parker
Name: Joshua B. Parker
Title: VP
11/22/2022 | 11:24 AM CST

By: _____
Name:
Title:

RPM for JLD 11.22.22

EXHIBIT A

Trademarks

XYREM® (sodium oxybate) 866-XYREM88®

Jazz Pharmaceuticals, Inc.®

Jazz® 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 B

ESSDS LOCATIONS

Express Scripts Building 3 4600 North Hanley Rd.
Suite B
St. Louis, MO 63134

Express Scripts Building 6 4700 North Hanley Rd.
Suite 1W
St. Louis, MO 63134

EXHIBIT C

WORK ORDER NO. __
TO PHARMACY MASTER SERVICES AGREEMENT

This Work Order No. __("Work Order "), dated as of the last date signed below, is made effective____, 20__("Work Order Effective Date"), pursuant to the terms of the Pharmacy Master Services Agreement ("Agreement") effective as of [Month] [day], 2022 between Jazz Pharmaceuticals, Inc. ("Jazz Pharmaceuticals") and Express Scripts Specialty Distribution Services, Inc. ("ESSDS"), (individually, "Party" and collectively, "Parties"), the terms of which are incorporated herein by reference.

No modification of this Work Order will be deemed effective unless in writing and signed by the Parties via an amendment hereto. No waiver of any obligation under this Work Order will be effective unless in writing and signed by the Party to be bound and then only to the extent expressly waived in such signed writing.

A. SCOPE OF SERVICES

B. PROGRAM FEES and PASS THROUGH EXPENSES

Accepted and Agreed:

EXPRESS SCRIPTS SPECIALTY DISTRIBUTION SERVICES, INC.		**JAZZ PHARMACEUTICALS, INC.**	
By:	_____	By:	_____
Signature:	_____	Signature:	_____
Title:	_____	Title:	_____
Date:	_____	Date:	_____

Exhibit A

Scope of Service

Exhibit B

Fees

EXHIBIT D

SERVICE LEVEL AGREEMENTS ("SLA")

This Exhibit identifies the expected level of service for certain Services during the term of the Agreement. The purpose of this SLA is to specify the requirements of certain Services with regards to:

Function	Activity	Measurement	Service Level Commitment
Operations	Inbound Calls to the Call Center across all departments	Average Speed to Answer (ASA)	Monthly[1] ASA ≤ 50 Seconds for RPH and RN; ≤ 30 Seconds for PSC and Reimbursement
Operations	Inbound Calls to the Call Center across all departments except for RPH	Inbound call Service Level (SL)	80% of all inbound calls to PSC, RN, and Reimbursement are answered in ≤ 20 seconds Monthly[1]
Operations	Inbound Calls to the Call Center across all departments	Maximum wait time	≥ 99% of all inbound calls will be answered in less than 5 minutes unless caller is proactively offered an automated, or manual, option to receive a returned call without losing his/her place in queue
Operations	Inbound Calls to the Call Center	Inbound Call Abandon Rate	≤ 3% abandon rate Monthly[1]
Customer Experience	Patient Feedback among patients who received shipment	Patient Satisfaction Percentage[2]	Greater than or equal to 90% Monthly[1]

[1]Excludes the month of January. ESSDS will make commercially reasonable efforts to achieve SLAs for the month of January.
[2]Patient Satisfaction Percentage is measured by a patient responding with 3, 4, or 5 to the question "*On a scale from 1 - 5 where 1 is Very Dissatisfied and 5 is Very Satisfied, how would you rate your overall experience with your specialty pharmacy?"*

EXHIBIT E

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

Lot No.	Bottles	Orders

Jazz Pharmaceuticals plc
2011 Equity Incentive Plan

1. General.

(a) Relationship to 2007 Plan and 2003 Plan. From and after 12:01 a.m. Pacific time on the Effective Date, all outstanding stock awards granted under the Jazz Pharmaceuticals plc 2007 Equity Incentive Plan (the "***2007 Plan***"), which was the successor to and continuation of the Jazz Pharmaceuticals plc 2003 Equity Incentive Plan (the "***2003 Plan***"), will remain subject to the terms of the 2007 Plan or the 2003 Plan, as applicable; *provided*, *however*, that any Ordinary Shares subject to outstanding stock awards granted under the 2007 Plan or the 2003 Plan that (i) expire or terminate for any reason prior to exercise or settlement, (ii) are forfeited because of the failure to meet a contingency or condition required to vest such Ordinary Shares or repurchased by the Company or an Affiliate at the original issuance price or (iii) are reacquired by the Company or an Affiliate or withheld (or not issued) to satisfy a tax withholding obligation in connection with an award (the "***Returning Shares***") will immediately be added to the Share Reserve (as further described in Section 3(a) below) as and when such Ordinary Shares become Returning Shares, and become available for issuance pursuant to Awards granted under this Plan.

(b) Eligible Award Recipients. The persons eligible to receive Awards are Employees.

(c) Available Awards. The Plan provides for the grant of the following Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) Stock Appreciation Rights (iv) Restricted Stock Awards, (v) Restricted Stock Unit Awards, (vi) Performance Stock Awards, (vii) Performance Cash Awards, and (viii) Other Stock Awards.

(d) Purpose. The Company, by means of the Plan, seeks to secure and retain the services of the group of persons eligible to receive Awards as set forth in Section 1(b), to provide incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and to provide a means by which such eligible recipients may be given an opportunity to benefit from increases in value of the Ordinary Shares through the granting of Awards.

2. Administration.

(a) Administration by Board. The Board shall administer the Plan unless and until the Board delegates administration of the Plan to a Committee or Committees, as provided in Section 2(c).

(b) Powers of Board. The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine from time to time (A) which of the persons eligible under the Plan shall be granted Awards; (B) when and how each Award shall be granted; (C) what type or combination of types of Award shall be granted; (D) the provisions of each Award granted (which need not be identical), including the time or times when a person shall be permitted to receive cash or Ordinary Shares pursuant to a Stock Award; (E) the number of Ordinary Shares with respect to which a Stock Award shall be granted to each such person; and (F) the Fair Market Value applicable to a Stock Award.

(ii) To construe and interpret the Plan and Awards granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement or in the written terms of a Performance Cash Award, in a manner and to the extent it shall deem necessary or expedient to make the Plan or Award fully effective.

(iii) To settle all controversies regarding the Plan and Awards granted under it.

(iv) To accelerate the time at which an Award may first be exercised or the time during which an Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Award stating the time at which it may first be exercised or the time during which it will vest.

(v) To effect, at any time and from time to time, with the consent of any adversely affected Participant, (A) the reduction of the exercise price (or strike price) of any outstanding Option or SAR under the Plan, provided this does not reduce the exercise price or strike price below the nominal value of an Ordinary Share; (B) the cancellation of any outstanding Option or SAR under the Plan and the grant in substitution therefor of (1) a new Option or SAR under the Plan or another equity plan of the Company covering the same or a different number of Ordinary Shares, (2) a Restricted Stock Award, (3) a Restricted Stock Unit Award, (4) an Other Stock Award, (5) cash and/or (6) other valuable consideration (as determined by the Board, in its sole discretion); or (C) any other action that is treated as a repricing under generally accepted accounting principles.

(vi) To suspend or terminate the Plan at any time. Suspension or termination of the Plan shall not impair rights and obligations under any Award granted while the Plan is in effect except with the written consent of the affected Participant.

(vii) To amend the Plan in any respect the Board deems necessary or advisable. However, except as provided in Section 9(a) relating to Capitalization Adjustments, to the extent required by applicable law or listing requirements, shareholder approval shall be required for any amendment of the Plan that either (A) materially increases the number of Ordinary Shares available for issuance under the Plan, (B) materially expands the class of individuals eligible to receive Awards under the Plan, (C) materially increases the benefits accruing to Participants under the Plan or materially reduces the price at which Ordinary Shares may be issued or purchased under the Plan, (D) materially extends the term of the Plan, or (E) expands the types of Awards available for issuance under the Plan. Except as provided above, rights under any Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (1) the Company requests the consent of the affected Participant, and (2) such Participant consents in writing.

(viii) To submit any amendment to the Plan for shareholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of (A) Section 162(m) of the Code regarding the exclusion of performance-based compensation from the limit on corporate deductibility of compensation paid to Covered Employees, (B) Section 422 of the Code regarding incentive stock options or (C) Rule 16b-3.

(ix) To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more Awards, including, but not limited to, amendments to provide terms more favorable to the Participant than previously provided in the Award Agreement, subject to any specified limits in the Plan that are not subject to Board discretion; *provided, however*, that except with respect to amendments that disqualify or impair the status of an Incentive Stock Option, a Participant's rights under any Award shall not be impaired by any such amendment unless (A) the Company requests the consent of the affected Participant, and

(B) such Participant consents in writing. Notwithstanding the foregoing, subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Awards without the affected Participant's consent if necessary to maintain the qualified status of the Award as an Incentive Stock Option or to bring the Award into compliance with Section 409A of the Code.

(x) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and any Affiliates and that are not in conflict with the provisions of the Plan or Awards.

(xi) To adopt such procedures and sub-plans as are necessary or appropriate to permit participation in the Plan by Employees who are foreign nationals or employed outside the United States.

(c) Delegation to Committee.

(i) General. The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in the Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Committee may, at any time, abolish the subcommittee and/or revest in the Committee any powers delegated to the subcommittee. The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated.

(ii) Section 162(m) and Rule 16b-3 Compliance. The Committee may consist solely of two or more Outside Directors, in accordance with Section 162(m) of the Code, or solely of two or more Non-Employee Directors, in accordance with Rule 16b-3.

(d) Delegation to Other Person or Body. The Board or any Committee may delegate to one or more persons or bodies the authority to do one or more of the following to the extent permitted by applicable law: (i) designate recipients, other than Officers, of Stock Awards, *provided* that no person or body may be delegated authority to grant a Stock Award to themself; (ii) determine the number of Ordinary Shares subject to such Stock Awards; and (iii) determine the terms of such Stock Awards; *provided*, *however*, that the Board or Committee action regarding such delegation will fix the terms of such delegation in accordance with applicable law, including without limitation Sections 152 and 157 of the Delaware General Corporation Law. Unless provided otherwise in the Board or Committee action regarding such delegation, each Stock Award granted pursuant to this section will be granted on the applicable form of Stock Award Agreement most recently approved for use by the Board or the Committee, with any modifications necessary to incorporate or reflect the terms of such Stock Award. Notwithstanding anything to the contrary herein, neither the Board nor any Committee may delegate to any person or body (who is not a Director or that is not comprised solely of Directors, respectively) the authority to determine the Fair Market Value pursuant to Section 13(w)(iii) below.

