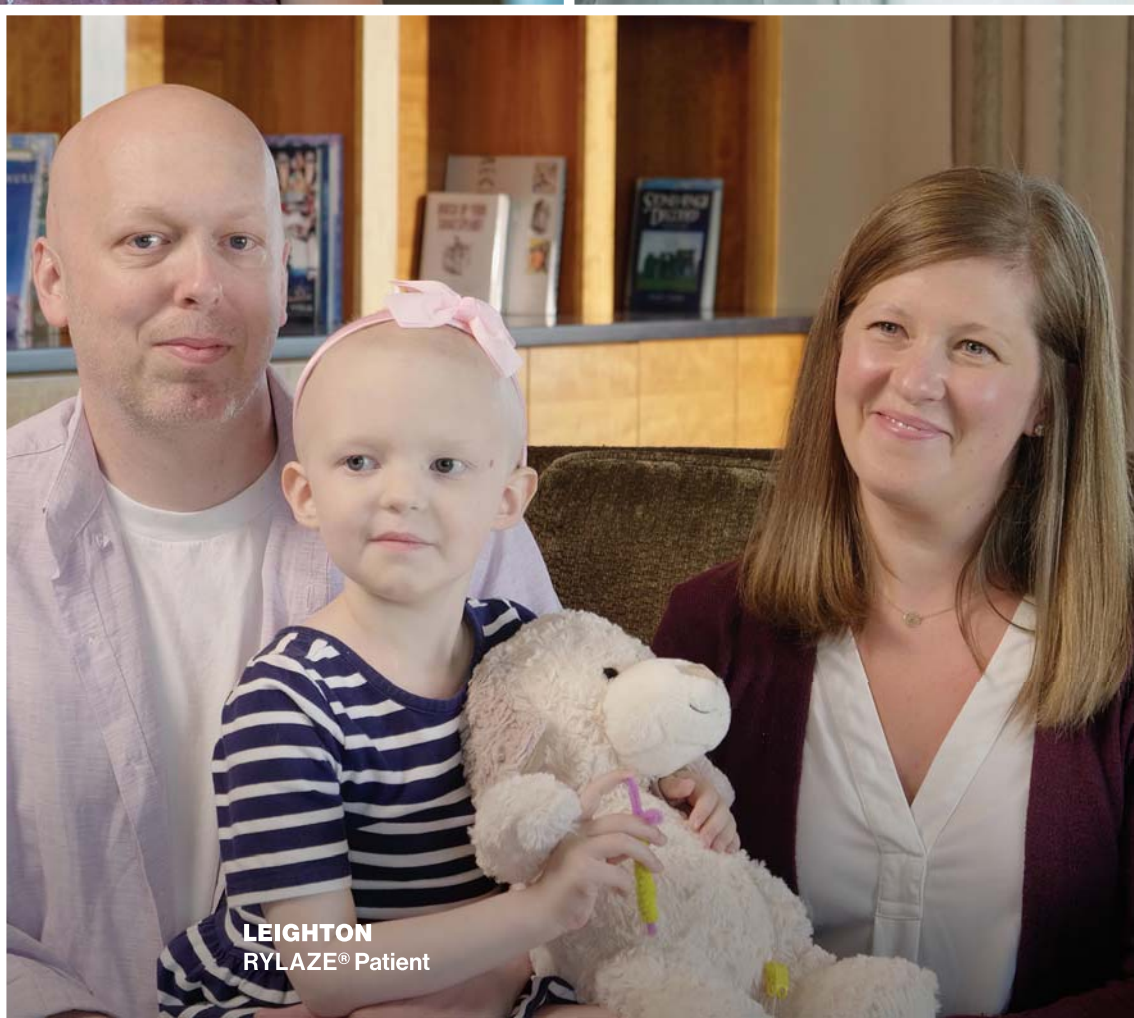
Jazz Pharmaceuticals

Jazz Pharmaceuticals plc
Proxy Statement
2022 Annual Report



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DEAR FELLOW SHAREHOLDERS,

JUNE 2023

I am pleased to report that 2022 was an outstanding year of execution at Jazz. We achieved record revenue based on the strong commercial performance of our diverse portfolio of neuroscience and oncology therapies, our expanded R&D organization has never been more productive and we maintained our focus on disciplined capital allocation and operational excellence. We are driven by our focus on developing life-changing medicines for people with serious diseases — often with limited or no therapeutic options. By keeping patients at the center of all that we do, we're able to transform the lives of patients and their families by providing vital medicines when there are few options available.

In early 2022, we introduced Vision 2025 to provide a clear perspective on what we expect to achieve in the coming years. Our goal is to deliver sustainable growth and enhanced value and drive the continued transformation of Jazz into an innovative, high-growth global biopharmaceutical leader as we bring new and innovative medicines to patients in critical need. Vision 2025 is built on our core strengths of commercial execution, enhanced R&D capabilities and our continued focus on strategic use of capital. I'm incredibly proud of our 2022 accomplishments, which have provided a foundation for our business to grow and position us well to achieve Vision 2025.

We're marking the 20th anniversary of the founding of Jazz in 2023, and over the past two decades, we've remained focused on our purpose to improve the lives of patients and commitment to being a great place to work while delivering consistent top-line growth. Thanks to the dedication, creativity and collaboration demonstrated by our approximately 2,800 talented employees around the world, we helped more patients and significantly advanced and broadened our pipeline in 2022.

VISION 2025 TO DELIVER SUSTAINABLE GROWTH AND ENHANCED VALUE

Vision 2025 has three key core components:

- **Commercial:** Generating $5 billion in revenue in 2025
- **Pipeline:** Delivering at least 5 novel product approvals by the end of the decade
- **Operational Excellence:** Driving 5% adjusted operating margin improvement from 2021 to 2025

2022 ACCOMPLISHMENTS

We delivered substantial top-line growth led by the strength of our commercial franchises, progressed

MEET LEIGHTON

Leighton was diagnosed with acute lymphoblastic leukemia (ALL) when she was four and immediately began treatment with the standard chemotherapy regimen, which included an *E. coli*-derived asparaginase. For more than 50 years, asparaginase has been a core component of multi-agent treatment regimens in ALL and lymphoblastic lymphoma (LBL).[1]

During her treatment, Leighton had an allergic reaction, also known as a hypersensitivity reaction (HSR), to the *E. coli*-derived asparaginase formulation, and her family were fearful that she would be unable to complete her asparaginase treatment. Approximately 20% of ALL and LBL patients receiving *E. coli*-derived asparaginase experience HSRs,[2] which can compromise the safety of patients and the effectiveness of treatment.[3] Discontinuation of an asparaginase treatment regimen may negatively affect treatment efficacy and patient outcomes. The ability to complete the full treatment course is of critical importance and strongly linked to improved outcomes in patients.[1] Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) provides a treatment option for appropriate patients who develop HSRs to *E. coli*-derived asparaginase and maintains a clinically meaningful level of asparaginase activity throughout the entire course of treatment.[4] Leighton joined the Phase 2/3 clinical trial and received *Rylaze*, a recombinant formulation of an *Erwinia*-derived asparaginase.

Treatment with *Rylaze* in the clinical trial enabled Leighton to complete the entire course of treatment, which is essential to treatment success for patients.[5] We're pleased to share Leighton had a positive outcome, and her family are grateful that Leighton was part of the trial that supported the FDA approval of *Rylaze*, which enables other appropriate ALL and LBL patients to have access to this important therapy.

> "When we found out we had the option to join the clinical trial, it made me feel so happy that there was something else out there – another avenue that we could explore to make sure Leighton got the treatment that her little body needed."
>
> — BILLY, LEIGHTON'S DAD

Rylaze *was rapidly developed from Phase 1 initiation to launch in approximately two and half years. Since it was first approved in 2021 with intramuscular administration,* Rylaze *has provided patients with an effective therapeutic option with reliable supply for the treatment of acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LBL). Jazz remains committed to providing access to the reliable, high-quality supply of* Rylaze, *so patients and healthcare providers have the opportunity to complete the full course of asparaginase therapy. Clinical trial results demonstrate* Rylaze *is efficacious and has a safety profile consistent with other asparaginases.*

On June 30, 2021, U.S. Food and Drug Administration (FDA) approved Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn) for use as a component of a multi-agent chemotherapeutic regimen given by intramuscular injection for the treatment of ALL and LBL in adult and pediatric patients one month or older who have developed hypersensitivity to E. coli-derived asparaginase.

The patient story shared in this communication depicts an individual patient's response to our medicine and is not representative of all patient responses.

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1. Egler RA, Ahuja SP, Matloub Y. L–asparaginase in the treatment of patients with acute lymphoblastic leukemia. J Pharmacol Pharmacother. 2016;7(2):62-71. 2. Burke MJ. How to manage asparaginase hypersensitivity in acute lymphoblastic leukemia. Future Oncol. 2014;10(16):2615-2627. 3. Asselin B. Immunology of infusion reactions in the treatment of patients with acute lymphoblastic leukemia. Future Oncol. 2016;12(13):1609-1621. 4. Maese, L, et al. Recombinant Erwinia asparaginase (JZP458) in acute lymphoblastic leukemia: results from the Phase 2/3 AALL1931 study. Blood. 2023;141(7): 704-712. 5. Salzer W, Bostrom B, Messinger Y, et al. Asparaginase activity levels and monitoring in patients with acute lymphoblastic leukemia. Leuk Lymphoma. 2018;59(8):1797-1806

multiple preclinical and clinical-stage programs, added three promising candidates to our pipeline and delivered strong financial results.

Commercial

- **Achieved total revenues of $3.7 billion with growing and durable commercial franchises; an 18% increase compared to 2021.** Revenue growth was driven by strong commercial execution of Xywav®, Epidiolex®, Zepzelca® and Rylaze®. We met our 2022 diversification target of 60% to 65% of net product sales coming from products launched or acquired since 2019.
- **Drove continued adoption of *Xywav* across both narcolepsy and idiopathic hypersomnia (IH).** In the fourth quarter of 2022, *Xywav* became our largest product by net sales, indicating that the benefits of *Xywav*, a low-sodium oxybate, continue to resonate with both physicians and patients. The large majority of new-to-oxybate narcolepsy patients are beginning their therapy with *Xywav*. We saw compelling uptake of *Xywav* in IH during its first full year on market as the only FDA-approved therapy for this debilitating sleep disorder. We expect *Xywav* to remain the oxybate of choice in 2023 and remain confident that *Xywav* is a durable product.
- **Significantly grew Epidiolex/Epidyolex®.** Net product sales increased 12% on a proforma basis compared to 2021, driven by a number of factors, including increased access to treatment centers and physician offices and volume of engagement with prescribers. We successfully completed the pricing and reimbursement process and commercial launch of *Epidyolex* in France, making *Epidyolex* available in all five key European markets: United Kingdom, Germany, Italy, Spain and France. We anticipate multiple new market and indication launches of *Epidyolex* outside of the U.S. throughout 2023. We remain excited about the future growth and blockbuster potential of *Epidiolex*.
- **Rapidly established Zepzelca® as the treatment of choice in second-line small cell lung cancer (SCLC).** We have a robust development program for Zepzelca to explore the utility in several new patient populations who may benefit from the medicine, including in first-line SCLC and other solid tumors.
- **Provided Rylaze to patients in critical need.** Rylaze remains the only therapy available to patients in the U.S. who have a hypersensitivity reaction to *E. coli*-derived asparaginase. In its first full year, it has been adopted universally in pediatric oncology protocols, reflecting the high-quality, reliable supply of this important treatment option for patients with acute lymphoblastic leukemia or lymphoblastic lymphoma.

> **“In 2022, we delivered substantial top-line growth led by the strength of our commercial franchises, progressed multiple preclinical and clinical-stage programs and added three promising candidates to our pipeline.”**

Pipeline

- **Added three promising candidates to our pipeline.** Zanidatamab is a novel, late-stage

"We believe that positively impacting patients' lives, investing in our people and our commitment to long-term sustainability are important to delivering on Vision 2025."

oncology asset with the potential to transform the standard of care in multiple HER2-expressing cancers. It has demonstrated compelling data in biliary tract cancers and gastroesophageal adenocarcinoma with the potential to benefit patients across multiple tumor types. JZP441 is a potent, highly selective, oral orexin-2 receptor agonist with potential to be applicable in the treatment of narcolepsy, IH and other sleep disorders, which entered Phase 1 clinical development in 2022. JZP898 is an engineered interferon alpha (IFNα) cytokine pro-drug that is activated specifically within the tumor microenvironment where it can stimulate IFNα receptors on cancer-fighting immune effector cells.