(e) Effect of Board's Decision. All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

3. Shares Subject to the Plan.

(a) Share Reserve. Subject to the provisions of Section 9(a) relating to Capitalization Adjustments, the aggregate number of Ordinary Shares that may be issued pursuant to Stock Awards from and after the Effective Date shall not exceed eight million three hundred thirty five thousand two hundred fifty five (8,335,255) Ordinary Shares (the "***Share Reserve***"), which number is the sum of (i) five million (5,000,000) Ordinary Shares, plus (ii) an additional number of Ordinary Shares in an amount not to exceed three million three hundred thirty five thousand two hundred fifty five (3,335,255) Ordinary Shares (which number consists of the Returning Shares, if any, as such shares become available from time to time). In addition, the number of Ordinary Shares available for issuance under the Plan shall automatically increase on January 1st of each year for a period of ten (10) years commencing on January 1, 2013 and ending on (and including) January 1, 2022, in an amount equal to the lesser of (i) four and one-half percent (4.5%) of the total number of Ordinary Shares outstanding on December 31st of the preceding calendar year or (ii) five million (5,000,000) Ordinary Shares. Notwithstanding the foregoing, the Board may act prior to the first day of any calendar year, to provide that there shall be no increase in the Share Reserve for such calendar year or that the increase in the Share Reserve for such calendar year shall be a lesser number of Ordinary Shares than would otherwise occur pursuant to the preceding sentence. For clarity, the Share Reserve in this Section 3(a) is a limitation on the number of Ordinary Shares that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Stock Awards except as provided in Section 7(a). Shares may be issued in connection with a merger or acquisition as permitted by, as applicable, NASDAQ Listing Rule 5635(c) or, if applicable, NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable rule, and such issuance shall not reduce the number of Ordinary Shares available for issuance under the Plan. Furthermore, if a Stock Award or any portion thereof (i) expires or otherwise terminates without all of the Ordinary Shares covered by such Stock Award having been issued or (ii) is settled in cash (*i.e.*, the Participant receives cash rather than Ordinary Shares), such expiration, termination or settlement shall not reduce (or otherwise offset) the number of Ordinary Shares that may be available for issuance under the Plan.

(b) Reversion of Shares to the Share Reserve. If (i) any Ordinary Shares issued pursuant to a Stock Award are forfeited back to or repurchased by the Company or any Affiliate because of the failure to meet a contingency or condition required for the vesting of such Ordinary Shares, or (ii) any Ordinary Shares are cancelled in accordance with the cancellation and regrant provisions of Section 2(b)(v), then the Ordinary Shares that are forfeited, repurchased or canceled shall revert to and again become available for issuance under the Plan. If any Ordinary Shares subject to a Stock Award are not delivered to a Participant because such Ordinary Shares are withheld for the payment of taxes pursuant to Section 8(g) or a Stock Award is exercised through a reduction of Ordinary Shares subject to the Stock Award (*i.e.*, "net exercised") or an appreciation distribution in respect of a Stock Appreciation Right is paid in Ordinary Shares, the number of Ordinary Shares subject to the Stock Award that are not delivered to the Participant shall remain available for subsequent issuance under the Plan. If the exercise price of any Stock Award is satisfied by tendering Ordinary Shares held by the Participant (either by actual delivery or attestation), then the number of Ordinary Shares so tendered shall remain available for issuance under the Plan.

(c) Incentive Stock Option Limit. Notwithstanding anything to the contrary in this Section 3 and, subject to the provisions of Section 9(a) relating to Capitalization Adjustments, the aggregate maximum number of Ordinary Shares that may be issued pursuant to the exercise of Incentive Stock Options shall be one hundred million (100,000,000) Ordinary Shares.

(d) Section 162(m) Limitation on Annual Grants. Subject to the provisions of Section 9(a) relating to Capitalization Adjustments, at such time as the Company may be subject

to the applicable provisions of Section 162(m) of the Code, a maximum of two million (2,000,000) Ordinary Shares subject to Options, Stock Appreciation Rights and Other Stock Awards whose value is determined by reference to an increase over an exercise or strike price of at least one hundred percent (100%) of the Fair Market Value on the date any such Stock Award is granted may be granted to any Participant during any calendar year. Notwithstanding the foregoing, if any additional Options, Stock Appreciation Rights or Other Stock Awards whose value is determined by reference to an increase over an exercise or strike price of at least one hundred percent (100%) of the Fair Market Value on the date the Stock Awards are granted to any Participant during any calendar year, compensation attributable to the exercise of such additional Stock Awards shall not satisfy the requirements to be considered "qualified performance-based compensation" under Section 162(m) of the Code unless such additional Stock Awards are approved by the Company's shareholders.

(e) Source of Shares. The shares issuable under the Plan shall be authorized but unissued or reacquired Ordinary Shares, including Ordinary Shares repurchased by the Company or any Affiliate on the open market or otherwise.

4. Eligibility.

(a) Eligibility for Specific Stock Awards. Incentive Stock Options may be granted only to employees of the Company or a "parent corporation" or "subsidiary corporation" thereof (as such terms are defined in Sections 424(e) and (f) of the Code). Stock Awards other than Incentive Stock Options may be granted to Employees; *provided, however*, that Nonstatutory Stock Options and SARs may not be granted to Employees who are providing Continuous Service only to any "parent" of the Company, as such term is defined in Rule 405 promulgated under the Securities Act, unless the Ordinary Shares underlying such Stock Awards are treated as "service recipient stock" under Section 409A of the Code because the Stock Awards are granted pursuant to a corporate transaction (such as a spin off transaction) or unless such Stock Awards comply with the distribution requirements of Section 409A of the Code.

(b) Ten Percent Shareholders. A Ten Percent Shareholder shall not be granted an Incentive Stock Option unless the exercise price of such Option is at least one hundred ten percent (110%) of the Fair Market Value on the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

5. Provisions Relating to Options and Stock Appreciation Rights.

Each Option or SAR shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. All Options shall be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates shall be issued for Ordinary Shares purchased on exercise of each type of Option. If an Option is not specifically designated as an Incentive Stock Option, then the Option shall be a Nonstatutory Stock Option. The provisions of separate Options or SARs need not be identical; *provided, however*, that each Option Agreement or Stock Appreciation Right Agreement shall conform to (through incorporation of provisions hereof by reference in the applicable Award Agreement or otherwise) the substance of each of the following provisions:

(a) Term. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, no Option or SAR shall be exercisable after the expiration of ten (10) years from the date of its grant or such shorter period specified in the Award Agreement.

(b) Exercise Price. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, the exercise price (or strike price) of each Option or SAR shall be not less than one

hundred percent (100%) of the Fair Market Value of the Ordinary Shares subject to the Option or SAR on the date the Option or SAR is granted. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise price (or strike price) lower than one hundred percent (100%) of the Fair Market Value of the Ordinary Shares subject to the Option or SAR if such Option or SAR is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Sections 409A and, if applicable, 424(a) of the Code, provided that in all cases the exercise price is not less than the nominal value of an Ordinary Share. Each SAR will be denominated in Ordinary Share equivalents.

(c) Purchase Price for Options. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option shall be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below; *provided, however*, that where Ordinary Shares are issued pursuant to the exercise of an Option the nominal value of each newly issued Ordinary Share is fully paid up. The Board shall have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to utilize a particular method of payment. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of the Ordinary Shares subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of Ordinary Shares;

(iv) if the option is a Nonstatutory Stock Option, by a "net exercise" arrangement pursuant to which the Company will reduce the number of Ordinary Shares issuable upon exercise by the largest whole number of Ordinary Shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that the Company shall accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole Ordinary Shares to be issued; *provided, further,* that Ordinary Shares will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) Ordinary Shares issuable upon exercise are reduced to pay the exercise price pursuant to the "net exercise," (B) Ordinary Shares are delivered to the Participant as a result of such exercise, and (C) Ordinary Shares are withheld to satisfy tax withholding obligations; or

(v) in any other form of legal consideration that may be acceptable to the Board.

(d) Exercise and Payment of a SAR. To exercise any outstanding Stock Appreciation Right, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right. The appreciation distribution payable on the exercise of a Stock Appreciation Right will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the Stock Appreciation Right) of a number of Ordinary Shares equal to the number of Ordinary Share equivalents in which the Participant is vested under such Stock Appreciation Right, and with respect to which the Participant is

exercising the Stock Appreciation Right on such date, over (B) the strike price that will be determined by the Board at the time of grant of the Stock Appreciation Right. The appreciation distribution in respect to a Stock Appreciation Right may be paid in Ordinary Shares, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right; *provided*, *however*, that where Ordinary Shares are issued pursuant to a Stock Appreciation Right the nominal value of each newly issued Ordinary Share is fully paid up.

(e) Transferability of Options and SARs. The Board may, in its sole discretion, impose such limitations on the transferability of Options and SARs as the Board shall determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options and SARs shall apply:

(i) Restrictions on Transfer. An Option or SAR shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant; *provided*, *however*, that the Board may, in its sole discretion, permit transfer of the Option or SAR in a manner that is not prohibited by applicable tax and securities laws upon the Participant's request. Except as explicitly provided herein, neither an Option nor a SAR may be transferred for consideration.

(ii) Domestic Relations Orders. Subject to the approval of the Board or a duly authorized Officer, an Option or SAR may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument as permitted by Treasury Regulation 1.421-1(b)(2). If an Option is an Incentive Stock Option, such Option may be deemed to be a Nonstatutory Stock Option as a result of such transfer.

(iii) Beneficiary Designation. Notwithstanding the foregoing, the Participant may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Company and any broker designated by the Company to effect Option exercises, designate a third party who, in the event of the death of the Participant, shall thereafter be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise. In the absence of such a designation, the executor or administrator of the Participant's estate shall be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise.

(f) Vesting Generally. The total number of Ordinary Shares subject to an Option or SAR may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option or SAR may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of Performance Goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options or SARs may vary. The provisions of this Section 5(f) are subject to any Option or SAR provisions governing the minimum number of Ordinary Shares as to which an Option or SAR may be exercised.

(g) Termination of Continuous Service. Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company or any Affiliate, if a Participant's Continuous Service terminates (other than for Cause or upon the Participant's death or Disability), the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Award as of the date of termination of Continuous Service) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Participant's Continuous Service (or such longer or shorter period specified in the applicable Award Agreement), or (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous

Service, the Participant does not exercise his or her Option or SAR within the time specified herein or in the Award Agreement (as applicable), the Option or SAR shall terminate.

(h) Extension of Termination Date. If the exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of Ordinary Shares would violate the registration requirements under the Securities Act, then the Option or SAR shall terminate on the earlier of (i) the expiration of a total period of three (3) months (that need not be consecutive) after the termination of the Participant's Continuous Service (other than for Cause) during which the exercise of the Option or SAR would not be in violation of such registration requirements or five (5) days (that need not be consecutive) after the termination of the Participant's Continuous Service for Cause, as applicable, or (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the immediate sale of any Ordinary Shares received upon exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option or SAR shall terminate on the earlier of (i) the expiration of a period equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Ordinary Shares received upon exercise of the Option or SAR would not be in violation of the Company's insider trading policy, or (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement.

(i) Disability of Participant. Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company or any Affiliate, if a Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Option or SAR as of the date of termination of Continuous Service), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination of Continuous Service (or such longer or shorter period specified in the Award Agreement), or (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR within the time specified herein or in the Award Agreement (as applicable), the Option or SAR (as applicable) shall terminate.

(j) Death of Participant. Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company or any Affiliate, if (i) a Participant's Continuous Service terminates as a result of the Participant's death, or (ii) the Participant dies within the period (if any) specified in the Award Agreement for exercisability after the termination of the Participant's Continuous Service (for a reason other than death), then the Option or SAR may be exercised (to the extent the Participant was entitled to exercise such Option or SAR as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Option or SAR by bequest or inheritance or by a person designated to exercise the Option or SAR upon the Participant's death, but only within the period ending on the earlier of (i) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Award Agreement), or (ii) the expiration of the term of such Option or SAR as set forth in the Award Agreement. If, after the Participant's death, the Option or SAR is not exercised within the time specified herein or in the Award Agreement (as applicable), the Option or SAR shall terminate.

(k) Termination for Cause. Except as explicitly provided otherwise in a Participant's Award Agreement or other individual written agreement between the Company or any Affiliate and the Participant, if a Participant's Continuous Service is terminated for Cause, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Award as of the date of termination of Continuous Service) but only

within such period of time ending on the earlier of (i) the date five (5) days following the termination of the Participant's Continuous Service (or such longer or shorter period specified in the applicable Award Agreement), or (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR within the time specified herein or in the Award Agreement (as applicable), the Option or SAR shall terminate.