- **Submitted four Investigational New Drug (IND) applications and initiated seven clinical trials.** We have expanded the breadth and depth of our pipeline to 30 R&D programs with 14 in late-stage development. We enrolled the first patient in several trials, including:
  - Phase 1 trial for JZP815 in patients with advanced or metastatic solid tumors with MAPK alterations
  - Phase 2 trial for suvecaltamide in patients with Parkinson's disease tremor
  - Phase 3 trial for *Epidyolex* in Lennox-Gastaut syndrome, Dravet syndrome and tuberous sclerosis complex in Japan.
- **Significantly expanded our in-house, end-to-end R&D capabilities.** We enhanced our medicinal chemistry and translational biology expertise to include differentiated capabilities such as cannabinoids and nanoparticle drug delivery.

Operational Excellence

- **Focused on driving five percentage points adjusted operating margin improvement from 2021 to 2025.** Our focus on operational excellence contributed to significantly increased cash from operations of $1.3 billion, an increase of $493 million or 63% compared to 2021.
- **Significantly delevered the balance sheet.** Disciplined capital allocation and strong cash flow enabled us to rapidly delever our balance sheet following the GW Pharmaceuticals acquisition in May 2021.

- **We remain focused on disciplined capital allocation aimed at our highest priority areas, including R&D programs and corporate development.** Our success in 2022 has given us additional flexibility to invest in our current business, as well as be active on potential future corporate development opportunities.

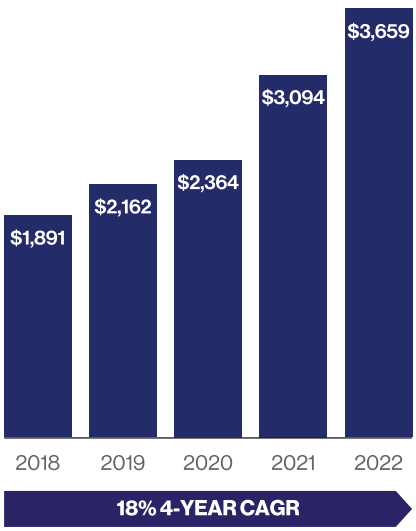
We believe that positively impacting patients' lives, investing in our people and our commitment to long-term sustainability are important to delivering on Vision 2025. In 2022, we published our inaugural environmental, social and governance (ESG) report. This report can be found on our website at https://www.jazzpharma.com/wp-content/uploads/2022/12/2021-JAZZ-ESG-Report.pdf.

Entering 2023, we remain optimistic about the year ahead and are well-positioned to achieve Vision 2025. This is an exciting time of transformation for Jazz and I thank you for your continued support as we innovate to transform the lives of patients and their families.

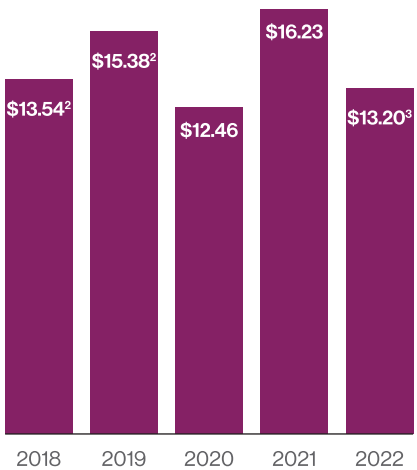
Bruce C. Cozadd
Chairperson and Chief Executive Officer

STRONG FINANCIAL EXECUTION

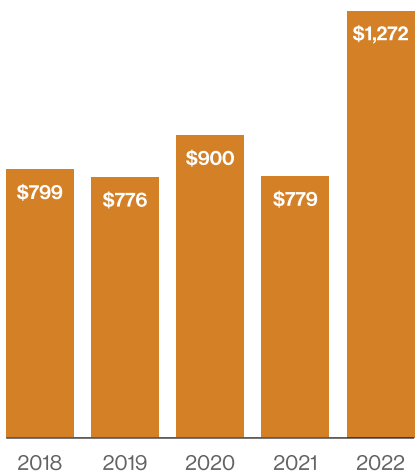
TOTAL REVENUES
$ in millions
(audited)



NON-GAAP ADJUSTED NET INCOME PER DILUTED SHARE[1]
(unaudited)



NET CASH PROVIDED BY OPERATING ACTIVITIES
$ in millions
(audited)



1. Non-GAAP adjusted net income per diluted share is a non-GAAP financial measure, for further information, see "Non-GAAP Financial Measures". Reconciliations of GAAP net income (loss) per diluted share to non-GAAP adjusted net income per diluted share can be found on pages 70 and 71 of the enclosed Proxy Statement. 2. Commencing in 2020, following consultation with the staff of the Division of Corporation Finance of the U.S. Securities and Exchange Commission, the Company no longer excludes upfront and milestone payments from the Company's non-GAAP adjusted net income. For the purposes of comparability, non-GAAP adjusted financial measures for the years ended December 31, 2018 and 2019 have been updated to reflect this change. 3. Non-GAAP adjusted net income per diluted share for the year ended December 31, 2022, was impacted by $1.48 per share following the adoption of ASU 2020-06, and by acquired IPR&D expense which had the effect of reducing adjusted net income per diluted share by $5.35 per share, compared to the year ended December 31, 2021.

CAGR = Compound Annual Growth Rate; IPR&D = In-process research and development

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NOTICE OF 2023 ANNUAL GENERAL MEETING OF SHAREHOLDERS

TO BE HELD ON AUGUST 3, 2023

Dear Shareholder:

The 2023 annual general meeting of shareholders (the "annual meeting") of Jazz Pharmaceuticals plc, a public limited company formed under the laws of Ireland (the "company"), will be held on Thursday, August 3, 2023, at 9:45 a.m. local time at our corporate headquarters located at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland, for the following purposes:

1. To elect by separate resolutions each of the four nominees for director named in the accompanying proxy statement (the "proxy statement") to hold office until the 2026 annual meeting of shareholders (Proposal 1).
2. To ratify, on a non-binding advisory basis, the appointment of KPMG as the independent auditors of the company for the fiscal year ending December 31, 2023 and to authorize, in a binding vote, the board of directors, acting through the audit committee, to determine the independent auditors' remuneration (Proposal 2).
3. To approve, on a non-binding advisory basis, the compensation of the company's named executive officers, or NEOs, as disclosed in the accompanying proxy statement (Proposal 3).
4. To grant the board of directors authority under Irish law to allot and issue ordinary shares for cash without first offering those ordinary shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply (Proposal 4).
5. To approve any motion to adjourn the annual meeting, or any adjournments thereof, to another time and place to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4 (Proposal 5).

To conduct any other business properly brought before the annual meeting.

Proposals 1, 2, 3 and 5 are ordinary resolutions, requiring the affirmative vote of a majority of the votes cast (in person or by proxy) at the annual meeting. Proposal 4 is a special resolution, requiring the approval of not less than 75% of the votes cast (in person or by proxy) at the annual meeting.

In addition to the above proposals, the annual meeting will also receive and consider the company's Irish statutory financial statements for the fiscal year ended December 31, 2022 and the reports of the directors and auditors thereon. There is no requirement under Irish law that the Irish statutory financial statements be approved by the shareholders, and no such approval will be sought at the annual meeting. Under the company's Memorandum and Articles of Association (our "articles"), and the Irish Companies Act 2014 (the "2014 Act"), Proposals 1 and 2 are deemed to be ordinary business, and Proposals 3, 4 and 5 are deemed to be special business.

The record date for the annual meeting is June 7, 2023. Only shareholders of record at the close of business on that date may vote at the annual meeting or any adjournment or postponement thereof. The Notice of Internet Availability of Proxy Materials and our proxy materials, which include this proxy statement, our annual letter to shareholders and our 2022 Annual Report on Form 10-K, are first being mailed to shareholders on or about June 20, 2023.

A shareholder entitled to attend and vote at the annual meeting is entitled to appoint one or more proxies to attend, speak and vote instead of him or her at the annual meeting, using the proxy card provided (or the form of proxy contained in section 184 of the 2014 Act) or using an electronic proxy card by telephone or via the internet in the manner described in this proxy statement. A proxy need not be a shareholder of record.

Whether or not you expect to attend the meeting, please vote as soon as possible. You may vote your shares:

Over the Telephone
1-800-690-6903

Via the Internet
www.proxyvote.com

By Mail
Complete, sign and return proxy card

In Person
Attend Annual Meeting

If you received a proxy card or voting instruction card by mail, you may submit your proxy card or voting instruction card by mailing your proxy card or voting instruction card in the envelope provided. Proxy cards must be received by August 2, 2023. Electronic proxy cards submitted via the internet or by telephone must be received by 11:59 p.m., U.S. Eastern Time, on August 2, 2023. It may not be possible to count proxy cards received after the relevant time towards voting. Proxy cards received will be forwarded to the company's registered office electronically before commencement of the annual meeting to comply with Irish law. Even if you have voted by proxy, you may still vote in person if you attend the meeting. Please note, however, that if the record holder of your ordinary shares is a broker, bank or other agent, and you wish to vote at the meeting, you must obtain a proxy issued in your name from that record holder.

Important Notice Regarding the Availability of Proxy Materials for the annual meeting of shareholders to be held on August 3, 2023, at 9:45 a.m. local time at our corporate headquarters located at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland.

The proxy statement, our letter to shareholders, our Irish statutory financial statements and our 2022 Annual Report on Form 10-K are available at https://materials.proxyvote.com/G50871.

By order of the board of directors,

/s/ Aislinn Doody
Aislinn Doody, Company Secretary
Dublin, Ireland
June 16, 2023

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TABLE OF CONTENTS

Index of Frequently Requested Information

PROXY OVERVIEW

This overview highlights certain information contained elsewhere in this proxy statement and does not contain all of the information that you should consider. You should read the entire proxy statement carefully before voting. For more complete information regarding our business and 2022 performance, please review our Annual Report on Form 10-K for the year ended December 31, 2022 that we filed with the Securities and Exchange Commission, or SEC, on March 1, 2023, which we refer to throughout this proxy statement as the 2022 Annual Report on Form 10-K.

In this proxy statement, unless otherwise indicated or the context otherwise requires, all references to "Jazz Pharmaceuticals," "Jazz," "the company," "we," "us" and "our" refer to Jazz Pharmaceuticals plc and its consolidated subsidiaries, except when the context makes clear that the time period being referenced is prior to January 18, 2012, in which case such terms are references to Jazz Pharmaceuticals, Inc. and its consolidated subsidiaries. On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company, or Azur Pharma, were combined in a merger transaction, or the Azur Merger, in connection with which Azur Pharma was renamed Jazz Pharmaceuticals plc, and we became the parent company of and successor to Jazz Pharmaceuticals, Inc., with Jazz Pharmaceuticals, Inc. becoming our wholly owned subsidiary.

Meeting and Voting Information

Time and Date:

9:45 a.m., local time on
Thursday, August 3, 2023

Place:

Our Corporate Headquarters
Fifth Floor, Waterloo Exchange
Waterloo Road Dublin 4, Ireland

Whether or not you expect to attend the meeting, please vote as soon as possible. Please see "Questions and Answers About These Proxy Materials and Voting—How do I vote?" beginning on page 104 below.

Business Overview

We are 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 sustainable growth is rooted in executing commercial launches and ongoing commercialization of our portfolio of products in global markets; 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.

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 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 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 (select markets).

Oncology

- **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;
- **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;

- **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; and
- **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.

Information About Our Board of Directors

Director Nominees and Continuing Directors

Summary information about our director nominees and continuing directors, including their key skills and experiences that are relevant to serving on our board, is provided in the charts below. See pages 17 to 39 for more information.

Our nominating and corporate governance committee examines the experience and expertise of our board as a whole to ensure alignment between the abilities and contributions of our board and our long-term strategic priorities by primarily emphasizing expertise in global and U.S. commercialization, in scientific development, in financial management and in corporate development transactions among other skill sets. All of our directors exhibit high commitment, integrity, collegiality, innovative thinking, sound business judgment and a knowledge of corporate governance requirements and practices.

Name	Age	Director Since	Principal Position	Independent	Other Current Public Boards
2023 Director Nominees					
Bruce C. Cozadd	59	2003(1)	Chairperson and Chief Executive Officer, Jazz Pharmaceuticals plc	No	1
Heather Ann McSharry	61	2013	Director, International Airlines Group, S.A.	Yes	1
Anne O'Riordan	55	2019	Group Director of Digital, Jardine Matheson Limited	Yes	0
Rick E Winningham	63	2010(1)	Chairperson and Chief Executive Officer, Theravance Biopharma, Inc.	Yes	1
Continuing Directors					
Jennifer E. Cook	57	2020	Director, BridgeBio Pharma, Inc. and Denali Therapeutics Inc.	Yes	2
Patrick G. Enright	61	2009(1)	Managing Director, Longitude Capital	Yes	1
Peter Gray	68	2013	Chairperson, Teckro, Inc. and Director, Abzena	Yes	0
Seamus Mulligan	62	2012	Director, Jazz Pharmaceuticals plc	Yes	0
Kenneth W. O'Keefe	56	2004(1)	Founder, BPOC, LLC	Yes	0
Norbert G. Riedel, Ph.D.	65	2013	Chairperson, Eton Pharmaceuticals, Inc. and Director, Cerevel Therapeutics Holdings, Inc.	Yes	2
Mark D. Smith, M.D.	71	2020	Professor, University of California, San Francisco and Director, Phreesia, Inc. and Teladoc Health, Inc.	Yes	2
Catherine A. Sohn, Pharm.D.	70	2012	Chairperson, BioEclipse Therapeutics, Inc. and Director, Altimmune, Inc. and Axcella Health Inc.	Yes	2

(1) Includes service on the board of directors of Jazz Pharmaceuticals, Inc., our predecessor.

Director Diversity

11 of our 12 directors are independent and our board has a mix of relatively newer and longer-tenured directors. The charts below show board makeup by various characteristics with respect to our director nominees and continuing directors:

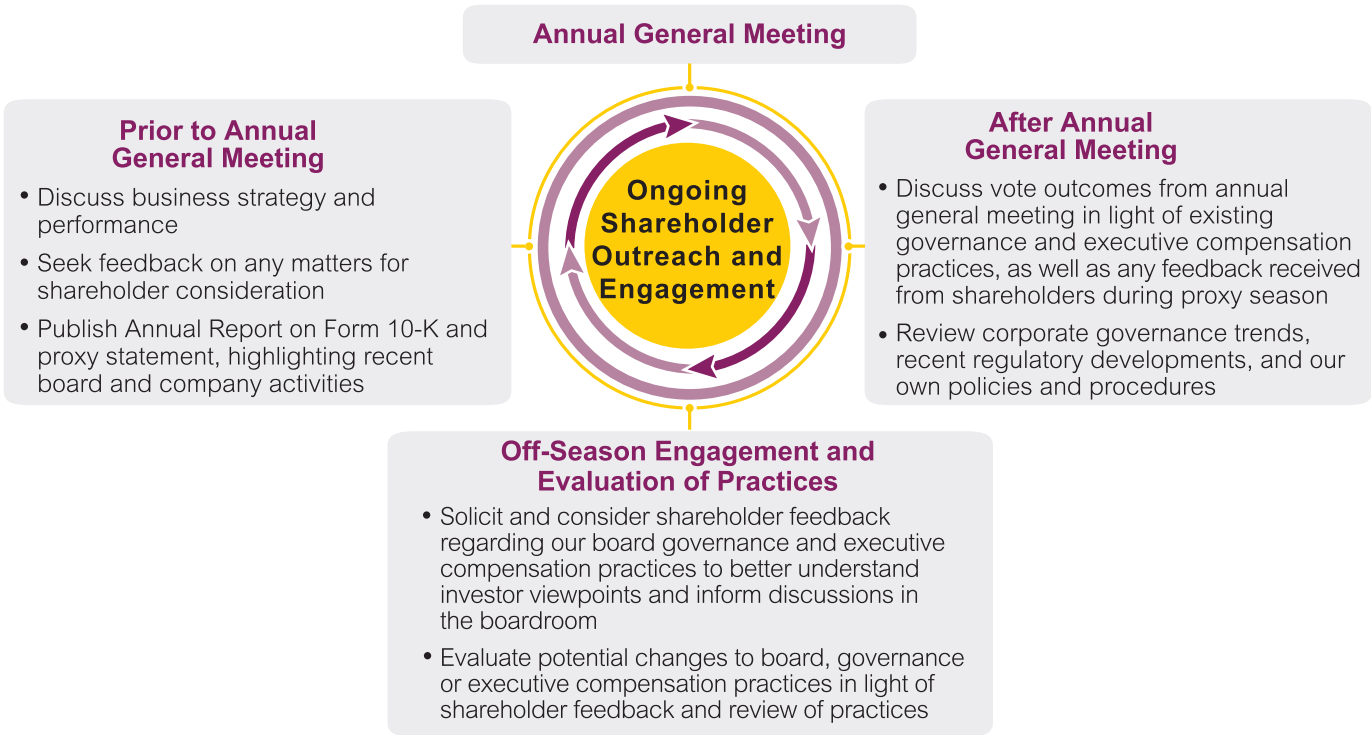
Board Diversity Matrix (as of June 1, 2023)				
Total Number of Directors	12			
	Female	Male	Non-Binary	Did Not Disclose Gender
Part 1: Gender Identity				
Directors	4	8	—	—
Part II: Demographic Background				
African American or Black	—	1	—	—
White	4	7	—	—
LGBTQ+	1			

Shareholder and Other Stakeholder Engagement

We value engaging with and obtaining feedback from our shareholders and view our shareholder engagement efforts as essential to Jazz's success. We continuously engage with our shareholders in many forms and forums from industry conferences, non-deal roadshows, to direct one-on-one meetings. Jazz seeks to act in the long-term interests of its shareholders and recognizes the value in building long lasting and trusting relationships with them. Through these relationships, Jazz has obtained valuable insight on a variety of topics, including our business and growth strategy, corporate governance practices, executive compensation matters, and various other environmental, social and governance (ESG) matters. Shareholder feedback is reported to our compensation & management development committee, or compensation committee, (and our nominating and corporate governance committee, as applicable) throughout the year.

Proxy Overview (continued)

The following graphic describes our typical shareholder outreach and engagement cycle.



In 2022 and early 2023, members of our management team, and in many cases members of our board of directors, including members of our compensation committee and our nominating and corporate governance committee, actively engaged with a significant number of our large shareholders to gain a better understanding of their views regarding our executive compensation program, our ESG strategy and other corporate governance matters. Specifically, we reached out to approximately 34 of our largest shareholders (representing over 58% of our outstanding ordinary shares). We held one-on-one governance related meetings with 11 of our largest shareholders (representing over 37% of our outstanding ordinary shares). We will continue outreach and dialogue with our largest shareholders in 2023.

Proxy Overview (continued)

We have taken a number of significant and responsive actions over the past several years to incorporate feedback received from shareholders, as highlighted in the following table.

Topic	What We Heard	What We Did
ESG	Shareholders and stakeholders continued to highlight the importance of ESG.	• In 2022, we obtained feedback from various external stakeholders to help us identify and prioritize the most impactful ESG matters for our business and our stakeholders. We plan to discuss the results of our materiality assessment in our next ESG Report for the year 2022. • In 2022, we issued our inaugural ESG Report for the year 2021 setting out the pillars of our ESG strategy, Patients, People, Community and Planet and recognizing the critical importance of these ESG pillars in achieving our near and long-term business objectives including Vision 2025. • Outlined in the committee charter, the nominating and corporate governance committee has oversight responsibilities for ESG strategy and practices. Our Executive Vice President and Chief Legal Officer has executive oversight for ESG strategic planning, risk management and reporting.
Board Skills	Shareholders wanted enhanced disclosure regarding the most significant skills and qualifications that each member of our board possesses.	We have enhanced our director skills disclosure by presenting our directors' skills on an individual basis and by providing a description of each skill to help shareholders understand how each skill helps contribute to effective oversight.
Director Commitments	Shareholders expressed interest in our policies and practices regarding director commitments.	We amended our Corporate Governance Guidelines to provide that directors may not serve on more than five public company boards (including Jazz's board) and if a director is also the chief executive officer of a public company, that director may not serve on more than three public company boards (including Jazz's board). We have also amended both the charter of the nominating and corporate governance committee and our Corporate Governance Guidelines to ensure that when performing our annual review of each of our director's time commitments and service on other companies' boards, we also review their service on other companies' board committees.
Board Refreshment	Shareholders continued to stress the importance of board refreshment and the role it plays in enhancing skills and capabilities and increasing board diversity.	Jazz recognizes the critical importance of balancing the appropriate representation of experience and skills on our board of directors to fit the current and future needs of our company. Our board of directors understands that strategic board refreshment is essential to Jazz's success and effective board oversight. With this purpose in mind, the nominating and corporate governance committee seeks out experienced candidates with a track record for commercial success and/or drug development, that exhibit strength of character, judgment and principles of diversity, including diversity of race, ethnicity, gender, age, geographic residency, cultural background and professional experiences.

Proxy Overview (continued)

Topic	What We Heard	What We Did
		We have an ongoing board evaluation process, with a mix of one-on-ones with the Lead Independent Director, surveys and external assessments. Board refreshment is a consistent theme of our board and committee evaluations.
Compensation	While shareholders provided positive feedback regarding our pay-for-performance alignment, we heard a strong preference that our long-term incentive program include performance-based equity awards. Shareholders raised concerns that our burn rate is higher than some of our peers. Shareholders disfavored the "evergreen provision" in our 2011 Equity Incentive Plan. Shareholders also expressed their desire for our annual performance bonus plan to have an explicit cap on payouts to avoid the potential of excessive payouts not tied to performance and to mitigate certain risks inherent in incentive plans.	In response to shareholder feedback: • We incorporated performance stock units (PSUs) into our program in 2021 and we continue to grant PSUs representing approximately 50% of each executive officer's target equity compensation; • Since 2021, stock options have been eliminated from our long-term incentive program, and 100% of the awards granted thereunder have been in the form of PSUs and restricted stock units (RSUs) which reduce our burn rate and result in less dilution than stock options; • The evergreen provision in the 2011 Equity Incentive Plan expired in January 2022 and we will not adopt a new one in the future; • We adopted and continue to maintain an explicit cap on payouts under annual performance bonus awards at 300% of an individual's target award; • We selected performance goals for our executive compensation program that focus specifically on (i) growing and diversifying our commercial portfolio and (ii) enhancing the value of our pipeline to create a meaningful incentive and reward for successfully driving transformation and delivery of long-term sustainable value to shareholders and life-changing medicines to patients; • We structured our PSUs so that payout is based on financial and operational goal performance, which is then adjusted, based on the rate of return of our stock price relative to peers, or a relative total shareholder return modifier (TSR). The compensation committee believes that having a TSR modifier helps balance the importance of providing executives clearer line of sight to payout opportunities using financial and operational measures with the need to ensure that those payouts are aligned with shareholders' experience during the performance period; • We further refined our 2022 PSUs so that objectives are measured over a three-year performance period; • We also have a policy for recoupment of incentive compensation, or a clawback policy, which is designed to mitigate risks generally associated with incentive compensation and allows us to recover amounts of incentive compensation under certain circumstances if we are required to restate our financial results due to material noncompliance with any financial requirement and the misconduct of an executive officer covered by the policy contributed to such noncompliance.

We also continue to evaluate feedback received from shareholders on other topics, including our classified board structure, setting climate change targets and reporting on workforce diversity.

Our ESG Approach

Jazz is committed to creating a company where the culture reflects three important goals—our purpose to serve patients, be a great place to work, and to live our core values of integrity, collaboration, passion, innovation, and pursuit of excellence. Our values, underpinned by good corporate governance, social responsibility and environmental stewardship anchor our corporate strategy and make up key elements of our vision to deliver on our commitment to generate long-term sustainable value for patients, employees, shareholders, and other stakeholders.

The pillars of our ESG strategy are Patients, People, Community and Planet. Jazz recognizes the critical importance of these ESG pillars in achieving our near and long-term business objectives including Vision 2025.

In 2022, as a key step in the development of our ESG strategy, we conducted a materiality assessment to identify and prioritize the most impactful ESG topics for our business and our stakeholders[1]. Jazz surveyed and solicited feedback from a selection of internal and external stakeholders, from global senior leaders and employees to shareholders, suppliers and patient groups. Jazz will use the assessment results to inform strategic decision-making, guide our ESG reporting, and further embed ESG considerations into our corporate strategy and company culture. Additionally, we believe this process will enhance our ability to engage stakeholders in meaningful ways.

As we build on the outcomes of this assessment and make progress on the development of our ESG multi-year strategy, further information on our ESG priorities will be shared in our future reporting activities.

ESG Board Oversight and Management

The board as a whole oversees the strategy for addressing ESG risks and opportunities that impact our business. Each committee of the board oversees ESG matters across our business operations in the areas that align with their respective responsibilities. The nominating and corporate governance committee has delegated oversight responsibilities for ESG strategy and works with senior management on implementing, reviewing, and providing guidance to the board where ESG matters are expected to have a significant impact on our performance, business activities or reputation. The compensation committee works with the full board to oversee human capital management matters, including Diversity, Equity, Inclusion and Belonging (DEIB), a core aspect of our ESG approach. The audit committee has primary responsibilities for overseeing risks related to information security, including cybersecurity. See the section entitled *"Corporate Governance and Board Matters"* on page 26 for a further discussion of our board and board committees.

Our Executive Vice President and Chief Legal Officer has executive oversight for ESG strategic planning, risk management, and reporting. A cross-functional team of senior leaders and subject matter experts supports ESG efforts across the organization. Senior management regularly briefs the board and its committees on ESG progress.

ESG Reporting

In 2022, we published our inaugural ESG Report reflecting our efforts through 2021. The Report was prepared with reference to the GRI Standards and aligns with the Sustainability Accounting Standards Board (SASB) Agricultural Products and Biotechnology & Pharmaceuticals Reporting Standards that apply to our business, to the extent indicated herein. In developing the Report, we also referenced insights from our materiality assessment and considered guidance, standards and relevant topics from external ESG and sustainability stakeholders. We intend to continuously evolve our ESG reporting and disclosure to better meet the expectations of our stakeholders.