(l) Non-Exempt Employees. No Option or SAR, whether or not vested, granted to an Employee who is a non-exempt employee for purposes of the Fair Labor Standards Act of 1938, as amended, shall be first exercisable for any Ordinary Shares until at least six months following the date of grant of the Option or SAR. Notwithstanding the foregoing, consistent with the provisions of the Worker Economic Opportunity Act, (i) in the event of the Participant's death or Disability, (ii) upon a Corporate Transaction in which such Option or SAR is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement or in another applicable agreement or in accordance with the Company's (or Affiliate's, if applicable) then current employment policies and guidelines), any such vested Options and SARs may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option or SAR will be exempt from his or her regular rate of pay.

6. Provisions of Stock Awards other than Options and SARs.

(a) Restricted Stock Awards. Each Restricted Stock Award Agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. To the extent consistent with the Company's Bylaws, at the Board's election, Ordinary Shares may be (i) held in book entry form subject to the Company's instructions until any restrictions relating to the Restricted Stock Award lapse; or (ii) evidenced by a certificate, which certificate shall be held in such form and manner as determined by the Board. The terms and conditions of Restricted Stock Award Agreements may change from time to time, and the terms and conditions of separate Restricted Stock Award Agreements need not be identical; *provided, however*, that each Restricted Stock Award Agreement shall conform to (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. A Restricted Stock Award may be awarded in consideration for (A) cash, check, bank draft or money order payable to the Company, (B) past services to the Company or an Affiliate, or (C) any other form of legal consideration (including future services) that may be acceptable to the Board, in its sole discretion, and permissible under applicable law; *provided, however*, that where Ordinary Shares are issued pursuant to a Restricted Stock Award the nominal value of each newly issued Ordinary Share is fully paid up.

(ii) Vesting. Ordinary Shares awarded under a Restricted Stock Award Agreement may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board.

(iii) Termination of Participant's Continuous Service. If a Participant's Continuous Service terminates, the Company or any Affiliate may receive through a forfeiture condition or a repurchase right any or all of the Ordinary Shares held by the Participant that have not vested as of the date of termination of Continuous Service under the terms of the Restricted Stock Award Agreement.

(iv) Transferability. Rights to acquire Ordinary Shares under the Restricted Stock Award Agreement shall be transferable by the Participant only upon such terms and

conditions as are set forth in the Restricted Stock Award Agreement, as the Board shall determine in its sole discretion, so long as the Ordinary Shares awarded under the Restricted Stock Award Agreement remain subject to the terms of the Restricted Stock Award Agreement.

(v) Dividends. A Restricted Stock Award Agreement may provide that any dividends paid on Restricted Stock will be subject to the same vesting and forfeiture restrictions as apply to the Ordinary Shares subject to the Restricted Stock Award to which they relate.

(b) Restricted Stock Unit Awards. Each Restricted Stock Unit Award Agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of Restricted Stock Unit Award Agreements may change from time to time, and the terms and conditions of separate Restricted Stock Unit Award Agreements need not be identical; *provided*, *however*, that each Restricted Stock Unit Award Agreement shall conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid upon delivery of each Ordinary Share subject to the Restricted Stock Unit Award. The consideration to be paid (if any) for each Ordinary Share subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law; *provided*, *however*, that where Ordinary Shares are issued pursuant to a Restricted Stock Unit Award the nominal value of each newly issued Ordinary Share is fully paid up.

(ii) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(iii) Payment. A Restricted Stock Unit Award may be settled by the delivery of Ordinary Shares, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement.

(iv) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the Ordinary Shares (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(v) Dividend Equivalents. Dividend equivalents may be credited in respect of Ordinary Shares covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional Ordinary Shares covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any additional Ordinary Shares covered by the Restricted Stock Unit Award credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying Restricted Stock Unit Award Agreement to which they relate.

(vi) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Restricted Stock Unit Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(vii) Transferability. Unless otherwise determined by the Board in its sole discretion and provided in the applicable Restricted Stock Unit Award Agreement, a Restricted Stock Unit Award shall not be transferable except by will or by the laws of descent and distribution. Notwithstanding the foregoing, subject to the approval of the Board or a duly authorized Officer, a Restricted Stock Unit Award may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument as permitted by Treasury Regulation 1.421-1(b)(2).

(c) Performance Awards.

(i) Performance Stock Awards. A Performance Stock Award is a Stock Award that may be granted, may vest or may be exercised contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Stock Award may, but need not, require the completion of a specified period of Continuous Service. The length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained with respect to a Performance Stock Award shall be conclusively determined by the Committee, in its sole discretion; *provided, however*, that the Board also may make any such determinations to the extent that the Performance Stock Award is not intended to comply with Section 162(m) of the Code. The maximum number of Ordinary Shares covered by an Award that may be granted to any Participant in a calendar year attributable to Performance Stock Awards (whether the grant, vesting or exercise is contingent upon the attainment during a Performance Period of the Performance Goals) shall not exceed two million (2,000,000) Ordinary Shares. The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Stock Award to be deferred to a specified date or event. In addition, to the extent permitted by applicable law and the applicable Award Agreement, the Board may determine that cash may be used in payment of Performance Stock Awards.

(ii) Performance Cash Awards. A Performance Cash Award is a cash award that may be paid contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Cash Award may, but need not, require the completion of a specified period of Continuous Service. The length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained with respect to a Performance Cash Award shall be conclusively determined by the Committee, in its sole discretion; *provided, however*, that the Board also may make any such determinations to the extent that the Performance Cash Award is not intended to comply with Section 162(m) of the Code. The maximum value that may be paid to any Participant in a calendar year pursuant to Performance Cash Awards shall not exceed fifteen million dollars ($15,000,000). The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Cash Award to be deferred to a specified date or event. The Board may specify the form of payment of Performance Cash Awards, which may be cash or other property, or may provide for a Participant to have the option for his or her Performance Cash Award, or such portion thereof as the Board may specify, to be paid in whole or in part in cash or other property.

(iii) Committee and Board Discretion. The Committee retains the discretion to reduce or eliminate the compensation or economic benefit due upon the attainment of any Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for a Performance Period with respect to a Performance Stock Award or Performance Cash Award; *provided*, *however*, that the Board also retains any such discretion to the extent that the Performance Stock Award or Performance Cash Award is not intended to comply with Section 162(m) of the Code.

(iv) Section 162(m) Compliance. Unless otherwise permitted in compliance with the requirements of Section 162(m) of the Code with respect to an Award intended to qualify as "performance-based compensation" thereunder, the Committee shall establish the Performance Goals applicable to, and the formula for calculating the amount payable under, the Award no later than the earlier of (a) the date ninety (90) days after the commencement of the applicable Performance Period, or (b) the date on which twenty-five percent (25%) of the Performance Period has elapsed, and in either event at a time when the achievement of the applicable Performance Goals remains substantially uncertain. Prior to the payment of any compensation under an Award intended to qualify as "performance-based compensation" under Section 162(m) of the Code, the Committee shall certify the extent to which any Performance Goals and any other material terms under such Award have been satisfied (other than in cases where such relate solely to the increase in the value of the Ordinary Shares). Notwithstanding the satisfaction of any Performance Goals, to the extent specified at the time of grant of an Award to any "covered employee" within the meaning of Section 162(m) of the Code that is intended to qualify as "performance-based compensation" thereunder, the number of Ordinary Shares, Options, cash or other benefits granted, issued, retainable and/or vested under the Award on account of the satisfaction of such Performance Goals may be reduced by the Committee on the basis of such further considerations as the Committee, in its sole discretion, shall determine.

(d) Other Stock Awards. Other forms of Stock Awards valued in whole or in part by reference to, or otherwise based on, Ordinary Shares, including the appreciation in value thereof (e.g., options or share rights with an exercise price or strike price less than 100% of the Fair Market Value of the Ordinary Shares at the time of grant) may be granted either alone or in addition to Stock Awards provided for under Section 5 and the preceding provisions of this Section 6. Subject to the provisions of the Plan, the Board shall have sole and complete authority to determine the persons to whom and the time or times at which such Other Stock Awards will be granted, the number of Ordinary Shares (or the cash equivalent thereof) to be granted pursuant to such Other Stock Awards and all other terms and conditions of such Other Stock Awards; *provided, however*, that where Ordinary Shares are issued pursuant to an Other Stock Award the nominal value of each newly issued Ordinary Share is fully paid up.

7. Covenants of the Company.

(a) Availability of Shares. During the terms of the Stock Awards, the Company shall keep available at all times the number of Ordinary Shares reasonably required to satisfy such Stock Awards.

(b) Securities Law Compliance. The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell Ordinary Shares upon exercise of the Stock Awards; *provided, however*, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any Ordinary Shares issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Ordinary Shares under the Plan, the Company shall be relieved from any liability for failure to issue and sell Ordinary Shares upon exercise of such Stock Awards unless and until such authority is obtained. A Participant shall not be eligible for the grant of a Stock Award or the subsequent issuance of Ordinary Shares pursuant to the Stock Award if such grant or issuance would be in violation of any applicable securities law.

(c) No Obligation to Notify or Minimize Taxes. The Company and any Affiliates shall have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising a Stock Award. Furthermore, the Company and any Affiliates shall have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a

Stock Award or a possible period in which the Stock Award may not be exercised. The Company and any Affiliates have no duty or obligation to minimize the tax consequences of a Stock Award to the holder of such Stock Award.

8. Miscellaneous.

(a) Use of Proceeds from Sales of Ordinary Shares. Proceeds from the sale of Ordinary Shares pursuant to Stock Awards shall constitute general funds of the Company.

(b) Corporate Action Constituting Grant of Stock Awards. Corporate action constituting a grant by the Company of a Stock Award to any Participant shall be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Stock Award is communicated to, or actually received or accepted by, the Participant.

(c) Shareholder Rights. No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any Ordinary Shares subject to such Stock Award unless and until (i) such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms, if applicable, and (ii) the issuance of the Ordinary Shares subject to such Stock Award has been entered into the books and records of the Company.

(d) No Employment or Other Service Rights. Nothing in the Plan, any Stock Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or shall affect the right of the Company or an Affiliate to terminate the employment of an Employee with or without notice and with or without cause.

(e) Incentive Stock Option $100,000 Limitation. To the extent that the aggregate Fair Market Value (determined at the time of grant) of Ordinary Shares with respect to which Incentive Stock Options are exercisable for the first time by any Optionholder during any calendar year (under all plans of the Company and any Affiliates) exceeds one hundred thousand dollars ($100,000), the Options or portions thereof that exceed such limit (according to the order in which they were granted) shall be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of the applicable Option Agreement(s).

(f) Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Ordinary Shares under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Ordinary Shares subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Ordinary Shares. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (A) the issuance of the Ordinary Shares upon the exercise or acquisition of Ordinary Shares under the Stock Award has been registered under a then currently effective registration statement under the Securities Act, or (B) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on share certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with

applicable securities laws, including, but not limited to, legends restricting the transfer of the Ordinary Shares.

(g) Withholding Obligations. Unless prohibited by the terms of a Stock Award Agreement, the Company or an Affiliate may, in its sole discretion, satisfy any federal, state, local or foreign tax withholding obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding Ordinary Shares from the Ordinary Shares issued or otherwise issuable to the Participant in connection with the Award; *provided, however,* that no Ordinary Shares are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such lesser amount as may be necessary to avoid classification of the Stock Award as a liability for financial accounting purposes); (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement.