[1] The ESG topics determined to be most impactful for purposes of the materiality assessment mentioned above, with reference to the Global Reporting Initiative (GRI) Standards and the Sustainability Accounting Standards Board (SASB) Agricultural Products and Biotechnology & Pharmaceuticals Reporting Standards, are not necessarily material for U.S. federal securities law reporting or other purposes.

ESG Highlights

Patients

We are innovating to develop life-changing medicines for patients who often have limited or no therapeutic options. We strive to help patients get access to the medications they need, and we advocate for policies that support the lives of patients.

- Patient safety is among our top concerns. We have implemented systems and processes designed to help us meet our legal and regulatory obligations related to product safety including to track and report adverse events/experiences, and product complaints. We continue to enhance our activities to meet the expectations of patients and other stakeholders
- For over two decades our commitment to public health and patient safety has included implementing a restricted distribution system for our oxybate products, which since 2007 has been known as a Risk Evaluation and Mitigation Strategy (REMS) in the U.S. We engage and work closely with stakeholders including regulatory authorities and physicians, with the goal of meeting the expectations of the evolving environment.
- Quality in our products and services is essential. We maintain quality and regulatory compliance systems that are designed to help us meet both internal and external standards. Each of us is responsible for the quality of our work and for implementing the appropriate quality standards.
- Continually working to expand patient access to medicines, including through our patient assistance programs, product donations to global aid organizations and monetary contributions to independent charities. We have been able to provide greater support and access to our medicines in markets around the world.
- We strive to help patients get access to the medications they need. Our JazzCares™ patient assistance programs offer Xywav, Xyrem, Epidiolex, Rylaze, Zepzelca, Defitelio and Vyxeos to eligible patients who otherwise cannot afford the medications. Our JazzCares programs are designed to give patients the support and assistance they need throughout their treatment journey.
- Enhancing our internal capabilities within the organization related to patient engagement and advocacy. We created a new advocacy role for R&D that was filled with a candidate with nearly 20 years of global experience in the biopharmaceutical industry building advocacy and engagement functions. We have focused strategies on incorporating patient and caregiver perspectives on needs into our review of trial protocols and target product profiles.
- Building significant awareness programs to educate and inform patient communities on important information relevant to treatment of conditions. This includes collaboration with various patient groups including the American Heart Association and sleep patient groups to educate and inform on the relationship between sleep disorders and cardiovascular comorbidities.
- In partnership with the Child Neurology Foundation, Jazz is supporting the establishment of a program in several Epilepsy Centers of Excellence to enhance genetic testing and reduce the time to diagnosis for rare epilepsies. In addition, we partner with several organizations to develop and deliver disease and CBD education.
- In partnership with Stand Up to Cancer (SU2C), we have development initiatives to raise awareness of the need for earlier diagnosis and screening of small cell lung cancer in communities of color. Utilizing digital ethnography research we are seeking to understand the path to treatment for Black and Hispanic patients and caregivers with SCLC and leveraging the insights to increase awareness of, and screenings for, SCLC among this population.

People

We are committed to creating a company where the culture embodies our corporate purpose to innovate to transform the lives of patients and their families 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.

- We conduct recurring employee pulse surveys to gather employee feedback on what they value about the workplace experience. We consistently achieve participation rates above 75% and over 80% of

employees would recommend Jazz as a good place to work based on our most recently completely pulse survey in February 2023. Survey results provide valuable insights into where to focus, prioritize, and create a greater sense of belonging while informing initiatives aligned with our corporate objectives.

- We continue to develop our flexible working model "Jazz Remix" which aims to provide eligible employees work location flexibility (including remote work capabilities). This dynamic and agile approach to working arrangements is designed to further our ability to connect globally, collaborate, innovate and perform.
- We believe that fostering an employee community that fosters diversity and inclusion leads to innovation. Our employee resource teams, Jazz ConcERTos, are self-led teams of employee volunteers with diverse backgrounds that deliver global events to educate the organization on important issues, celebrate important dates on our cultural calendar, and act as employee listening hubs sharing feedback with decision makers on inclusive work practices. In addition, we have five active affinity forums at Jazz which provide a space for employees from various traditionally underrepresented groups and their allies to build community. The five forums include, ¡HOLA Jazz! (Hispanic Organization for Leadership Advancement), JazzSoul, JAWS (Jazz Associate of Women Supporters), Jazz Pride, and Pan-Asian. As of the end of the first quarter of 2023, 27% of our global workforce were active in employee resource teams.
- We have established goals related to increasing the diversity of the representation of women and people of color in our workforce, 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:
    - 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 global leadership level (employees at executive director and above).
    - People of color represent 33% of our U.S. workforce and 19% at the U.S. leadership level.
- Our Global Talent Acquisition Sourcing Strategy seeks to attract, select, and secure diverse talent for our organization through building connections, attending diversity events, providing training workshops, posting to diverse job boards and partnering with local community channels.
- Jazz encourages employees to complete development plans with their managers that outline growth interests and focus areas. Plans include customized, continuous learning opportunities that align with their career ambitions. Development and succession plans are regularly reviewed to successfully maintain business operations. We continue to evolve performance management, striving for a more meaningful and inclusive experience for all employees.
- We invest in our talent pipeline by providing leadership development experiences (including and not limited to training) appropriate to management level and professional experience for many levels. In 2022, over 600 functional and people leaders participated in three quarterly targeted leadership development activities supporting transformation and integration. We continue 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.
- 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.
- Jazz offers full company participation in our long-term incentive plan providing employees with an ownership stake.
- Our manufacturing operations have Health and Safety Systems that are designed to fully comply with the requirements of the European Union Framework Directive for Health and Safety and that are designed to meet the requirements of section 6.4.6 of ISO 26000 (Labour Practices – Health and Safety at Work).

Community

We aim to be an engaged corporate citizen globally and in our communities. We work through direct philanthropy, employee volunteerism and with partners to execute key initiatives that reflect our social impact goals and values.

In 2022 Jazz provided charitable support to over 70 organizations globally related to improving patient access and care, addressing healthcare and wellbeing of our communities, disaster relief and humanitarian crises as well as helping to enhance diversity in our industry.

- Jazz provided financial donations to Direct Relief in support of Hurricane disasters in Florida and Puerto Rico in addition to earthquake relief in Turkey and Syria.
- Jazz encourages global volunteer day which provides employees time off with full pay to give back to their communities. In recognition of International Volunteers' Day, several of our UK colleagues spent a day working with FareShare, the UK's national network of charitable food redistributors. German colleagues used volunteer day to support facilities for patients with Down syndrome and helped to remove old furniture from local nurseries.
- In Italy, Jazz partnered with the Rise Against Hunger association to develop a charity initiative to benefit families and children in Zimbabwe, and organized a day dedicated to packing and assembling thousands of food rations for Schooling Programs in developing countries.
- Our actions to support health equity include a commitment to improving the diversity within STEM fields and among healthcare professionals. Jazz also developed a novel program in partnership with Momentum and Value for People of Color whereby members of our R&D organization mentored students interested in the healthcare field and hosted a group of summer interns.
- Jazz is actively involved in fostering diversity within the legal profession through our participation in various groups including the Leadership Council of Legal Diversity. Since 2020, the company has hosted multiple diverse interns within the legal department. Attorneys within the legal department provide pro-bono legal services through a variety of programs including providing assistance to seniors in preparation of life planning documents and assisting individuals in the renewal of their Deferred Action for Childhood Arrivals (DACA) applications.

Planet

We seek to operate our business in an environmentally responsible way and are committed to meeting evolving regulatory standards for climate impact, to take steps to reduce our environmental impact and to using sustainable practices wherever feasible.

- In 2022, we published our first set of environmental performance data reflecting calendar year 2021 including energy consumption and information on energy management and water management.
- Jazz maintains an environmental management system (EMS) and policies across our manufacturing and development operations to comply with applicable laws, directives, and regulations on environmental protection and sustainability. In addition to the harmonized EMS, Jazz continues to identify opportunities to reduce our environmental footprint in relation to greenhouse gas emissions, energy consumption, water use, and waste generation and disposal.
- The manufacturing and development site Villa Guardia, Italy maintains ISO 14001:2015 and EU Eco-Management and Audit Scheme certification which sets the standard for an EMS and supports Jazz in its efforts to improve our environmental performance through more efficient use of resources and reduction of waste.
- Both our Athlone, Ireland and Villa Guardia, Italy manufacturing and development sites purchase and consume renewable electricity.
- Our Athlone, Ireland, Kent Science Park, U.K., and Villa Guardia, Italy manufacturing sites have implemented energy efficiency and conservation measures including LED light conversions, energy efficient chiller replacements, as well as installations electric vehicle charging stations.

Summary of Shareholder Voting Matters and Board Recommendations

For the reasons set forth below and in the rest of this proxy statement, our board of directors recommends that you vote your shares "FOR" each of the nominees named below for director to hold office until the 2026 annual meeting of shareholders and "FOR" each of the other proposals.

Proposal 1 — Election of Directors

The board of directors recommends a vote "FOR" each of the named nominees.

Vote required to elect each nominee to hold office until the 2026 annual meeting of shareholders: Affirmative vote of a majority of the votes cast on his or her election.

For more information, see Proposal 1 starting on page 17.

We are asking our shareholders to vote, by separate resolutions, on the election of each of Bruce C. Cozadd, Heather Ann McSharry, Anne O'Riordan and Rick E Winningham to hold office until the 2026 annual meeting of shareholders. Detailed information about each nominee's background and experience can be found beginning on page 17.

Each of the nominees for director was nominated for election by the board of directors upon the recommendation of our nominating and corporate governance committee. Our board of directors believes that each nominee has the specific experience, qualifications, attributes and skills to serve as a member of the board of directors and has demonstrated the ability to devote sufficient time and attention to board duties and to otherwise fulfill the responsibilities required of directors. See *"Corporate Governance and Board Matters—Director Commitments"* beginning on page 30 for more information.

Proposal 2 — Ratify, on a Non-Binding Advisory Basis, the Appointment of Independent Auditors and Authorize, in a Binding Vote, the Board of Directors, Acting Through the Audit Committee, to Determine the Independent Auditors' Remuneration

The board of directors recommends a vote "FOR" this proposal.

Vote required for approval: Affirmative vote of a majority of the votes cast on the proposal.

For more information, see Proposal 2 starting on page 96.

Under Irish law, KPMG will be deemed to be reappointed as our independent auditors for the financial year ending December 31, 2023, without needing a shareholder vote at the annual meeting. However, our shareholders are being asked to ratify KPMG's appointment on a non-binding advisory basis because we value our shareholders' views on the company's independent auditors. The board of directors and the audit committee intend to consider the results of this vote in making determinations in the future regarding the appointment of the company's independent auditors.

Our shareholders are also being asked to authorize the board of directors, acting through the audit committee, to determine KPMG's remuneration. This authorization is required by Irish law.

Less than 1% of the total fees that KPMG billed us for services last year were for services other than audit, audit-related and tax compliance services.

Proposal 3 — Non-Binding Advisory Vote on Executive Compensation

The board of directors recommends a vote "FOR" this proposal.

Vote required for approval: Affirmative vote of a majority of the votes cast on the proposal.

For more information, see Proposal 3 starting on page 98.

We are asking our shareholders for advisory approval of our NEOs' compensation. This non-binding advisory vote is commonly referred to as a "say-on-pay" vote. Our executive compensation program is aligned with our business strategy and priorities and encourages executive officers to work for meaningful shareholder returns consistent with our pay-for-performance philosophy. Our executive compensation program focuses on *target total direct compensation*, combining short-term and long-term components, cash and equity, and fixed and variable payments, in the proportions that we believe are the most appropriate to incentivize and reward our executive officers for achieving our corporate goals while minimizing incentives for excessive risk-taking or unethical conduct. Our annual performance bonus awards are not earned unless pre-determined levels of performance are achieved against annual corporate objectives approved by our board of directors at the beginning of the year. We also have executive share ownership guidelines to further support our ownership culture and align the interests of executive officers and shareholders. Further, in 2021 we implemented a new performance-based equity program tied to the achievement of critical multi-year financial and other strategic objectives as well as relative total shareholder return goals, with performance-based restricted stock unit awards making up approximately 50% of each NEO's target annual equity grant, and time-vested restricted stock unit awards making up the other approximately 50%. Our 2022 advisory say-on-pay proposal was approved by approximately 94% of total votes cast.

Proposal 4 — Board Authority to Issue Shares for Cash Without First Offering Shares to Existing Shareholders

The board of directors recommends a vote "FOR" this proposal.

Vote required for approval: Affirmative vote of 75% of the votes cast on the proposal.

For more information, see Proposal 4 starting on page 100.

We are asking our shareholders to renew the authority granted to the board of directors at the 2022 annual meeting of shareholders, or 2022 AGM , to opt out of the pre-emption rights provision in the event of an issuance of shares for cash up to the amount of 20% of our issued ordinary share capital in the aggregate, for a period expiring on the date being 18 months from the passing of the resolution set forth in Proposal 4, unless otherwise varied, renewed or revoked.

In general, unless otherwise authorized by shareholders, before an Irish public limited company can issue shares for cash (including rights to subscribe for, convert into or otherwise acquire any shares) to any new shareholders, it must first offer the shares or rights to existing shareholders of the company pro-rata to their existing shareholdings. Under Irish law, the authority to opt-out of this pre-emption right, which we call the pre-emption opt-out authority, can be granted by shareholders for a maximum period of five years, at which point it lapses unless renewed by shareholders.

Granting our board of directors the pre-emption opt-out authority on the terms set forth in Proposal 4 is vital to the way we intend to advance our business. In this regard, our strategy for sustainable growth is rooted in executing commercial launches and ongoing

commercialization initiatives; advancing robust research and development 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. 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. In this regard, strategic capital allocation will continue to be an important driver of our growth, including investing in our current pipeline and facilitating our ability to continue corporate development.

Our strategy for growth depends in part on our ability to quickly take advantage of strategic opportunities, including potential acquisitions and other capital-intensive transactions that we believe would increase shareholder value. Many of these opportunities are highly competitive, with multiple parties often offering comparable or even the same economics. If Proposal 4 is not approved, in each case where we propose to issue shares for cash consideration after January 28, 2024 and/or beyond the limits of our current pre-emption opt-out authority, we would first have to offer those shares on the same or more favorable terms to our existing shareholders pro-rata following a specific Irish statutory procedure and timeline in the absence of a new shareholder approval to dis-apply the pre-emption rights provision to the issuance of those shares. This could put us at a distinct disadvantage vis-à-vis many of our peers in competing for acquisitions and similar transactions (particularly since many of the companies with which we compete strategically are listed and incorporated in the U.S. and are not subject to similar pre-emption right restrictions), and might make it difficult for us to complete such transactions in a timely manner or at all, thus potentially limiting our ability to further our strategy for growth by deploying capital to meet strategic goals that are in the best interests of our shareholders. And importantly, Jazz remains, like all U.S.-incorporated companies listed on Nasdaq, subject to compliance with Nasdaq listing rules, including the Nasdaq shareholder approval requirements related to equity issuances.

We expect to next propose renewal of the Board's pre-emption opt-out authority at our 2024 AGM.

Proposal 5 — Adjournment Proposal

The board of directors recommends a vote "FOR" this proposal.

Vote required for approval: Affirmative vote of a majority of the votes cast on the proposal.

For more information, see Proposal 5 starting on page 102.

We are asking our shareholders to vote on a proposal to approve any motion to adjourn the annual meeting, or any adjournments thereof, to another time and place to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4.

Under Irish law, Proposal 4 is a special resolution, which requires no less than 75% of the votes of shareholders cast (in person or by proxy) at a general meeting to be voted "FOR" the proposal in order to be passed. Given the high vote threshold associated with Proposal 4, we are seeking your authority to adjourn the meeting to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4.

PROXY STATEMENT

FOR THE 2023 ANNUAL GENERAL MEETING OF SHAREHOLDERS TO BE HELD ON AUGUST 3, 2023

GENERAL

Purpose of this Proxy Statement and Other General Information

Our board of directors is soliciting proxies for use at our 2023 annual general meeting of shareholders, or the annual meeting. This proxy statement contains important information for you to consider when deciding how to vote on the matters brought before the annual meeting. Please read it carefully. The Notice of Internet Availability of Proxy Materials and our proxy materials, which include this proxy statement, our annual letter to shareholders and our 2022 Annual Report on Form 10-K, are first being mailed to shareholders on or about June 20, 2023. Our proxy materials are also available online at https://materials.proxyvote.com/G50871. The specific proposals to be considered and acted upon at the annual meeting are summarized in the accompanying Notice of 2023 Annual General Meeting of Shareholders. Each proposal is described in more detail in this proxy statement.

This solicitation is made on behalf of our board of directors and all solicitation expenses, including costs of preparing, assembling and mailing proxy materials and notices, will be borne by us. In addition to these proxy materials, our directors and employees may also solicit proxies in person, by telephone, or by other means of communication. Directors and employees will not be paid any additional compensation for soliciting proxies. We may also reimburse brokerage firms, banks and other agents for the cost of forwarding proxy materials to beneficial owners. In addition, we have retained Alliance Advisors, a proxy solicitation firm, to assist in the solicitation of proxies for a fee of approximately $28,000 plus reimbursement of expenses.

Our board of directors has set the close of business on June 7, 2023 as the record date for the annual meeting. Shareholders of record who owned our ordinary shares on that date are entitled to vote at and attend the annual meeting. Each ordinary share is entitled to one vote. There were 64,139,500 of our ordinary shares outstanding and entitled to vote on the record date.

PROPOSAL 1
ELECTION OF DIRECTORS

Our board of directors is divided into three classes, designated Class I, Class II and Class III. The term of the Class III directors will expire on the date of this annual meeting; the term of the Class I directors will expire on the date of the 2024 annual meeting of shareholders; and the term of the Class II directors will expire on the date of the 2025 annual meeting of shareholders. At each annual meeting of shareholders, successors to the directors whose term expires at that annual meeting are put forward for election for a three-year term.

The board of directors currently has 12 members and there are no vacancies. There are currently four directors in Class III, the class whose term of office expires at the annual meeting, all of whom are standing for election at the annual meeting: Bruce C. Cozadd, Heather Ann McSharry, Anne O'Riordan and Rick E Winningham. All four Class III director nominees were nominated for election by the board of directors upon the recommendation of our nominating and corporate governance committee. Each of Mr. Cozadd, Ms. McSharry, Ms. O'Riordan and Mr. Winningham were previously elected to our board of directors by our shareholders.

In order to be elected as a director at the annual meeting to hold office until the 2026 annual meeting of shareholders, each nominee must be appointed by an ordinary resolution, meaning each must individually receive the affirmative vote of a majority of the votes cast by the holders of ordinary shares represented in person or by proxy at the annual meeting (including any adjournment thereof). Under our articles, if, at any annual meeting of shareholders, the number of directors is reduced below the minimum prescribed by the board of directors pursuant to our articles due to the failure of any director nominee to receive the affirmative vote of a majority of the votes cast, then in those 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 such director would remain a director (subject to the provisions of the 2014 Act and our articles) only until the conclusion of the next annual meeting of shareholders unless he or she is re-elected at such time.

If any nominee becomes unavailable for election as a result of an unexpected occurrence, the proxy holders will vote your proxy for the election of any substitute nominee as may be proposed by the nominating and corporate governance committee. Each nominee has consented to being named as a nominee in this proxy statement and has agreed to serve if elected, and we have no reason to believe that any nominee will be unable to serve. If elected at the annual meeting by the affirmative vote of a majority of the votes cast on his election, each nominee would serve as a director until the 2026 annual meeting of shareholders and until his successor has been elected and qualified, or, if sooner, until his death, resignation, retirement, disqualification or removal. It is our policy to invite directors and nominees for director to attend annual meetings of shareholders. All twelve of our directors attended our 2022 annual meeting of shareholders.

Vacancies on the board of directors, including a vacancy that results from an increase in the authorized number of directors, may be filled only by the affirmative vote of a majority of the directors then in office, provided that a quorum is present at the relevant board meeting. A director elected by the board of directors to fill a vacancy in a class will serve for the remainder of the full term of that class and until the director's successor is elected and qualified, or, if sooner, until his or her death, resignation, retirement, disqualification or removal. Under our articles, if the number of directors is increased, directors are apportioned among the classes to maintain the number of directors in each class as nearly equal as possible, or as the Chairperson of our board may otherwise direct.

We believe our director nominees bring a variety of expertise, qualifications and skills. The table below summarizes some of the expertise, qualifications and skills of each individual director nominee. Further information on each director nominee, including some of their specific experience, qualifications or skills, is set forth in their biographies below.

Jazz Pharmaceuticals Board Skills and Experience Matrix

Director	Public Company Board Experience	C-Suite / Management Experience	Industry Expertise	Financial Experience	Merger and Acquisition / Corporate Development	Commercial Experience	Scientific Research and Drug Development Experience	International Perspective	Public Policy and Regulation	Human Capital
Jennifer E. Cook	●	●	●	●		●	●	●		●
Bruce C. Cozadd	●	●	●	●	●	●		●	●	●
Patrick G. Enright	●	●	●	●	●	●	●	●	●	●
Peter Gray	●	●	●	●	●		●	●		●
Heather Ann McSharry	●	●	●	●	●	●		●	●	●
Seamus Mulligan	●	●	●		●	●	●	●		
Kenneth W. O'Keefe	●	●	●	●	●				●	
Anne O'Riordan		●	●	●				●		●
Norbert G. Riedel, Ph.D.	●	●	●	●	●	●	●	●	●	●
Mark D. Smith, M.D.	●	●					●		●	●
Catherine A. Sohn, Pharm. D.	●	●	●	●	●	●	●	●	●	●
Rick E Winningham	●	●	●	●	●	●	●	●	●	●

● Indicates experience/expertise in subject matter.

Capabilities Description

Public Company Board Experience	Experience as a board member of a publicly-traded company
C-Suite/Management Experience	Experience as a C-suite officer or as a member of senior management of a large or growing business
Industry Expertise	Knowledge of the healthcare and biopharmaceutical industry, including, as applicable, science, manufacturing, regulatory compliance and payer dynamics
Financial Experience	Experience in positions requiring financial knowledge and analysis with expertise in the evaluation a large or growing company's capital structure
Merger & Acquisition/ Corporate Development	Experience or expertise in structuring financing and executing strategic acquisitions, partnerships, and other corporate development activities
Commercial Experience	Experience or expertise in cultivating a large or growing business's brand equity, the development and management of business relationships with customers and the process of reimbursement of pharma products
Scientific Research and Drug Development Experience	Relevant backgrounds in academia, clinical practice, science and technology and, in particular, the research and development of pharmaceutical products
International Perspective	Experience or expertise in the operation of complex multinational organizations
Public Policy and Regulation	Experience operating in a highly regulated industry, navigating governmental or public policy matters in related to medicines and healthcare products
Human Capital	Experience leading larger, diverse teams and human capital management initiatives generally, including leadership development, succession planning, executive recruitment, oversight of corporate culture, diversity and inclusion, and compensation

The following includes a brief biography of each nominee for director and each of our other directors whose terms of office will continue following the annual meeting, including their respective ages, as of June 1, 2023. Each biography includes information regarding the specific experience, qualifications, attributes or skills that led the nominating and corporate governance committee and the board of directors to determine that the applicable nominee or other current director should serve as a member of the board of directors. We evaluate diversity considerations as well as the experience and expertise of our board as a whole to ensure alignment between the abilities and contributions of our board and our strategic priorities and long-range plan, emphasizing, among other things, expertise in global and U.S. sales and marketing, in product development, in financial management and in corporate development transactions.

Director Nominees

Bruce C. Cozadd — Age: 59

DIRECTOR SINCE: 2003*

BOARD COMMITTEES:
None

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Commercial Experience
International Perspective
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
ACELYRIN, INC.

SPECIFIC EXPERTISE:

Mr. Cozadd's extensive leadership experience having served as co-founder and our Chief Executive Officer for over 10 years and having served previously as Chairperson and Chief Executive Officer of Jazz Pharmaceuticals, Inc, for 3 years, brings to our board of directors a deep and comprehensive knowledge of our business, as well as shareholder-focused insight into effectively executing the company's strategy and business plans to maximize shareholder value.

BACKGROUND:

Bruce C. Cozadd has served as our Chairperson and Chief Executive Officer since the closing of the Azur Merger in January 2012, and from October 2019 through March 2020, he served as our interim principal financial officer. Mr. Cozadd co-founded Jazz Pharmaceuticals, Inc. and has served as Chairperson and Chief Executive Officer of Jazz Pharmaceuticals, Inc. since April 2009. From 2003 until 2009, he served as Jazz Pharmaceuticals, Inc.'s Executive Chairperson and as a member of its board of directors. From 1991 until 2001, he held various positions with ALZA Corporation, a pharmaceutical company acquired by Johnson & Johnson, including as Executive Vice President and Chief Operating Officer, with responsibility for research and development, manufacturing and sales and marketing. Previously at ALZA Corporation, he held the roles of Chief Financial Officer and Vice President, Corporate Planning and Analysis. Since February 2022, Mr. Cozadd has served on the board of ACELYRIN, INC., a late-stage clinical biopharma company which became public in May 2023, and has served as Chairperson of ACELYRIN's board since February 2023. Mr. Cozadd also serves on the board of Biotechnology Innovation Organization, a biotechnology trade association, where he serves on its Health Section Governing Board. He also serves on the boards of two non-profit organizations, The Nueva School and SFJAZZ. He received a B.S. from Yale University and an M.B.A. from the Stanford Graduate School of Business.