(h) Electronic Delivery. Any reference herein to a "written" agreement or document shall include any agreement or document delivered electronically or posted on the Company's (or Affiliate's, if applicable) intranet (or other shared electronic medium controlled by the Company (or Affiliate, if applicable) to which the Participant has access).

(i) Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Ordinary Shares or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company or an Affiliate. The Board is authorized to make deferrals of Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(j) Compliance with Section 409A. To the extent that the Board determines that any Award granted hereunder is subject to Section 409A of the Code, the Award Agreement evidencing such Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Award Agreements shall be interpreted in accordance with Section 409A of the Code. Notwithstanding anything to the contrary in this Plan (and unless the Award Agreement specifically provides otherwise), if the Ordinary Shares are publicly traded and a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount shall be made upon a "separation from service" before a date that is six (6) months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death.

(k) Clawback Policy. Any amounts paid hereunder shall be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law.

9. Adjustments upon Changes in Ordinary Shares; Other Corporate Events.

(a) Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board shall appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a); (ii) the class(es) and maximum number of securities by which the Share Reserve is to increase automatically each year pursuant to Section 3(a); (iii) the class(es) and maximum number of securities that may be issued pursuant to the exercise of Incentive Stock Options pursuant to Section 3(c); (iv) the class(es) and maximum number of securities that may be awarded to any person pursuant to Sections 3(d) and 6(c)(i); and (v) the class(es) and number of securities and price per Ordinary Share subject to outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive.

(b) Dissolution or Liquidation. Except as otherwise provided in a Stock Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Stock Awards (other than Stock Awards consisting of vested and outstanding Ordinary Shares not subject to a forfeiture condition or the Company's or any Affiliate's right of repurchase) shall terminate immediately prior to the completion of such dissolution or liquidation, and any Ordinary Shares subject to the Company's or any Affiliate's repurchase rights or subject to a forfeiture condition may be repurchased or reacquired by the Company or Affiliate notwithstanding the fact that the holder of such Stock Award is providing Continuous Service; *provided, however*, that the Board may, in its sole discretion, cause some or all Stock Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Stock Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c) Corporate Transaction. Notwithstanding any other provision of the Plan, the Board may take one or more of the following actions in the event of a Corporate Transaction with respect to Stock Awards, contingent upon the closing or completion of the Corporate Transaction, unless otherwise provided in the instrument evidencing the Stock Award or any other written agreement between the Company or any Affiliate and the Participant or unless otherwise expressly provided by the Board at the time of grant of a Stock Award:

(i) arrange for the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) to assume or continue the Stock Award or to substitute a similar stock award for the Stock Award (including, but not limited to, an award to acquire the same consideration paid to the shareholders of the Company pursuant to the Corporate Transaction);

(ii) arrange for the assignment of any reacquisition or repurchase rights held by the Company or any Affiliate in respect of Ordinary Shares issued pursuant to the Stock Award to the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company);

(iii) accelerate the vesting, in whole or in part, of the Stock Award (and, if applicable, the time at which the Stock Award may be exercised) to a date prior to the effective time of such Corporate Transaction as the Board shall determine (or, if the Board shall not determine such a date, to the date that is five (5) days prior to the effective date of the Corporate Transaction), with such Stock Award terminating if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction;

(iv) arrange for the lapse of any reacquisition or repurchase rights held by the Company or any Affiliate with respect to the Stock Award;

(v) cancel or arrange for the cancellation of the Stock Award, to the extent not vested or not exercised prior to the effective time of the Corporate Transaction, in exchange for such cash consideration, if any, as the Board, in its sole discretion, may consider appropriate; or

(vi) make a payment, in such form as may be determined by the Board equal to the excess, if any, of (A) the value of the property the Participant would have received upon the exercise of the Stock Award, over (B) any exercise price payable by such holder in connection with such exercise.

The Board need not take the same action or actions with respect to all Stock Awards or portions thereof or with respect to all Participants.

(d) Change in Control. A Stock Award may be subject to additional acceleration of vesting and exercisability upon or after a Change in Control as may be provided in the Stock Award Agreement for such Stock Award or as may be provided in any other written agreement between the Company or any Affiliate and the Participant, but in the absence of such provision, no such acceleration shall occur.

10. Termination or Suspension of the Plan.

(a) Plan Term. The Board may suspend or terminate the Plan at any time. No Incentive Stock Option will be granted after October 24, 2021. No Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) No Impairment of Rights. Suspension or termination of the Plan shall not impair rights and obligations under any Award granted while the Plan is in effect except with the written consent of the affected Participant.

11. Effective Date of Plan.

This Plan shall become effective on the Effective Date.

12. Choice of Law.

The laws of the State of Delaware shall govern all questions concerning the construction, validity and interpretation of this Plan, without regard to that state's conflict of laws rules.

13. Definitions. As used in the Plan, the following definitions shall apply to the capitalized terms indicated below:

(a) "***Affiliate***" means, at the time of determination, any "parent" or "subsidiary" of the Company as such terms are defined in Rule 405 promulgated under the Securities Act and any "holding company" or "subsidiary" of the Company as such terms are defined in Section 8 and 7 respectively of the Companies Act. The Board shall have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(b) "***Award***" means a Stock Award or a Performance Cash Award.

(c) "***Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of an Award.

(d) "***Board***" means the Board of Directors of the Company.

(e) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Ordinary Shares subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, share dividend, dividend in property other than cash, large nonrecurring cash dividend, share split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or any similar equity restructuring transaction, as that term is used in Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto), including, for the avoidance of doubt, capitalization of profits or reserves, capital distribution, rights issue, the conversion of one class of share to another or reduction of capital or otherwise. Notwithstanding the foregoing, the conversion of any convertible securities of the Company shall not be treated as a Capitalization Adjustment.

(f) "***Cause***" shall have the meaning ascribed to such term in any written agreement between the Participant and the Company or an Affiliate defining such term and, in the absence of such agreement, such term shall mean, with respect to a Participant, the occurrence of any of the following events that has a material negative impact on the business or reputation of the Company or an Affiliate: (i) such Participant's commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) such Participant's attempted commission of, or participation in, a fraud or act of dishonesty against the Company or an Affiliate; (iii) such Participant's intentional, material violation of any contract or agreement between the Participant and the Company or an Affiliate or of any statutory duty owed to the Company or an Affiliate; (iv) such Participant's unauthorized use or disclosure of the Company's or an Affiliate's confidential information or trade secrets; or (v) such Participant's gross misconduct. The determination that a termination of the Participant's Continuous Service is either for Cause or without Cause shall be made by the Company (or an Affiliate, if applicable) in its sole discretion. Any determination by the Company (or an Affiliate, if applicable) that the Continuous Service of a Participant was terminated with or without Cause for the purposes of outstanding Awards held by such Participant shall have no effect upon any determination of the rights or obligations of the Company or Affiliate or such Participant for any other purpose.

(g) "***Change in Control***" means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than thirty percent (30%) of the combined voting power of the Company's then outstanding securities. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur on account of the acquisition of securities of the Company directly from the Company;

(ii) there is consummated a compromise or arrangement sanctioned by the Irish courts under the Companies Act, a scheme, contract or offer which has become binding on all shareholders of the Company pursuant to Section 457 of the Companies Act or a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC)) Regulations 2006 (as may be amended, updated or replaced from time to time), an offer or reverse takeover transaction which has been completed pursuant to the Irish Takeover Panel Act, 1997, Takeover Rules, 2013, or a reorganization, merger, statutory share exchange, consolidation or similar transaction involving (directly or indirectly) the Company (each, a "***Business Combination***") and (A) immediately after the consummation of such Business Combination, the shareholders of the Company immediately prior thereto do not Own, directly or indirectly, either outstanding voting securities representing more than fifty percent (50%) of the combined outstanding voting power of the surviving Entity or ultimate parent of the surviving Entity in such Business Combination in substantially the same proportions as their Ownership of the

outstanding voting securities of the Company immediately prior to such Business Combination, (B) an Exchange Act Person becomes the Owner, directly or indirectly, of securities representing more than thirty percent (30%) of the combined voting power of the surviving Entity or ultimate parent of the surviving Entity through the Business Combination, or (C) at least a majority of the members of the board of directors of the ultimate parent (or if there is no parent, the surviving Entity) immediately following such Business Combination were not Incumbent Board Members (as defined below) at the time the Board approved the execution of the definitive agreement providing for such Business Combination;

(iii) the shareholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation;

(iv) there is consummated a sale, lease, exclusive license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, exclusive license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than fifty percent (50%) of the combined voting power of the voting securities of which are Owned by shareholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, exclusive license or other disposition; or

(v) individuals who, on the date the Plan is adopted by the Board, are members of the Board (the "***Incumbent Board Members***") cease for any reason to constitute at least a majority of the members of the Board; *provided, however*, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the Incumbent Board Members then still in office, such new member shall, for purposes of the Plan, be considered as an Incumbent Board Member, but excluding for purposes of the Plan any such individual whose initial assumption of office occurs as a result of either an actual or threatened election contest or other actual or threatened solicitation of proxies or consents by or on behalf of any person or Entity other than the Board.

Notwithstanding the foregoing or any other provision of this Plan, the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Awards subject to such agreement; *provided, however*, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply.

The Board may, in its sole discretion and without a Participant's consent, amend the definition of "Change in Control" to conform to the definition of "Change in Control" under Section 409A of the Code, and the regulations thereunder.

(h) "***Code***" means the Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(i) "***Committee***" means a committee of one (1) or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(j) "***Companies Act***" means the Companies Act 2014 of Ireland, together with all statutory modifications and re-enactments thereof and all statutes and statutory instruments which are to be read as one with, or construed or read together as one with, the aforementioned enactments and every statutory modification and re-enactment thereof for the time being in force.

(k) "***Company***" means:

(i) prior to a Change in Control, Jazz Pharmaceuticals plc; and

(ii) on or after a Change in Control, (A) Jazz Pharmaceuticals plc in the event that the surviving Entity resulting from a Change in Control is Jazz Pharmaceuticals plc, (B) the surviving Entity resulting from a Change in Control in the event that such surviving Entity is not Jazz Pharmaceuticals plc, (C) any Entity to which the assets of Jazz Pharmaceuticals plc and its Subsidiaries are sold, leased, exclusively licensed or otherwise disposed of in the event of a Change in Control under Section 13(g)(iv), or (D) any other successor to Jazz Pharmaceuticals plc in the event of a Change in Control, as applicable;

provided, however, that in the event Jazz Pharmaceuticals plc completes a reorganization that is not in connection with a Change in Control that results in Jazz Pharmaceuticals plc no longer being the ultimate parent company and reporting company under the Exchange Act, then "Company" means the ultimate parent that directly or indirectly holds Jazz Pharmaceuticals plc.

(l) "***Consultant***" means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Director, or payment of a fee for such service, shall not cause a Director to be considered a "Consultant" for purposes of the Plan. Notwithstanding the foregoing, a person is treated as a Consultant under this Plan only if a Form S-8 Registration Statement under the Securities Act is available to register either the offer or the sale of the Company's securities to such person.