* Includes service on the board of directors of Jazz Pharmaceuticals, Inc., our predecessor.

Proposal 1 (continued)

Heather Ann McSharry — Age: 61

DIRECTOR SINCE: 2013
INDEPENDENT

NOMINATING & CORPORATE GOVERNANCE COMMITTEE (Chair)

AUDIT COMMITTEE (Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Commercial Experience
International Perspective
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
International Airlines Group, S.A

SPECIFIC EXPERTISE:

Ms. McSharry brings to our board of directors over 30 years of experience in multiple international industries, including healthcare, consumer goods and financial services, as well as expertise in crisis management, risk oversight and financial services relevant to our business.

BACKGROUND:

Heather Ann McSharry has served as a member of our board of directors since May 2013 and was appointed as chair of our nominating and corporate governance committee in August 2017. Ms. McSharry has served as a non-executive director on the board of directors of International Airlines Group, S.A since 2020 and as Senior Independent Director of International Airlines Group, S.A. since June 2022. From 2006 to 2009, Ms. McSharry was Managing Director Ireland of Reckitt Benckiser, a multinational health, home and hygiene consumer products company. From 1989 to 2006, she held various positions at Boots Healthcare, a leading global consumer healthcare company, most recently as Managing Director of Boots Healthcare Ireland Limited. Ms. McSharry served on the boards of directors of the Bank of Ireland from 2007 to 2011, the Industrial Development Agency in Ireland from 2010 to 2014, Uniphar plc from 2019 to 2020, CRH plc from 2012 to 2021 and Greencore Group plc from 2013 to 2021. Ms. McSharry holds a Bachelor of Commerce and a Master of Business Studies degree from University College Dublin.

Anne O'Riordan — Age: 55

DIRECTOR SINCE: 2019
INDEPENDENT

NOMINATING & CORPORATE GOVERNANCE COMMITTEE (Member)

AUDIT COMMITTEE (Member)

KEY SKILLS:
C-Suite/Management Experience
Industry Expertise
Financial Experience
International Perspective
Human Capital

OTHER CURRENT PUBLIC BOARDS:
None

SPECIFIC EXPERTISE:

Ms. O'Riordan brings to our board of directors 30 years of knowledge and leadership experience advising life sciences and healthcare companies across the globe, with a uniquely diverse perspective attributable to her geographic residency in Asia. Ms. O'Riordan is a leader in digital and innovation strategy. Ms. O'Riordan's background in advising life sciences companies with respect to significant global markets provides an important contribution to our board of director's mix of backgrounds, experiences and skills.

BACKGROUND:

Anne O'Riordan has served as a member of our board of directors since February 2019. Since June 2019, Ms. O'Riordan has served as a Group Director of Digital at Jardine Matheson Limited, a multinational conglomerate, headquartered in Hong Kong, focused on multiple industry segments throughout North and South East Asia. Ms. O'Riordan is a member of the board of directors of Jardine Matheson Limited (JML). From 1990 to March 2019, Ms. O'Riordan worked with Accenture (formerly Andersen Consulting) in their Life Sciences practice, where she held various leadership positions in North America (1992-1998), Europe (1998-2007) and Asia Pacific (2007-2014). From 2014-2019, she served as the Global Industry Senior Managing Director for Life Sciences responsible for the growth and management of the business across all geographies. In addition, Ms. O'Riordan currently serves on the board of governors of the American Chamber of Commerce in Hong Kong where she serves as the board liaison for the Healthcare Committee and is on the board of the International Women's Forum Hong Kong where she serves as the Treasurer. She is also a long-standing member of the Women's Foundation and the 30% Club. Ms. O'Riordan received a B.Sc in Biotechnology from Dublin City University as well as a postgraduate diploma in Financial Accounting and MIS from the University of Galway.

Rick E Winningham — **Age:** 63

DIRECTOR SINCE: 2010*
INDEPENDENT

NOMINATING & CORPORATE GOVERNANCE COMMITTEE
(Member)

SCIENCE & MEDICINE COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Commercial Experience
Scientific Research and Drug Development Experience
International Perspective
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
Theravance Biopharma, Inc.

SPECIFIC EXPERTISE:

Mr. Winningham's experience in senior management positions in the pharmaceutical industry provides significant industry knowledge and operational and management expertise to our board of directors, along with a deep knowledge of global marketing, commercialization and market access.

BACKGROUND:

Rick E Winningham has served as a member of our board of directors since the closing of the Azur Merger in January 2012 and was a director of Jazz Pharmaceuticals, Inc. from 2010 until the closing of the Azur Merger. In May 2014, Mr. Winningham was appointed as Lead Independent Director of our board of directors. Mr. Winningham has served as Chairperson of the board of directors of Theravance Biopharma, Inc., a biopharmaceutical company, since July 2013. He has served as Chief Executive Officer of Theravance Biopharma, Inc. since its spin-off from Theravance, Inc. (now Innoviva, Inc.) in June 2014. From October 2001 to August 2014, Mr. Winningham served as Chief Executive Officer of Theravance, Inc., where he also served as Chairperson of the board of directors from April 2010 to October 2014. From 1997 to 2001, he served as President of Bristol-Myers Squibb Oncology/Immunology/Oncology Therapeutics Network and, from 2000 to 2001, as President of Global Marketing. Mr. Winningham is a member of Biotechnology Industry Organization's board of directors and serves on the Health Section Governing Board Standing Committee on Reimbursement. He previously served as a member of the board of directors of Retrotope, Inc., a private biotechnology company focused on cell degeneration, from February 2021 to January 2022 and OncoMed Pharmaceuticals, Inc. from June 2015 until the company's merger with Mereo BioPharma Group plc in April 2019. He also served as a member of the board of directors of the California Healthcare Institute, or CHI, from November 2011 to March 2015 and served as its Chairperson from January 2014 until CHI merged with Bay Area Bioscience Association to become the California Life Sciences Association, or CLSA, in March 2015. Mr. Winningham is on the board of directors of CLSA, and served as its Chairperson from March 2015 until November 2015. Mr. Winningham holds an M.B.A. from Texas Christian University and a B.S. from Southern Illinois University.

The board of directors recommends a vote "FOR" each nominee named above

* Includes service on the board of directors of Jazz Pharmaceuticals, Inc., our predecessor.

Proposal 1 (continued)

Class I Directors Continuing in Office Until the 2024 Annual General Meeting

Peter Gray — Age: 68

DIRECTOR SINCE: 2013
INDEPENDENT

AUDIT COMMITTEE
(Chair)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Scientific Research and Drug Development Experience
International Perspective
Human Capital

OTHER CURRENT PUBLIC BOARDS:
None

SPECIFIC EXPERTISE:

Mr. Gray brings to our board of directors and audit committee over 30 years of experience in financial and operational management within the pharmaceutical industry, with extensive experience in the development of pharmaceutical products and operational execution.

BACKGROUND:

Peter Gray has served as a member of our board of directors since May 2013 and was appointed as chair of our audit committee in April 2014. He is Chairperson of a privately-held company providing outsourced technology services to the biopharma industry, a director of a privately-held large molecule development company, and chairs a non-profit educational establishment. He served as Chairperson of the board of directors of UDG Healthcare plc, an international provider of healthcare services, from February 2012 to September 2020. In September 2011, Mr. Gray retired from his position as Chief Executive Officer of ICON plc, a global provider of outsourced development services to the pharmaceutical, biotechnology and medical device industries, which he held since November 2002. At ICON plc, Mr. Gray previously served as Group Chief Operating Officer from June 2001 to November 2002 and Chief Financial Officer from June 1997 to June 2001. From November 1983 to November 1989, Mr. Gray served as senior financial officer at Elan Corporation plc, a pharmaceutical company. Mr. Gray holds a degree in law from Trinity College Dublin and qualified as a chartered accountant in 1981.

Kenneth W. O'Keefe — Age: 56

DIRECTOR SINCE: 2004*
INDEPENDENT

AUDIT COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Public Policy and Regulation

OTHER CURRENT PUBLIC BOARDS:
None

SPECIFIC EXPERTISE:

As Founder and Advisor to BPOC, LLC, Mr. O'Keefe brings to our board of directors significant expertise in accounting and financial matters and in analyzing and evaluating financial statements, as well as substantial experience managing high growth investments. As the former chairperson and current member of our audit committee, Mr. O'Keefe brings to our board of directors detailed knowledge of our financial position and finance strategy.

BACKGROUND:

Kenneth W. O'Keefe has served as a member of our board of directors since the closing of the Azur Merger in January 2012 and was a director of Jazz Pharmaceuticals, Inc. from 2004 until the closing of the Azur Merger. He served as Managing Director from January 1996 to January 2010 and Chief Executive Officer from January 2010 to January 2018 of BPOC, LLC, a healthcare private equity firm he co-founded. Since January 2018 he has served as Founder of and Advisor to BPOC, LLC. He serves on the boards of several privately-held healthcare companies. He received a B.A. from Northwestern University and an M.B.A. from the University of Chicago.

* Includes service on the board of directors of Jazz Pharmaceuticals, Inc., our predecessor.

Mark D. Smith , M.D. — Age: 71

DIRECTOR SINCE: 2020
INDEPENDENT

NOMINATING & CORPORATE GOVERNANCE COMMITTEE
(Member)

SCIENCE AND MEDICINE COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Scientific Research and Drug Development Experience
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
Phreesia, Inc.
Teladoc Health, Inc

SPECIFIC EXPERTISE:

Dr. Smith brings to our board of directors an impressive background that marries the worlds of active medical practice and business development. A practicing physician and professor, Dr. Smith also has experience working for a variety of health focused companies both public and private. Dr. Smith has a deep understanding of the trends in public policy and future trends in healthcare delivery systems in the United States. Additionally, Dr. Smith allocates part of his time for nonprofit organizations and a health policy foundation.

BACKGROUND:

Mark D. Smith, M.D. has served as a member of our board of directors since December 2020. Dr. Smith is a practicing physician and professor of clinical medicine at the University of California at San Francisco, where he has served since 1994. He also serves as a non-executive director on the boards of directors of two other publicly-held companies, Teladoc Health, Inc., a telemedicine and virtual healthcare company, and Phreesia, Inc., a healthcare software company. Dr. Smith also serves on the board of directors of the Commonwealth Fund, a private health policy foundation. From 1996 to 2013, Dr. Smith was the founding President and Chief Executive Officer of the California HealthCare Foundation, an independent nonprofit philanthropy organization. From 1991 to 1996, he served as Executive Vice President at the Henry J. Kaiser Family Foundation. Dr. Smith received a B.A. from Harvard College, an M.D. from the University of North Carolina at Chapel Hill and an M.B.A. from The Wharton School at the University of Pennsylvania.

Catherine A. Sohn, Pharm.D. — Age: 70

DIRECTOR SINCE: 2012
INDEPENDENT

COMPENSATION COMMITTEE
(Member)

SCIENCE & MEDICINE COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Commercial Experience
Scientific Research and Drug Development Experience
International Perspective
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
Axcella Health Inc.
Altimmune, Inc.

SPECIFIC EXPERTISE:

Dr. Sohn brings to our board of directors three decades of product development, strategy, commercial launch and business development transaction experience in the pharmaceutical industry and a global perspective that is directly relevant to our company.

BACKGROUND:

Catherine A. Sohn, Pharm.D. has served as a member of our board of directors since July 2012. Dr. Sohn also serves as a non-executive director on the boards of directors of two other public biotechnology companies: Axcella Health Inc and Altimmune, Inc. Dr. Sohn previously served as an independent director on the board of directors of the publicly traded life sciences company: Rubius Therapeutics, Inc. from January 2018 to February 2023, and Lifecore Biomedical (previously known as Landec Corporation) from November 2012 to November 2022. She also serves as Chairperson of the board of BioEclipse Therapeutics, Inc., a privately-held clinical-stage biopharmaceutical company. Dr. Sohn currently holds the position of Adjunct Professor at the University of California, San Francisco. From 1998 to 2010, she was Senior Vice President, Worldwide Business Development and Strategic Alliances at GlaxoSmithKline Consumer Healthcare responsible for leading numerous US, regional and global partnering deals, and acquisitions. From 1994 to 1998, she was Vice President, Worldwide Strategic Product Development at SmithKline Beecham Pharmaceuticals plc in the pharmaceutical division. From 1982 to 1994, she held a series of positions in Medical Affairs, Pharmaceutical Business Development and U.S. Product Marketing, including leading the creation of and commercial launch of the US Vaccine business and subsequently the commercialization of the company's neuroscience product. Dr. Sohn was named the Distinguished Alum of the Year by the University of California, San Francisco (2000), was recognized as The Woman of the Year by the Healthcare Businesswomen's Association (2003), received the Frank Barnes Mentoring Award from the Licensing Executive Society (2009) and was recognized as one of the PharmaVoice100 (2016). Dr. Sohn received a Pharm.D. from UCSF, a Corporate Directors Certificate from Harvard Business School, a Certificate of Professional Development from Wharton, a Certificate from Berkeley Law for ESG: Navigating the Board's Role and is a Certified Licensing Professional Emeritus.

Proposal 1 (continued)

Class II Directors Continuing in Office Until the 2025 Annual General Meeting

Jennifer E. Cook — Age: 57

DIRECTOR SINCE: 2020
INDEPENDENT

COMPENSATION COMMITTEE
(Chair)

SCIENCE & MEDICINE COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Commercial Experience
Scientific Research and Drug Development Experience
International Perspective
Human Capital

OTHER CURRENT PUBLIC BOARDS:
BridgeBio Pharma, Inc.
Denali Therapeutics, Inc.

SPECIFIC EXPERTISE:

Ms. Cook brings to our board of directors over 30 years of biopharmaceutical experience with significant C-suite, global product development and commercialization expertise, with a focus on transformative growth.

BACKGROUND:

Jennifer E. Cook has served as a member of our board of directors since December 2020 and was appointed chair of our compensation committee in April 2022. Ms. Cook serves as a non-executive director on the boards of directors of two other publicly-held companies, Denali Therapeutics Inc. and BridgeBio Pharma, Inc., both biotechnology companies. Ms. Cook founded Jennifer Cook Consulting, a consulting company, and has served as Principal since July 2019. From January 2018 to June 2019, Ms. Cook was the Chief Executive Officer at GRAIL, Inc., a privately-held early cancer detection diagnostic company. Prior to that, Ms. Cook worked at Roche Pharmaceuticals/ Genentech for 25 years, where she held a number of senior management positions covering the full lifecycle of product development and commercialization. From 2010 to 2013, she oversaw Genentech's U.S. Immunology and Ophthalmology Business Unit, and from 2013 to 2016, she led Roche's European commercial business. She also served as Roche's Global Head of Clinical Operations throughout 2017. In 2016, Ms. Cook was recognized as Woman of the Year by the Healthcare Businesswoman's Association. Ms. Cook received a B.A. in Human Biology and a M.S. in Biology from Stanford University and an M.B.A. from the Haas School of Business at University of California, Berkeley.

Patrick G. Enright — Age: 61

DIRECTOR SINCE: 2009*
INDEPENDENT

AUDIT COMMITTEE
(Member)

COMPENSATION COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Commercial Experience
Scientific Research and Drug Development Experience
International Perspective
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
Vera Therapeutics, Inc.

SPECIFIC EXPERTISE:

Based on his experience serving on the boards of several clinical-stage biotechnology companies and his investment experience in the life sciences industry, Mr. Enright brings to our board of directors operating experience and financial expertise in the life sciences industry.

BACKGROUND:

Patrick G. Enright has served as a member of our board of directors since the closing of the Azur Merger in January 2012 and was a director of Jazz Pharmaceuticals, Inc. from 2009 until the closing of the Azur Merger. Mr. Enright co-founded Longitude Capital, a healthcare venture capital firm, where he has served as a Managing Director since 2006. Mr. Enright currently serves on the board of directors of Vera Therapeutics, Inc. and privately held healthcare companies as well as the National Venture Capital Association. Previously, Mr. Enright was a Managing Director of Pequot Ventures where he co-led the life sciences investment practice. Mr. Enright also has significant life sciences operations experience including holding senior executive positions at Valentis, Boehringer Mannheim (acquired by Roche) and Sandoz (now known as Novartis). Mr. Enright previously served on the boards of directors of over twenty companies, including Aptinyx Inc. from 2016 to 2022, Aimmune Therapeutics, Inc. from 2013 until its acquisition by Nestlé in 2020 and Vaxcyte, Inc. from 2015 to 2020. Mr. Enright received a B.S. in Biological Sciences from Stanford University and an M.B.A. from the Wharton School of the University of Pennsylvania.

* Includes service on the board of directors of Jazz Pharmaceuticals, Inc., our predecessor.

Seamus Mulligan — Age: 62

DIRECTOR SINCE: 2012
INDEPENDENT

SCIENCE & MEDICINE COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Merger and Acquisition/Corporate Development
Commercial Experience
Scientific Research and Drug Development Experience
International Perspective

OTHER CURRENT PUBLIC BOARDS:
None

SPECIFIC EXPERTISE:

As a founder of Adapt Pharma and Azur Pharma, and a pharmaceutical industry executive, Mr. Mulligan brings to our board of directors an expertise in business development and over 35 years of experience in the pharmaceutical industry.

BACKGROUND:

Seamus Mulligan has served as a member of our board of directors since the closing of the Azur Merger in January 2012. Mr. Mulligan was a founder and principal investor of Azur Pharma and was Azur Pharma's Chairperson and Chief Executive Officer as well as being a member of its board of directors from 2005 until January 2012. Mr. Mulligan also served as our Chief Business Officer, International Business Development from January 2012 until February 2013. Between 2014 and 2018, Mr. Mulligan served as Chairperson and Chief Executive Officer of Adapt Pharma Limited or Adapt Pharma, a specialty pharmaceutical company, which was acquired in October 2018 by Emergent BioSolutions Inc., a multinational specialty biopharmaceutical company. Mr. Mulligan acted as a Consultant to Emergent BioSolutions Inc. from October 2018 to March 2019, when he was appointed to its board of directors on which he served until his resignation from the board in May 2020. From 2006 to 2017, Mr. Mulligan served as Executive Chairperson of Circ Pharma Limited and its subsidiaries, a pharmaceutical development stage group. From 1984 until 2004, Mr. Mulligan held various positions with Elan Corporation, plc, a pharmaceutical company, most recently as Executive Vice President, Business and Corporate Development, and prior to that position, held the roles of President of Elan Pharmaceutical Technologies, the drug delivery division of Elan Corporation, plc, Executive Vice President, Pharmaceutical Operations, Vice President, U.S. Operations and Vice President, Product Development. Mr. Mulligan served as a member of the board of directors of the U.S. National Pharmaceutical Council until 2004. Mr. Mulligan holds a B.Sc. (Pharm) and M.Sc. from Trinity College Dublin.

Norbert G. Riedel, Ph.D. — Age: 65

DIRECTOR SINCE: 2013
INDEPENDENT

SCIENCE & MEDICINE COMMITTEE
(Chair)

COMPENSATION COMMITTEE
(Member)

KEY SKILLS:
Public Company Board Experience
C-Suite/Management Experience
Industry Expertise
Financial Experience
Merger and Acquisition/Corporate Development
Commercial Experience
Scientific Research and Drug Development Experience
International Perspective
Public Policy and Regulation
Human Capital

OTHER CURRENT PUBLIC BOARDS:
Cerevel Therapeutics Holdings, Inc.
Eton Pharmaceuticals, Inc.

SPECIFIC EXPERTISE:

Dr. Riedel brings over 20 years of experience in the biotechnology and pharmaceutical industries to our board of directors with significant scientific, drug discovery and development, and commercial expertise. Dr. Riedel also leverages this pharmaceutical research experience in his position as Chair of the science and medicine committee.

BACKGROUND:

Norbert G. Riedel, Ph.D. has served as a member of our board of directors since May 2013 and was appointed chair of our science and medicine committee in April 2022. Dr. Riedel currently serves on the boards of directors of two other publicly-held companies, Eton Pharmaceuticals, Inc., a development stage pharmaceutical company, where he serves as Chairperson of the board, and Cerevel Therapeutics Holdings, Inc., a biopharmaceutical company, where he serves as Lead Independent Director. Dr. Riedel also currently serves on the board of directors of a non-profit organization, the Illinois Biotechnology Industry Organization, and is a member of the Austrian Academy of Sciences. Dr. Riedel is an Adjunct Professor at Boston University School of Medicine and an Adjunct Professor of Medicine at Northwestern University's Feinberg School of Medicine. Dr. Riedel served as Executive Chairperson of Aptinyx Inc. from January 2022 to May 2023, as Chief Executive Officer from September 2015 to December 2021 and as President from September 2015 to December 2020. Aptinyx Inc. is a biopharmaceutical company spun out of its predecessor company, Naurex, Inc., where Dr. Riedel served as Chief Executive Officer and President from January 2014 to September 2015. From 2001 to 2013, he served as Corporate Vice President and Chief Scientific Officer of Baxter International Inc., a diversified healthcare company, where from 1998 to 2001, he also served as President and General Manager of the recombinant therapeutic proteins business unit and Vice President of Research and Development of the bioscience business unit. From 1996 to 1998, Dr. Riedel served as head of worldwide biotechnology and worldwide core research functions at Hoechst-Marion Roussel, now Sanofi, a global pharmaceutical company. Dr. Riedel served on the board of directors of Ariad Pharmaceuticals, Inc., an oncology company, from May 2011 until the company was acquired in February 2017. Dr. Riedel holds a Diploma in biochemistry and a Ph.D. in biochemistry from the University of Frankfurt.

CORPORATE GOVERNANCE AND BOARD MATTERS

Overview

We are committed to exercising exemplary corporate governance practices. In furtherance of this commitment, we regularly monitor developments in the area of corporate governance and enhancing our processes, policies and procedures in light of such developments. Key information regarding our corporate governance initiatives can be found on our website, *www.jazzpharmaceuticals.com*, including our Corporate Governance Guidelines, Code of Conduct, and the charters for all of our committees including the audit, compensation and nominating and corporate governance committees. We believe that our strong corporate governance policies and practices, including the substantial percentage of independent directors on our board of directors and the robust duties of our Lead Independent Director, empower our independent directors to effectively oversee our management team—including the performance of our Chief Executive Officer—and provide an effective and appropriately balanced board governance structure. In addition, we believe that our directors are all actively and constructively engaged in the exercise of their duties and responsibilities, with each independent director serving on at least one board committee and engaging with management between board meetings to remain well-informed of our strategy and our business.

Independence of the Board of Directors

As required under the Nasdaq listing standards, a majority of the members of a listed company's board of directors must qualify as "independent," as affirmatively determined by the board of directors. Our board of directors consults with counsel to ensure that the board's determinations are consistent with relevant securities and other laws and regulations regarding the definition of "independent," including those set forth in the applicable Nasdaq listing standards, as in effect from time to time. Consistent with these considerations, after review of all relevant transactions or relationships between each director, or any of his or her family members, and our company, our senior management and our independent registered public accounting firm, the board of directors affirmatively determined that all of our current directors are independent directors within the meaning of the applicable Nasdaq listing standards, except that Mr. Cozadd, our Chairperson and Chief Executive Officer, is not independent by virtue of his employment with our company. In addition, our board of directors has determined that each member of the audit committee, compensation committee and nominating and corporate governance committee meets the applicable Nasdaq and SEC rules and regulations regarding "independence" and that each member is free of any relationship that would impair his or her individual exercise of independent judgment with regard to the company.

Board Leadership Structure

Mr. Cozadd has served as our Chairperson and Chief Executive Officer since the closing of the Azur Merger in January 2012. He co-founded Jazz Pharmaceuticals, Inc. in 2003 and served as its Chairperson and Chief Executive Officer since April 2009 and, prior to that, as Executive Chairperson.

The board of directors believes that the Chief Executive Officer is best suited to serve as our Chairperson because he is the member of the board of directors who is most familiar with our business as a whole, and the most capable of identifying and bringing to the attention of the full board of directors the strategic priorities and key issues facing the company. The board of directors also believes that having Mr. Cozadd in particular in a combined Chairperson/Chief Executive Officer role helps provide strong, unified leadership for our management team and optimizes communication with our board of directors. In addition, having previously served for many years as a director of other publicly-traded and privately-held companies, as well as in executive management roles, Mr. Cozadd brings both a strategic and operational perspective to this combined position.

In addition to our Chairperson, our Lead Independent Director plays an important role on the board. Our Corporate Governance Guidelines require the independent directors to elect a Lead Independent Director when the roles of Chairperson and Chief Executive Officer are held by the same person. Rick E Winningham currently serves as our Lead Independent Director.

The Lead Independent Director plays an essential and indispensable role on the board. A critical function of the Lead Independent Director is to help to reinforce the effective independent functioning of the board of directors.

Accordingly, specific roles and responsibilities of the Lead Independent Director, which are detailed in our Corporate Governance Guidelines, include:

- serving as the principal liaison between the independent directors and the Chairperson;
- coordinating the activities of the independent directors, including developing agendas for and presiding at executive sessions of the independent directors;
- advising the Chairperson on board and committee agendas, meeting schedules and information provided to other board members, including the quality, quantity and timeliness of such information that is necessary or appropriate for the directors to effectively and responsibly perform their duties;
- discussing the results of the Chief Executive Officer's performance evaluation with the chair of the compensation committee; and
- presiding at all meetings of the board of directors at which the Chairperson is not present.