(m) "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. Except as provided in the following sentence, a change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, shall not terminate a Participant's Continuous Service; *provided, however*, if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service shall be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. Notwithstanding the foregoing, unless the Board or the Compensation Committee of the Board agrees otherwise in writing, in the event a Participant's service as an Employee or Consultant terminates and upon such termination, the only capacity in which the Participant continues to render service to the Company is as a Director, then such Participant's Continuous Service shall be considered to have terminated on the date of such termination of employment or termination of service as a Consultant, as the case may be, and regardless of whether such Participant continues to render service to the Company as a Director following such termination. To the extent permitted by law, the Board or the chief executive officer of the Company (or an Affiliate, if applicable), in that party's sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of: (i) any leave of absence approved by the Board or the chief executive officer of the Company (or an Affiliate, if applicable), including sick leave, military leave or any other personal leave; or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence shall be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's (or Affiliate's, if applicable) leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

(n) "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) a sale or other disposition of at least ninety percent (90%) of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the Ordinary Shares outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to a compromise or arrangement sanctioned by the Irish courts under the Companies Act, a scheme, contract or offer which has become binding on all shareholders of the Company pursuant to Section 457 of the Companies Act or a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC)) Regulations 2006 (as may be amended, updated or replaced from time to time), or an offer or reverse takeover transaction which has been completed pursuant to the Irish Takeover Panel Act, 1997, Takeover Rules, 2013.

(o) "***Covered Employee***" shall have the meaning provided in Section 162(m)(3) of the Code.

(p) "***Director***" means a member of the Board.

(q) "***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than twelve (12) months, as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and shall be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(r) "***Effective Date***" means the effective date of this Plan document, which is January 18, 2012, which is immediately prior to the effective time of the merger between Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company pursuant to the Agreement and Plan of Merger and Reorganization dated September 19, 2011, provided that the Plan is approved by the stockholders of the Company prior to such merger and such merger is consummated.

(s) "***Employee***" means any person employed by the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such services, shall not cause a Director to be considered an "Employee" for purposes of the Plan.

(t) "***Entity***" means a corporation, partnership, limited liability company or other entity.

(u) "***Exchange Act***" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(v) "***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, or (iv) an Entity Owned, directly or indirectly, by the shareholders of the Company in substantially the same proportions as their Ownership of shares of the Company.

(w) "***Fair Market Value***" means, as of any date, the value of the Ordinary Shares determined as follows:

(i) If the Ordinary Shares are listed on any established stock exchange or traded on any established market, the Fair Market Value of an Ordinary Share shall be the closing sales price for such Ordinary Share as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Ordinary Shares) on the date of determination, as reported in a source the Board deems reliable.

(ii) Unless otherwise provided by the Board, if there is no closing sales price for the Ordinary Shares on the date of determination, then the Fair Market Value shall be the closing selling price on the last preceding date for which such quotation exists.

(iii) In the absence of such markets for the Ordinary Shares, the Fair Market Value shall be determined by the Board in good faith and in a manner that complies with Sections 409A and 422 of the Code.

(x) "***Incentive Stock Option***" means an option granted pursuant to Section 5 of the Plan that is intended to be, and qualifies as, an "incentive stock option" within the meaning of Section 422 of the Code.

(y) "***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("***Regulation S-K***")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

(z) "***Nonstatutory Stock Option***" means any option granted pursuant to Section 5 of the Plan that does not qualify as an Incentive Stock Option.

(aa) "***Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

(bb) "***Option***" means an Incentive Stock Option or a Nonstatutory Stock Option to purchase Ordinary Shares granted pursuant to the Plan.

(cc) "***Option Agreement***" means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.

(dd) "***Optionholder***" means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(ee) "Ordinary Share" or "Ordinary Shares" means the ordinary shares of the Company of nominal value US$0.0001 per share.

(ff) "***Other Stock Award***" means an award based in whole or in part by reference to the Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(d).

(gg) "***Other Stock Award Agreement***" means a written agreement between the Company and a holder of an Other Stock Award evidencing the terms and conditions of an Other Stock Award grant. Each Other Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(hh) "***Outside Director***" means a Director who either (i) is not a current employee of the Company or an "affiliated corporation" (within the meaning of Treasury Regulations promulgated under Section 162(m) of the Code), is not a former employee of the Company or an "affiliated corporation" who receives compensation for prior services (other than benefits under a tax-qualified retirement plan) during the taxable year, has not been an officer of the Company or an "affiliated corporation," and does not receive remuneration from the Company or an "affiliated corporation," either directly or indirectly, in any capacity other than as a Director, or (ii) is otherwise considered an "outside director" for purposes of Section 162(m) of the Code.

(ii) "***Own,***" "***Owned,***" "***Owner,***" "***Ownership***" A person or Entity shall be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(jj) "***Participant***" means a person to whom an Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(kk) "***Performance Cash Award***" means an award of cash granted pursuant to the terms and conditions of Section 6(c)(ii).

(ll) "***Performance Criteria***" means, with respect to a Performance Stock Award or Performance Cash Award, the one or more criteria that the Committee shall select for purposes of establishing the Performance Goals for a Performance Period; *provided, however*, that the Board also may select any such criteria to the extent that the Performance Stock Award or Performance Cash Award is not intended to comply with Section 162(m) of the Code. The Performance Criteria that shall be used to establish such Performance Goals may be based on any one of, or combination of, the following as determined by the Committee (or Board, if applicable): (i) earnings (including earnings per share and net earnings); (ii) earnings before interest, taxes and depreciation; (iii) earnings before interest, taxes, depreciation and amortization; (iv) total shareholder return; (v) return on equity or average shareholder's equity; (vi) return on assets, investment, or capital employed; (vii) share price; (viii) margin (including gross margin); (ix) income (before or after taxes); (x) operating income; (xi) operating income after taxes; (xii) pre-tax profit; (xiii) operating cash flow; (xiv) sales or revenue targets (including volume-based measures); (xv) increases in revenue or product revenue; (xvi) expenses and cost reduction goals; (xvii) improvement in or attainment of working capital levels; (xiii) economic value added (or an equivalent metric); (xix) market share; (xx) cash flow; (xxi) cash flow per share; (xxii) share price performance; (xxiii) debt reduction; (xxiv) implementation or completion of projects or processes; (xxv) customer satisfaction; (xxvi) shareholders' equity; (xxvii) capital expenditures; (xxiii) debt levels; (xxix) operating profit or net operating profit;

(xxx) workforce diversity; (xxxi) growth of net income or operating income; (xxxii) billings; and (xxxiii) to the extent that an Award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by the Committee or Board.

(mm) "***Performance Goals***" means, with respect to a Performance Stock Award or Performance Cash Award, for a Performance Period, the one or more goals established by the Committee for the Performance Period based upon the Performance Criteria; *provided, however*, that the Board also may establish any such goals to the extent that the Performance Stock Award or Performance Cash Award is not intended to comply with Section 162(m) of the Code. Performance Goals may be based on a Company-wide basis, with respect to one or more business units, divisions, Affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise by the Committee (or the Board to the extent that an Award is not intended to comply with Section 162(m) of the Code), (i) in the Award Agreement at the time the Award is granted or (ii) in such other document setting forth the Performance Goals at the time the Performance Goals are established, the Committee (or Board, if applicable) shall appropriately make adjustments in the method of calculating the attainment of Performance Goals for a Performance Period as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated Performance Goals; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; and (5) to exclude the effects of items that are "unusual" in nature or occur "infrequently" as determined under generally accepted accounting principles.

(nn) "***Performance Period***" means, with respect to a Performance Stock Award or Performance Cash Award, the period of time selected by the Committee over which the attainment of one or more Performance Goals will be measured for the purpose of determining a Participant's right to and the payment of the Performance Stock Award or Performance Cash Award; *provided, however*, that the Board also may select any such period to the extent that the Performance Stock Award or Performance Cash Award is not intended to comply with Section 162(m) of the Code. Performance Periods may be of varying and overlapping duration, at the sole discretion of the Committee (or the Board, if applicable).

(oo) "***Performance Stock Award***" means a Stock Award granted under the terms and conditions of Section 6(c)(i).

(pp) "***Plan***" means this Jazz Pharmaceuticals plc 2011 Equity Incentive Plan.

(qq) "***Restricted Stock Award***" means an award of Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(a).

(rr) "***Restricted Stock Award Agreement***" means a written agreement between the Company and a holder of a Restricted Stock Award evidencing the terms and conditions of a Restricted Stock Award grant. Each Restricted Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(ss) "***Restricted Stock Unit Award***" means a right to receive Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(b).

(tt) "***Restricted Stock Unit Award Agreement***" means a written agreement between the Company and a holder of a Restricted Stock Unit Award evidencing the terms and conditions of a Restricted Stock Unit Award grant. Each Restricted Stock Unit Award Agreement shall be subject to the terms and conditions of the Plan.

(uu) "***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(vv) "***Securities Act***" means the Securities Act of 1933, as amended.

(ww) "***Stock Appreciation Right***" or "***SAR***" means a right to receive the appreciation on Ordinary Shares that is granted pursuant to the terms and conditions of Section 5.

(xx) "***Stock Appreciation Right Agreement***" means a written agreement between the Company and a holder of a Stock Appreciation Right evidencing the terms and conditions of a Stock Appreciation Right grant. Each Stock Appreciation Right Agreement shall be subject to the terms and conditions of the Plan.

(yy) "***Stock Award***" means any right to receive Ordinary Shares granted under the Plan, including an Incentive Stock Option, a Nonstatutory Stock Option, a Restricted Stock Award, a Restricted Stock Unit Award, a Stock Appreciation Right, a Performance Stock Award or any Other Stock Award.

(zz) "***Stock Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of a Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(aaa) "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation shall have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other Entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than fifty percent (50%).

(bbb) "***Ten Percent Shareholder***" means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) shares possessing more than ten percent (10%) of the total combined voting power of all classes of shares of the Company or any Affiliate.

Adopted by the Board of Directors of Jazz Pharmaceuticals, Inc. on October 24, 2011.

Approved by the stockholders of Jazz Pharmaceuticals, Inc. on December 12, 2011.

Adopted by the Board of Directors of Azur Pharma plc on December 21, 2011.

Approved by the shareholders of Azur Pharma plc on January 3, 2012.

Amended and restated by the Board of Directors of Jazz Pharmaceuticals plc on May 5, 2016.

Approved by the shareholders of Jazz Pharmaceuticals plc on August 4, 2016.

Amended and restated by the Board of Directors of Jazz Pharmaceuticals plc on November 3, 2016.

Amended by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on November 2, 2022.

JAZZ PHARMACEUTICALS PLC

AMENDED AND RESTATED

2007 EMPLOYEE STOCK PURCHASE PLAN

1. GENERAL.

(a) The purpose of the Plan is to provide a means by which Eligible Employees of the Company and certain designated Related Corporations may be given an opportunity to purchase Ordinary Shares. The Plan is intended to permit the Company to grant a series of Purchase Rights to Eligible Employees under an Employee Stock Purchase Plan.

(b) The Company, by means of the Plan, seeks to retain the services of such Employees, to secure and retain the services of new Employees and to provide incentives for such persons to exert maximum efforts for the success of the Company, its Related Corporations and Affiliates.

(c) This Plan includes two components: a 423 Component and a Non-423 Component. It is the intention of the Company to have the 423 Component qualify as an Employee Stock Purchase Plan. The provisions of the 423 Component, accordingly, shall be construed so as to extend and limit participation in a uniform and nondiscriminatory basis consistent with the requirements of Section 423 of the Code. In addition, this Plan authorizes the grant of Purchase Rights under the Non-423 Component that does not qualify as an Employee Stock Purchase Plan; such Purchase Rights shall be granted pursuant to any rules, procedures, agreements, appendices, or sub-plans adopted by the Board for such purpose. Except as otherwise provided herein or determined by the Board, the Non-423 Component will operate and be administered in the same manner as the 423 Component.

2. ADMINISTRATION.

(a) The Board shall administer the Plan unless and until the Board delegates administration of the Plan to a Committee or Committees, as provided in Section 2(c).

(b) The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine how and when Purchase Rights to purchase Ordinary Shares shall be granted and the provisions of each Offering comprised of such Purchase Rights (which need not be identical).

(ii) To designate from time to time which Related Corporations shall be eligible to participate in the 423 Component as Designated Related Corporations and which Related Corporations or Affiliates shall be eligible to participate in the Non-423 Component as Designated Companies; provided, however, that at any given time, a Related Corporation that is a Designated Company under the 423 Component will not be a Designated Company under the Non-423 Component.

(iii) To construe and interpret the Plan and Purchase Rights, and to establish, amend and revoke rules and regulations for administration of the Plan. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan, in a manner and to the extent it shall deem necessary or expedient to make the Plan or Purchase Rights fully effective.

(iv) To settle all controversies regarding the Plan and Purchase Rights granted under it.

(v) To suspend or terminate the Plan at any time as provided in Section 13.

(vi) To amend the Plan at any time as provided in Section 13.

(vii) Generally, to exercise such powers and to perform such acts as it deems necessary or expedient to promote the best interests of the Company, its Related Corporations and Affiliates and to carry out the intent that the 423 Component be treated as an Employee Stock Purchase Plan.

(viii) To adopt such rules, procedures, agreements, appendices, or sub-plans as are necessary or appropriate to permit participation in the Plan by Employees who are foreign nationals or employed outside the United States. Without limiting the generality of the foregoing, the Board specifically is authorized to adopt rules, procedures, agreements, appendices, or sub-plans, which, for purposes of the Non-423 Component, may be outside the scope of Section 423 of the Code, regarding, without limitation, eligibility to participate in the Plan, handling and making of Contributions, establishment of bank or trust accounts to hold Contributions, payment of interest, conversion of local currency, obligations to pay payroll tax, determination of beneficiary designation requirements, withholding procedures and handling of share issuances, which may vary according to local requirements.

(ix) To make any other determination and take any other action that the Board deems necessary or desirable for the administration of the Plan.

(c) The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. Further, to the extent not prohibited by applicable law, the Board or Committee may, from time to time, delegate some or all of its authority under to the Plan to one or more officers of the Company or other persons or groups of persons as it deems necessary, appropriate or advisable under conditions or limitations that it may set at or after the time of delegation. The Board may retain the authority to concurrently administer the Plan with the Committee (or other applicable delegate) and may, at any time, revest in the Board some or all of the powers previously delegated. Whether or not the Board has delegated administration of the Plan to a Committee or other delegate, the Board shall have the final power to determine all questions of policy and expediency that may arise in the administration of the Plan.

(d) All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

3. ORDINARY SHARES SUBJECT TO THE PLAN.

(a) Subject to the provisions of Section 12(a) relating to Capitalization Adjustments, the number of Ordinary Shares that may be sold pursuant to Purchase Rights shall not exceed in the aggregate one million two thousand one hundred twenty five (1,002,125) Ordinary Shares. In addition, the number of Ordinary Shares available for issuance under the Plan shall automatically increase on January 1st of each year for a period of ten (10) years commencing on January 1, 2013 and ending on (and including) January 1, 2022, in an amount equal to the lesser of (i) one and one-half percent (1.5%) of the total number of Ordinary Shares outstanding on December 31st of the preceding calendar year or (ii) one million (1,000,000) Ordinary Shares. Notwithstanding the foregoing, the Board may act prior to the first day of any calendar year, to provide that there shall

be no increase in the share reserve for such calendar year or that the increase in the share reserve for such calendar year shall be a lesser number of Ordinary Shares than would otherwise occur pursuant to the preceding sentence.

(b) If any Purchase Right granted under the Plan shall for any reason terminate without having been exercised, the Ordinary Shares not purchased under such Purchase Right shall again become available for issuance under the Plan.

(c) The shares purchasable under the Plan shall be authorized but unissued or reacquired Ordinary Shares, including Ordinary Shares repurchased by the Company or any Affiliate on the open market or otherwise

(d) For avoidance of doubt, up to the maximum number of Ordinary Shares reserved under Section 3(a) may be used to satisfy purchases of Ordinary Shares under the 423 Component and any remaining portion of such maximum number of Ordinary Shares may be used to satisfy purchases of Shares under the Non-423 Component.

4. GRANT OF PURCHASE RIGHTS; OFFERING.

(a) The Board may from time to time grant or provide for the grant of Purchase Rights to purchase Ordinary Shares under the Plan to Eligible Employees in an Offering (consisting of one or more Purchase Periods) on an Offering Date or Offering Dates selected by the Board. Each Offering shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate, and with respect to the 423 Component shall comply with the requirement of Section 423(b)(5) of the Code that all Employees granted Purchase Rights shall have the same rights and privileges. The terms and conditions of an Offering shall be incorporated by reference into the Plan and treated as part of the Plan. The provisions of separate Offerings need not be identical, but each Offering shall include (through incorporation of the provisions of this Plan by reference in the document comprising the Offering or otherwise) the period during which the Offering shall be effective, which period shall not exceed twenty-seven (27) months beginning with the Offering Date, and the substance of the provisions contained in Sections 5 through 8, inclusive relevant to the Offering as either a 423 Component Offering or a Non-423 Component Offering.

(b) If a Participant has more than one Purchase Right outstanding under the Plan, unless he or she otherwise indicates in agreements or notices delivered hereunder: (i) each agreement or notice delivered by that Participant shall be deemed to apply to all of his or her Purchase Rights under the Plan, and (ii) a Purchase Right with a lower exercise price (or an earlier-granted Purchase Right, if different Purchase Rights have identical exercise prices) shall be exercised to the fullest possible extent before a Purchase Right with a higher exercise price (or a later-granted Purchase Right if different Purchase Rights have identical exercise prices) shall be exercised.

(c) The Board shall have the discretion to structure an Offering so that if the Fair Market Value of an Ordinary Share on any Purchase Date within that Offering is less than or equal to the Fair Market Value of an Ordinary Share on the Offering Date for that Offering, then
(i) that Offering shall terminate immediately following the purchase of Ordinary Shares on such Purchase Date, and (ii) Participants in such terminated Offering shall be automatically enrolled in a new Offering beginning on the first day following such Purchase Date.

5. ELIGIBILITY.

(a) Purchase Rights may be granted only to Employees of the Company or, as the Board may designate as provided in Section 2(b), to Employees of a Related Corporation or, in the case of the Non-423 Component, an Affiliate. Except as provided in Section 5(b), an Employee shall not be eligible to be granted Purchase Rights under the Plan unless, on the Offering Date, such

Employee has been in the employ of the Company, Related Corporation or Affiliate, as the case may be, for such continuous period preceding such Offering Date as the Board may require, but in no event shall the required period of continuous employment be greater than two (2) years. In addition, the Board may provide that no Employee shall be eligible to be granted Purchase Rights under the Plan unless, on the Offering Date, such Employee's customary employment with the Company or the Related Corporation or, in the case of the Non-423 Component, an Affiliate is at least twenty (20) hours per week and at least five (5) months per calendar year or such other criteria as the Board may determine, and with respect to the Section 423 Component, any such determination shall be consistent with Section 423 of the Code. Further, an Eligible Employee (or group of Eligible Employees) may be excluded from participation in the Non-423 Component or an Offering thereunder if the Committee has determined, in its sole discretion, that participation of such Eligible Employee(s) is not advisable or practicable for any reason.

(b) The Board may provide that each person who, during the course of an Offering, first becomes an Eligible Employee shall, on a date or dates specified in the Offering which coincides with the day on which such person becomes an Eligible Employee or which occurs thereafter, receive a Purchase Right under that Offering, which Purchase Right shall thereafter be deemed to be a part of that Offering. Such Purchase Right shall have the same characteristics as any Purchase Rights originally granted under that Offering, as described herein, except that:

(i) the date on which such Purchase Right is granted shall be the "Offering Date" of such Purchase Right for all purposes, including determination of the exercise price of such Purchase Right;

(ii) the period of the Offering with respect to such Purchase Right shall begin on its Offering Date and end coincident with the end of such Offering; and

(iii) the Board may provide that if such person first becomes an Eligible Employee within a specified period of time before the end of the Offering, he or she shall not receive any Purchase Right under that Offering.

(c) No Employee shall be eligible for the grant of any Purchase Rights under the Plan if, immediately after any such Purchase Rights are granted, such Employee owns shares possessing five percent (5%) or more of the total combined voting power or value of all classes of shares of the Company or of any Related Corporation. For purposes of this Section 5(c), the rules of Section 424(d) of the Code shall apply in determining the share ownership of any Employee, and shares which such Employee may purchase under all outstanding Purchase Rights and options shall be treated as shares owned by such Employee.

(d) As specified by Section 423(b)(8) of the Code, an Eligible Employee may be granted Purchase Rights under the Plan only if such Purchase Rights, together with any other rights granted under all Employee Stock Purchase Plans of the Company and any Related Corporations, do not permit such Eligible Employee's rights to purchase shares of the Company or any Related Corporation to accrue at a rate which exceeds twenty five thousand dollars ($25,000) of Fair Market Value of such shares (determined at the time such rights are granted, and which, with respect to the Plan, shall be determined as of their respective Offering Dates) for each calendar year in which such rights are outstanding at any time.

(e) Officers of the Company and any Designated Company, if they are otherwise Eligible Employees, shall be eligible to participate in Offerings under the Plan. Notwithstanding the foregoing, the Board may provide in an Offering that Employees who are highly compensated Employees within the meaning of Section 423(b)(4)(D) of the Code shall not be eligible to participate.

6. PURCHASE RIGHTS; PURCHASE PRICE.

(a) On each Offering Date, each Eligible Employee, pursuant to an Offering made under the Plan, shall be granted a Purchase Right to purchase up to that number of Ordinary Shares purchasable either with a percentage or with a maximum dollar amount, as designated by the Board, but in either case not exceeding fifteen percent (15%) of such Employee's earnings (as defined by the Board in each Offering) during the period that begins on the Offering Date (or such later date as the Board determines for a particular Offering) and ends on the date stated in the Offering, which date shall be no later than the end of the Offering.

(b) The Board shall establish one (1) or more Purchase Dates during an Offering as of which Purchase Rights granted pursuant to that Offering shall be exercised and purchases of Ordinary Shares shall be carried out in accordance with such Offering. In connection with each Offering made under the Plan, the Board may specify a maximum number of Ordinary Shares that may be purchased by any Participant on any Purchase Date during such Offering. In connection with each Offering made under the Plan, the Board may specify a maximum aggregate number of Ordinary Shares that may be purchased by all Participants pursuant to such Offering. In addition, in connection with each Offering that contains more than one Purchase Date, the Board may specify a maximum aggregate number of Ordinary Shares that may be purchased by all Participants on any Purchase Date under the Offering. If the aggregate purchase of Ordinary Shares issuable upon exercise of Purchase Rights granted under the Offering would exceed any such maximum aggregate number, then, in the absence of any Board action otherwise, a pro rata allocation of the Ordinary Shares available shall be made in as nearly a uniform manner as shall be practicable and equitable.

(c) The purchase price of Ordinary Shares acquired pursuant to Purchase Rights shall be not less than the lesser of:

(i) an amount equal to eighty-five percent (85%) of the Fair Market Value of the Ordinary Shares on the Offering Date; or

(ii) an amount equal to eighty-five percent (85%) of the Fair Market Value of the Ordinary Shares on the applicable Purchase Date;

provided, *however*, that in all cases the purchase price is not less than the nominal value of an Ordinary Share on the applicable Purchase Date.

7. PARTICIPATION; WITHDRAWAL; TERMINATION.

(a) A Participant may elect to authorize payroll deductions pursuant to an Offering under the Plan by completing and delivering to the Company, within the time specified in the Offering, an enrollment form (in such form as the Company may provide). Each such enrollment form shall authorize an amount of Contributions expressed as a percentage of the submitting Participant's earnings (as defined in each Offering) during the Offering (not to exceed the maximum percentage specified by the Board). Each Participant's Contributions shall be credited to a bookkeeping account for such Participant under the Plan and shall be deposited with the general funds of the Company except where applicable law requires that Contributions be deposited with a third party. To the extent provided in the Offering, a Participant may begin such Contributions after the beginning of the Offering. To the extent provided in the Offering, a Participant may thereafter reduce (including to zero) or increase his or her Contributions. To the extent required under applicable law or if specifically provided in the Offering, in addition to or instead of making Contributions by payroll deductions, a Participant may make Contributions through the payment by cash or check prior to each Purchase Date of the Offering.

(b) During an Offering, a Participant may cease making Contributions and withdraw from the Offering by delivering to the Company a notice of withdrawal in such form as the Company may provide. Such withdrawal may be elected at any time prior to the end of the Offering, except as provided otherwise in the Offering. Upon such withdrawal from the Offering by a Participant, the Company shall distribute to such Participant all of his or her accumulated Contributions (reduced to the extent, if any, such Contributions have been used to acquire Ordinary Shares for the Participant) under the Offering, and such Participant's Purchase Right in that Offering shall thereupon terminate. A Participant's withdrawal from an Offering shall have no effect upon such Participant's eligibility to participate in any other Offerings under the Plan, but such Participant shall be required to deliver a new enrollment form in order to participate in subsequent Offerings.

(c) Unless otherwise required by applicable law, Purchase Rights granted pursuant to any Offering under the Plan shall terminate immediately upon a Participant ceasing to be an Employee for any reason or for no reason or other lack of eligibility. The Company shall distribute to such terminated or otherwise ineligible Employee all of his or her accumulated Contributions (reduced to the extent, if any, such Contributions have been used to acquire Ordinary Shares for the terminated or otherwise ineligible Employee) under the Offering.

(d) With respect to the 423 Component, unless otherwise determined by the Board, in the event a Participant transfers employment from the Company or a Related Corporation that has been designated as being eligible to participate in the 423 Component to a Related Corporation that has not been designated as being eligible to participate in the 423 Component, such transfer shall not cause such Participant to cease being eligible to participate in the Plan, provided that there is no interruption or termination of such Participant's employment with the Company or a Related Corporation. Further, unless otherwise determined by the Board, a Participant who transfers employment between the Company or a Designated Company or between Designated Companies will not be treated as having terminated employment for purposes of participating in the Plan or an Offering; however, if a Participant transfers employment from the Company or any Designated Related Corporation participating in the 423 Component to a Designated Affiliate participating in the Non-423 Component, the exercise of the Participant's Purchase Right will be qualified under the Section 423 Component Offering only to the extent that such exercise complies with Section 423 of the Code. If a Participant transfers from a Designated Affiliate participating in the Non-423 Component to the Company or any Designated Related Corporation participating in the 423 Component, such Participant shall remain a Participant in the Non-423 Component until the earlier of (i) the end of the applicable Offering Period under the Non-423 Component in which such transfer occurs, or (ii) the Offering Date of the first Offering in which he or she participates following such transfer.

(e) Purchase Rights shall not be transferable by a Participant except by will, the laws of descent and distribution, or by a beneficiary designation as provided in Section 10. During a Participant's lifetime, Purchase Rights shall be exercisable only by such Participant.

(f) Unless otherwise specified in an Offering, the Company shall have no obligation to pay interest on Contributions, unless otherwise required by applicable law.

8. EXERCISE OF PURCHASE RIGHTS.

(a) On each Purchase Date during an Offering, each Participant's accumulated Contributions shall be applied to the purchase of Ordinary Shares up to the maximum number of Ordinary Shares permitted pursuant to the terms of the Plan and the applicable Offering, at the purchase price specified in the Offering. No fractional Ordinary Shares shall be issued upon the exercise of Purchase Rights unless specifically provided for in the Offering.

(b) Except as otherwise determined by the Committee in a manner that complies with Treasury Regulation Section 1.423-2(f)(5), if applicable, if any amount of accumulated Contributions remains in a Participant's account after the purchase of Ordinary Shares on the Purchase Date, then such remaining amount shall be distributed in full to such Participant as soon as administratively practicable following the end of the applicable Purchase Period, without interest (unless otherwise required by applicable law).

(c) No Purchase Rights may be exercised to any extent unless the Ordinary Shares to be issued upon such exercise under the Plan are covered by an effective registration statement pursuant to the Securities Act and the Plan is in material compliance with all applicable federal, state, foreign and other securities and other laws applicable to the Plan. If on a Purchase Date during any Offering hereunder the Ordinary Shares are not so registered or the Plan is not in such compliance, no Purchase Rights or any Offering shall be exercised on such Purchase Date, and the Purchase Date shall be delayed until the Ordinary Shares are subject to such an effective registration statement and the Plan is in such compliance, except that the Purchase Date shall not be delayed more than twelve (12) months and the Purchase Date shall in no event be more than twenty-seven (27) months from the Offering Date. If, on the Purchase Date under any Offering hereunder, as delayed to the maximum extent permissible, the Ordinary Shares are not registered and the Plan is not in such compliance, no Purchase Rights or any Offering shall be exercised and all Contributions accumulated during the Offering (reduced to the extent, if any, such Contributions have been used to acquire Ordinary Shares) shall be distributed to the Participants without interest (unless otherwise required by applicable law).

9. Taxes.

At the time a Participant's Purchase Right is exercised, in whole or in part, or at the time a Participant disposes of some or all of the Ordinary Shares acquired under the Plan, the Participant will make adequate provision for any Tax-Related Items. In their sole discretion, and except as otherwise determined by the Committee, the Company or the Designated Company that employs the Participant may satisfy their obligations to withhold Tax-Related Items by (a) withholding from the Participant's wages or other compensation, (b) withholding a sufficient number of Ordinary Shares otherwise issuable following purchase having an aggregate fair market value sufficient to pay the Tax-Related Items required to be withheld with respect to the Ordinary Shares, (c) withholding from proceeds from the sale of Ordinary Shares issued upon purchase, either through a voluntary sale or a mandatory sale arranged by the Company, or (d) any other method deemed acceptable by the Committee and permitted under applicable law.

10. COVENANTS OF THE COMPANY.

The Company shall seek to obtain from each federal, state, foreign or other regulatory commission or agency having jurisdiction over the Plan such authority as may be required to issue and sell Ordinary Shares upon exercise of the Purchase Rights. If, after commercially reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Ordinary Shares under the Plan, and at a commercially reasonable cost, the Company shall be relieved from any liability for failure to issue and sell Ordinary Shares upon exercise of such Purchase Rights unless and until such authority is obtained.

11. DESIGNATION OF BENEFICIARY.

(a) Unless otherwise determined by the Company, the Participant may file a written designation of a beneficiary who is to receive any Ordinary Shares and/or cash, if any, from the Participant's account under the Plan in the event of such Participant's death subsequent to the end of an Offering but prior to delivery to the Participant of such Ordinary Shares or cash. In addition, a Participant may file a written designation of a beneficiary who is to receive any cash from the

Participant's account under the Plan in the event of such Participant's death during an Offering. Any such designation shall be on a form provided by or otherwise acceptable to the Company.

(b) The Participant may change such designation of beneficiary at any time by written notice to the Company. In the event of the death of a Participant and in the absence of a beneficiary validly designated under the Plan who is living at the time of such Participant's death, the Company shall deliver such Ordinary Shares and/or cash to the executor or administrator of the estate of the Participant, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its sole discretion, may deliver such Ordinary Shares and/or cash to the spouse or to any one or more dependents or relatives of the Participant, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

12. MISCELLANEOUS PROVISIONS.

(a) The Plan and Offering do not constitute an employment contract. Nothing in the Plan or in the Offering shall in any way alter the at will nature of a Participant's employment, if applicable, or be deemed to create in any way whatsoever any obligation on the part of any Participant to continue in the employ of the Company, a Related Corporation or an Affiliate, or on the part of the Company, a Related Corporation or an Affiliate to continue the employment of a Participant.

(b) The provisions of the Plan shall be governed by the laws of the State of Delaware without resort to that state's conflicts of laws rules.

(c) Proceeds from the sale of Ordinary Shares pursuant to Purchase Rights shall constitute general funds of the Company.

(d) A Participant shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, Ordinary Shares subject to Purchase Rights unless and until the Participant's Ordinary Shares acquired upon exercise of Purchase Rights are recorded in the books of the Company (or its transfer agent).

(e) If any particular provision of the Plan is found to be invalid or otherwise unenforceable, such provision shall not affect the other provisions of the Plan, but the Plan shall be construed in all respects as if such invalid provision were omitted.

13. ADJUSTMENTS UPON CHANGES IN ORDINARY SHARES; CORPORATE TRANSACTIONS.

(a) In the event of a Capitalization Adjustment, the Board shall appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a), (ii) the class(es) and maximum number of securities by which the share reserve is to increase automatically each year pursuant to Section 3(a), (iii) the class(es) and number of securities subject to, and the purchase price applicable to outstanding Offerings and Purchase Rights, and (iv) the class(es) and number of securities imposed by purchase limits under each ongoing Offering. The Board shall make such adjustments, and its determination shall be final, binding and conclusive.

(b) In the event of a Corporate Transaction, then: (i) any surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) may assume or continue Purchase Rights outstanding under the Plan or may substitute similar rights (including a right to acquire the same consideration paid to the shareholders in the Corporate Transaction) for those outstanding under the Plan, or (ii) if any surviving or acquiring corporation (or its parent company) does not assume or continue such Purchase Rights or does not substitute similar rights for Purchase Rights outstanding under the Plan, then the Participants' accumulated Contributions

shall be used to purchase Ordinary Shares within ten (10) business days prior to the Corporate Transaction under any ongoing Offerings, and the Participants' Purchase Rights under the ongoing Offerings shall terminate immediately after such purchase.

14. AMENDMENT, TERMINATION OR SUSPENSION OF THE PLAN.

(a) The Board may amend the Plan at any time in any respect the Board deems necessary or advisable. However, except as provided in Section 13(a) relating to Capitalization Adjustments, shareholder approval shall be required for any amendment of the Plan for which shareholder approval is required by applicable law or listing requirements, including any amendment that either (i) materially increases the number of Ordinary Shares available for issuance under the Plan, (ii) materially expands the class of individuals eligible to become Participants and receive Purchase Rights under the Plan, (iii) materially increases the benefits accruing to Participants under the Plan or materially reduces the price at which Ordinary Shares may be purchased under the Plan, (iv) materially extends the term of the Plan, or (v) expands the types of awards available for issuance under the Plan, but in each of (i) through (v) above only to the extent shareholder approval is required by applicable law or listing requirements.

(b) The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate at the time that all of the Ordinary Shares reserved for issuance under the Plan, as increased and/or adjusted from time to time, have been issued under the terms of the Plan. No Purchase Rights may be granted under the Plan while the Plan is suspended or after it is terminated.

(c) Any benefits, privileges, entitlements and obligations under any outstanding Purchase Rights granted before an amendment, suspension or termination of the Plan shall not be impaired by any such amendment, suspension or termination except (i) with the consent of the person to whom such Purchase Rights were granted, (ii) as necessary to comply with any laws, listing requirements, or governmental regulations (including, without limitation, the provisions of Section 423 of the Code and the regulations and other interpretive guidance issued thereunder relating to Employee Stock Purchase Plans) including without limitation any such regulations or other guidance that may be issued or amended after the Effective Date of the Plan, or (iii) as necessary to obtain or maintain favorable tax, listing, or regulatory treatment.

15. CODE SECTION 409A; TAX QUALIFICATION.

(a) Purchase Rights granted under the 423 Component are exempt from the application of Section 409A of the Code. Purchase Rights granted under the Non-423 Component to U.S. taxpayers are intended to be exempt from the application of Section 409A of the Code under the short-term deferral exception thereunder and any ambiguities shall be construed and interpreted in accordance with such intent. Subject to Section 15(b) hereof, Purchase Rights granted to U.S. taxpayers under the Non-423 Component shall be subject to such terms and conditions that will permit such Purchase Rights to satisfy the requirements of the short-term deferral exception available under Section 409A of the Code, including the requirement that the Ordinary Shares purchased on exercise of a Purchase Right be delivered within the short-term deferral period. Subject to Section 14(b) hereof, in the case of a Participant who would otherwise be subject to Section 409A of the Code, to the extent the Board determines that a Purchase Right or the exercise, payment, settlement or deferral thereof is subject to Section 409A of the Code, the Purchase Right shall be granted, exercised, paid, settled or deferred in a manner that will comply with Section 409A of the Code. Notwithstanding the foregoing, the Company shall have no liability to a Participant or any other party if the Purchase Right that is intended to be exempt from or compliant with Section 409A of the Code is not so exempt or compliant or for any action taken by the Board with respect thereto.

(b) Although the Company may endeavor to (i) qualify a Purchase Right for favorable tax treatment under the laws of the United States or jurisdictions outside of the United States or (ii) avoid adverse tax treatment (e.g., under Section 409A of the Code), the Company makes no representation to that effect and expressly disavows any covenant to maintain favorable or avoid unfavorable tax treatment, notwithstanding anything to the contrary in this Plan, including Section 14(a) hereof. The Company shall be unconstrained in its corporate activities without regard to the potential negative tax impact on Participants under the Plan.

15. EFFECTIVE DATE OF PLAN.

The Plan became effective on May 31, 2007.

16. DEFINITIONS.

As used in the Plan, the following definitions shall apply to the capitalized terms indicated below:

(a) ***"423 Component"*** means part of the Plan, which excludes the Non-423 Component, pursuant to which Purchase Rights that are intended to satisfy the requirements for Employee Stock Purchase Plans may be granted to Eligible Employees.

(b) ***"Affiliate"*** means any entity that, directly or indirectly, is controlled by or controls the Company, as determined by the Board, whether now or hereafter existing.

(c) "***Board***" means the Board of Directors of the Company.

(d) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Ordinary Shares subject to the Plan or subject to any Purchase Right after the effective date of the Plan without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, share dividend, dividend in property other than cash, large nonrecurring cash dividend, share split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or any similar equity restructuring transaction, as that term is used in Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto), including, for the avoidance of doubt, capitalization of profits or reserves, capital distribution, rights issue, the conversion of one class of share to another or reduction of capital or otherwise. Notwithstanding the foregoing, the conversion of any convertible securities of the Company shall not be treated as a Capitalization Adjustment.

(e) "***Code***" means the United States Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(f) "***Committee***" means a committee of one (1) or more members of the Board to whom authority has been delegated by the Board in accordance with Section 2(c).

(g) "***Company***" means Jazz Pharmaceuticals plc, a company formed under the laws of Ireland.

(h) "***Contributions***" means the payroll deductions and other additional payments specifically provided for in the Offering, that a Participant contributes to fund the exercise of a Purchase Right. A Participant may make additional payments into his or her account, if specifically provided for in the Offering, and then only if the Participant has not already had the maximum permitted amount withheld during the Offering through payroll deductions.

(i) "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) a sale or other disposition of at least ninety percent (90%**)** of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the Ordinary Shares outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (A) a compromise or arrangement sanctioned by the court under section 201 of the Companies Act 1963 of the Republic of Ireland or (B) section 204 of the Companies Act 1963 of the Republic of Ireland.

Notwithstanding the foregoing or any other provision of this Plan, unless the Board determines otherwise, the term Corporate Transaction shall not include the creation of a new holding company where the Company becomes a wholly-owned subsidiary of that holding company and the holding company will be owned in substantially the same proportions by the persons who held the Company's issued shares immediately before such transaction (in which case Purchase Rights granted hereunder will be treated as if they were in all respects purchase rights over shares in the holding company but so that (i) the new purchase right shall vest in the same manner as the Purchase Right; (ii) the total market value of the new shares subject to the new purchase right shall, immediately after such reorganization, be equal to the total market value of the Ordinary Shares comprised in the Purchase Right immediately prior to such reorganization; (iii) the new shares shall have the same rights attaching thereto as the Ordinary Shares; and (iv) the new purchase right shall be deemed to have been granted as at the date of grant of the Purchase Right).

(j) ***"Designated Affiliate"*** means any Affiliate selected by the Board as eligible to participate in the Non-423 Component.

(k) ***"Designated Company"*** means a Designated Affiliate or Designated Related Corporation.

(l) ***"Designated Related Corporation"*** means any Related Corporation selected by the Board as eligible to participate in the 423 Component.

(m) "***Director***" means a member of the Board.

(n) "***Eligible Employee***" means an Employee who meets the requirements set forth in the Offering for eligibility to participate in the Offering, provided that such Employee also meets the requirements for eligibility to participate set forth in the Plan.

(o) "***Employee***" means any person, including Officers and Directors, who is employed for purposes of Section 423(b)(4) of the Code by the Company, a Related Corporation or an Affiliate. However, service solely as a Director, or payment of a fee for such services, shall not cause a Director to be considered an "Employee" for purposes of the Plan. Consultants, independent contractors or other types of service providers are not "Employees" for purposes of the Plan.

(p) "***Employee Stock Purchase Plan***" means a plan that grants Purchase Rights intended to be options issued under an "employee stock purchase plan," as that term is defined in Section 423(b) of the Code.

(q) "***Exchange Act***" means the United States Securities Exchange Act of 1934, as amended.

(r) "***Fair Market Value***" means, as of any date, the value of the Ordinary Shares determined as follows:

(i) If the Ordinary Shares are listed on any established stock exchange or traded on any established market, the Fair Market Value of an Ordinary Share shall be the closing sales price for such Ordinary Share as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Ordinary Shares) on the date of determination, as reported in such source as the Board deems reliable. Unless otherwise provided by the Board, if there is no closing sales price for the Ordinary Shares on the date of determination, then the Fair Market Value shall be the closing selling price (or closing bid if no sales were reported) on the last preceding date for which such quotation exists.

(ii) In the absence of such markets for the Ordinary Shares, the Fair Market Value shall be determined by the Board in good faith.

(s) ***"Non-423 Component"*** means an employee stock purchase plan which is not intended to meet the requirements set forth in Code Section 423 and the regulations thereunder.

(t) "***Offering***" means the grant of Purchase Rights to purchase Ordinary Shares under the Plan to Eligible Employees. Unless otherwise determined by the Board, each Offering under the Plan in which Eligible Employees of one or more Designated Companies may participate will be deemed a separate offering for purposes of Section 423 of the Code, even if the dates of each such Offering are identical, and the provisions of the Plan will separately apply to each Offering.

(u) "***Offering Date***" means a date selected by the Board for an Offering to commence.

(v) "***Officer***" means a person who is an officer of the Company, an Affiliate or a Related Corporation within the meaning of Section 16 of the Exchange Act and the rules and regulations promulgated thereunder.

(w) "***Ordinary Share***" or "***Ordinary Shares***" means the ordinary shares of the Company of nominal value US$0.0001 per share.

(x) "***Participant***" means an Eligible Employee who holds an outstanding Purchase Right granted pursuant to the Plan.

(y) "***Plan***" means this Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan, including both the 423 and Non-423 Components, as amended from time to time.

(z) "***Purchase Date***" means one or more dates during an Offering established by the Board on which Purchase Rights shall be exercised and as of which purchases of Ordinary Shares shall be carried out in accordance with such Offering.

(aa) "***Purchase Period***" means a period of time specified within an Offering beginning on the Offering Date or on the next day following a Purchase Date within an Offering and ending on a Purchase Date. An Offering may consist of one or more Purchase Periods.

(bb) "***Purchase Right***" means an option to purchase Ordinary Shares granted pursuant to the Plan.

(cc) "***Related Corporation***" means any "parent corporation" or "subsidiary corporation" of the Company whether now or subsequently established, as those terms are defined in Sections 424(e) and 424(f), respectively, of the Code.

(dd) "***Securities Act***" means the United States Securities Act of 1933, as amended.

(ee) "***Tax-Related Items***" means any income tax, social insurance, payroll tax, payment on account or other tax-related items arising in relation to the Participant's participation in the Plan

(ff) "***Trading Day***" means any day on which the exchange(s) or market(s) on which the Ordinary Shares are listed, including the Nasdaq Global Select Market or the Nasdaq Global Market, is open for trading.

Adopted by the Board of Directors of Jazz Pharmaceuticals, Inc. on May 1, 2007. Approved by the stockholders of

Jazz Pharmaceuticals, Inc. on May 9, 2007.

Amended and restated by the Board of Directors of Jazz Pharmaceuticals, Inc. on September 29, 2010.

Amended and restated by the Board of Directors of Jazz Pharmaceuticals, Inc. on October 24, 2011.

Approved by the stockholders of Jazz Pharmaceuticals, Inc. on December 12, 2011. Adopted by the Board of

Directors of Azur Pharma plc on December 21, 2011.

Approved by the shareholders of Azur Pharma plc on January 3, 2012.

Amended and restated by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on October 26, 2012.

Amended and restated by the Compensation Committee of the Board of Directors of Jazz Pharmaceuticals plc on November 2, 2022.

Exhibit 21.1

Subsidiaries of the Registrant

Name	**State/Jurisdiction of Incorporation**
Jazz Pharmaceuticals Ireland Limited	Ireland
Jazz Financing I DAC	Ireland
GW Pharma Limited	United Kingdom
Jazz Pharmaceuticals, Inc.	Delaware
Celator Pharmaceuticals Inc.	Delaware
GW Research Limited	United Kingdom
Gentium S.r.l.	Italy
Jazz Pharmaceuticals UK Holdings Limited	United Kingdom
Jazz Securities DAC	Ireland
Jazz Financing Holdings Limited	Ireland
Jazz Financing Lux S.à.r.l	Luxembourg
Jazz Pharmaceuticals International Limited	Bermuda
Jazz Investments Europe Limited	Malta
Jazz Investments I Limited	Bermuda
Jazz Capital Limited	Ireland
Jazz Pharmaceuticals UK Limited	United Kingdom
GW Pharmaceuticals Limited	United Kingdom
Cavion Inc	Delaware

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (No. 333-179075, No. 333-186886, No. 333-194131, No. 333-202269, No. 333-209767, No. 333-216338, No. 333-224757, No. 333-229889, No. 333-236636, No. 333-249807, No. 333-253417, No. 333-255895 and No. 333-263195) on Form S-8 of our reports dated March 1, 2023, with respect to the consolidated financial statements and financial statement schedule at Item 15(a)2 of Jazz Pharmaceuticals plc and the effectiveness of internal control over financial reporting.

/s/ KPMG

Dublin, Ireland
March 1, 2023

Exhibit 31.1

CERTIFICATION

I, Bruce C. Cozadd, certify that:

1. I have reviewed this Annual Report on Form 10-K 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: March 1, 2023

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 Annual Report on Form 10-K 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: March 1, 2023

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 Annual Report on Form 10-K for the year ended December 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: March 1, 2023

/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 Annual Report on Form 10-K 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-K), 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.