The Lead Independent Director also has the authority to call meetings of the independent directors of the board of directors and is available for consultation and communication with significant shareholders. The Lead Independent Director also plays a central role in the board's annual self-evaluation process, including holding one-to-one meetings with each board member and briefing the board on the findings. See "*Corporate Governance and Board Matters—Nominating and Corporate Governance Committee*". In addition to fulfilling the basic requirements of his role as Lead Independent Director, Mr. Winningham attends meetings of committees where he is not a member to remain informed and engaged, communicates with the Chief Executive Officer on matters involving the company on a regular basis, regularly seeks input from other independent directors relating to significant developments at the company between regular board meetings, attends certain meetings at the company involving strategic portfolio and/or scientific reviews, and makes himself available for direct communication with significant shareholders as necessary.

Mr. Winningham is an expert in public company board experience with strong industry and business acumen. Mr. Winningham is an effective communicator and acts as a highly versatile intermediary between the Chairperson, the board and Jazz's stakeholders. Furthermore Mr. Winningham, with his unique insight and objectivity, carefully monitors the Board's performance and ensures regular independent executive discussion.

In addition, our board of directors is currently comprised of 12 directors, of whom 11 are independent. At meetings of our board of directors, the independent directors regularly convene executive sessions without the presence of our Chairperson and Chief Executive Officer and other members of management.

Risk Oversight

We believe that our board of directors provides effective oversight of risk management for our company (including financial, operational, business, intellectual property, information technology (including cybersecurity), public policy, reputational risk, governance and compliance), particularly as a result of the work of our committees and the ongoing dialogue between the full board, our Chairperson and Chief Executive Officer and our active and engaged Lead Independent Director.

At its meetings, our full board of directors receives reports concerning the management of the relevant risks from each committee, in addition to reports concerning material risks and concerns or significant updates on such matters from our Chief Legal Officer, Chief Compliance and Ethics Officer and other executive officers, as necessary.

Audit Committee

Our audit committee is responsible for overseeing our financial reporting process on behalf of our board of directors and reviewing with management and our auditors, as appropriate, our major financial risk exposures and the steps taken by management to monitor and control these exposures. Our board of directors has also formalized our audit committee's role in oversight of risks related to information security, including cybersecurity. In its oversight role, the audit committee receives quarterly updates on information security developments, cybersecurity incidents and the steps taken by management to monitor and mitigate risk exposures in these areas.

Compensation & Management Development Committee

Our compensation & management development committee, or compensation committee, approves compensation of executive officers and all material compensation plans for our company and reviews our compensation practices to ensure that they do not encourage excessive risk taking and provide appropriate incentives for meeting both short-term and long-term objectives and increasing shareholder value over time. Our compensation committee also works with our full board of directors to oversee matters related to diversity, talent, and culture strategy including human capital programs and policies regarding management development, talent planning, diversity and inclusion initiatives, and employee engagement, as well as human capital management, which includes reviewing workforce trends, executive succession plans and talent risk and maintaining compensation objectives and corporate policies that appropriately incentivize creating and maintaining a positive workplace and corporate culture.

Nominating and Governance Committee

Our nominating and corporate governance committee oversees the company's risk management other than those concerning the company's major financial, business or cybersecurity risk exposures or risks related to our compensation programs and policies, on behalf of our board of directors. Our nominating and corporate governance committee has oversight responsibility over our ESG program and strategy. The nominating and corporate governance committee has oversight responsibility related to administration of and certifies to, compliance with the company's corporate integrity agreement, or CIA, including compliance with CIA requirements related to training and disclosures of instances of potential non- compliance with certain federal laws, regulations, or company policy and meets at least quarterly. Additionally, our nominating and corporate governance committee maintains oversight over the company's enterprise risk management program. Because enterprise risk management is holistic risk management, reported risks and their mitigation often include risks more fully governed by other committees, such as cybersecurity. The nominating and corporate governance committee review program methodology and results to ensure management has properly identified and are monitoring enterprise risks.

Ethical Business Practices

We are committed to conducting our business with integrity and the pursuit of excellence in all that we do. Our management team and our board of directors are committed to honesty and compliance with all laws, rules, regulations and corporate policies that apply to our business, and we expect the same commitment from our employees, consultants, business partners and service providers. In particular, we are committed to acting responsibly, safely and with transparency in our interactions with patients, doctors and other stakeholders in the healthcare system.

Compliance and Ethics Program – I-CARE. I-CARE is our philosophy that acknowledges it takes more than just striving to adhere to the law and company policy to create a healthy and ethical corporate culture. The following elements comprise I-CARE:

- Integrity: Our corporate value of integrity is the foundation of our approach.
- Compliance: The elements of an effective compliance program are managed to *deter, detect, and respond* appropriately to potential wrongdoing.
- Accountability: Every employee plays a role in ensuring our actions live up to the company's expectations, and every employee is encouraged to speak up if something looks wrong.
- Respect: Respect for our patients, company and each other keep us on the right path.
- Ethics: Being lawful is the minimum bar we must meet. Our commitment to patients and other stakeholders requires a higher ethical standard.

I-CARE strives to create a strong, effective compliance and ethics program by educating and advising our employees to empower smart risk decisions, advance our value of integrity, and promote operational efficiencies.

We have established various methods of confidential communication for our employees, vendors and others to report suspected violations of laws, rules, regulations or company policies. Where permitted by local laws, anonymous reporting is available.

Chief Compliance and Ethics Officer. The Chief Compliance and Ethics Officer is responsible for designing and implementing our compliance program, managing the I-CARE team and compliance program elements, and administering the obligations and reporting requirements of the CIA. The Chief Compliance and Ethics Officer reports to the Chief Executive Officer, and makes periodic reports to our board of directors.

Corporate Compliance Committee. The corporate compliance committee is comprised of members of our management team and is responsible for overseeing the implementation and effectiveness of our compliance program to support the Chief Compliance and Ethics Officer. The corporate compliance committee's responsibilities include:

- Adopting a system of standards of conduct, policies, procedures, trainings, communications, reporting mechanisms, monitoring, investigations and internal control system reasonably designed to prevent and detect violations of applicable laws, rules and regulations;
- Overseeing the enforcement of compliance policies program and procedures by directing that all received reports of potential compliance violations are investigated and resolved, and that appropriate incentives and disciplinary measures are utilized, including discipline of employees responsible for violations;
- Taking steps designed to ensure that the individuals responsible for our compliance program have adequate resources, authority and competencies to carry out their responsibilities;
- Periodically reviewing the effectiveness of the day-to-day compliance activities engaged in by Jazz and
- Taking such other actions, or making such other recommendations, designed to promote a compliant and ethical organizational culture at Jazz.

Board Oversight of Compliance. The board of directors oversees matters related to compliance requirements and our compliance program generally, including: the adequacy of resources dedicated to the compliance

function; the identification and handling of instances of non-compliance; and the overall effectiveness of the design and implementation of the compliance program. The nominating and corporate governance committee has responsibility for review and oversight of matters related to compliance with U.S. federal health care program requirements and the obligations of the CIA, including the performance of the Chief Compliance and Ethics Officer and corporate compliance committee. The nominating and corporate governance committee meets at least quarterly with the Chief Compliance and Ethics Officer to review our compliance program and annually adopt a resolution summarizing its review and oversight of Jazz's compliance with U.S. federal health care program requirements and the obligations of the CIA. In addition, our board of directors meets regularly with the Chief Compliance and Ethics Officer.

Anti-Corruption Policy. Our global Anti-Corruption Policy applies to all of our employees, directors and officers, our subsidiaries and affiliates, and third party vendors and other agents acting on our behalf. We are committed to complying with applicable anti-corruption and anti-bribery laws, including the Foreign Corrupt Practices Act (FCPA) and the UK Bribery Act (UKBA). The Anti-Corruption Policy is available on our website at *www.jazzpharmaceuticals.com* under the section entitled "Ethical Standards" under "Our Purpose."

Anti-Slavery and Human Trafficking Commitment. We are committed to operating our global business with integrity and upholding a high level of ethical conduct among our employees and business partners including assessing and addressing the risk of modern slavery and human trafficking within our business operations and supply chain. Jazz has existing procedures designed to assess our suppliers that provide materials for use in our tangible goods for sale, and we have enhanced these procedures to include steps for reasonably evaluating whether these suppliers have policies and procedures in place that are designed to promote compliance with applicable laws related to eradication of human trafficking, slavery and illegal child labor.

Code of Conduct. 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 "Ethical Standards" under "Our Purpose." We intend to satisfy the disclosure requirements under Item 5.05 of 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.

Political Contributions Guidance. Our Political Contributions Guidance outlines a process intended to ensure all political contributions (including political action committee contributions) are made with transparency, segregated from lobby activities and also intended to ensure that these activities are conducted in accordance with the applicable federal, state, and local campaign and lobbying laws.

Meetings of the Board of Directors

The board of directors met six times during 2022. All directors attended at least 75% of the aggregate number of meetings of the board of directors and of the committees on which they served that were held during 2022. As required under applicable Nasdaq listing standards, in 2022, the independent directors generally met at each regular board meeting in scheduled executive sessions at which only independent directors were present.

Indirectly through the Lead Independent Director and directly through quarterly independent executive sessions our full board informs the development of board agendas and focus of our board meetings.

Director Commitments

Our Corporate Governance Guidelines provide that directors may not serve on more than five public company boards (including Jazz's board), and if a director is also the chief executive officer of a public company, that director may not serve on more than three public company boards (including Jazz's board). In addition, our Corporate Governance Guidelines require directors to seek prior approval from our Chairperson, our Lead Independent Director (to the extent one has been appointed) and the chair of our nominating and corporate governance committee before accepting an invitation to serve on any additional boards of directors. We monitor

our directors' time commitments throughout the year and we have determined that, as of the date of this proxy statement, all of our directors are currently in compliance with our Corporate Governance Guidelines. We have also amended both the nominating and corporate governance committee charter and the Corporate Governance Guidelines to ensure that when performing our annual review of each of our director's time commitments and service on other companies' boards, we also review their service on other companies' board committees.

Our Board engages regularly with senior management throughout board meetings, one-on-ones, and attendance at key meetings and events including attendance at regional kick off and other business meetings.

Classified Board Structure

Our board of directors is divided into three classes, designated Class I, Class II and Class III. Our nominating and corporate governance committee has discussed the shareholder feedback received on the topic of our classified board structure and continues to believe that this structure is appropriate for our company and beneficial to our shareholders. In particular, the nominating and corporate governance committee believes that the classified board structure:

- promotes stability and continuity, allowing our board and management to remain focused on our long-term strategy and value generation for our shareholders;
- allows for the development of institutional knowledge at the board level, which is particularly important in our industry, given the multi-year life cycles of our product development programs; and
- enhances director independence by decreasing pressures from special interest groups that might have short-term agendas contrary to the long-term interests of our shareholders.

Moreover, a classified board for an Irish company does not present the same entrenchment risk as for a typical U.S.-incorporated company due to the statutory right of shareholders to remove directors and the ability of shareholders to replace any board vacancies created by such removal under Irish law.

Information About Board Committees

The standing committees of the board of directors include an audit committee, a compensation committee, a nominating and corporate governance committee, and a science and medicine committee. Each of these committees is comprised solely of independent directors, has a chair and has a written charter approved by the board of directors reflecting applicable standards and requirements adopted by the SEC and Nasdaq. A copy of the standing committees' charters can be found on our website, www.jazzpharmaceuticals.com, in the section titled "About" under the subsection titled "Board of Directors."

Committee Membership

Our board of directors has four standing committees: the audit committee, the compensation & management development committee (referred to herein as the compensation committee), nominating and corporate governance committee, and science and medicine committee. The following table provides membership information for 2022 for each standing committee.

Name	Audit	Compensation	Nominating and Corporate Governance	Science and Medicine[1]
Jennifer E. Cook[2]		C		●
Patrick G. Enright	●	●		
Peter Gray	C			
Heather Ann McSharry	●		C	
Seamus Mulligan				●
Kenneth W. O'Keefe	●			
Anne O'Riordan[3]	●		●	
Norbert G. Riedel, Ph.D.[4]		●		C
Mark D. Smith, M.D.			●	●
Catherine A. Sohn, Pharm.D.[5]		●		●
Rick E Winningham			●	●

C = committee chair ● = committee member

1 The science and medicine committee was formed in April 2022.
2 Ms. Cook was appointed as chair of our compensation committee in April 2022.
3 Ms. O'Riordan was appointed as a member of our nominating and corporate governance committee in April 2022.
4 Mr. Riedel ceased serving as chair of our compensation committee in April 2022.
5 Dr. Sohn ceased serving on our nominating and corporate governance committee in April 2022.

Audit Committee

The audit committee of the board of directors oversees our corporate accounting and financial reporting processes, our systems of internal control over financial reporting and audits of our financial statements, the quality and integrity of our financial statements and reports, the qualifications, independence and performance of the auditors engaged as our independent registered public accounting firm for purposes of preparing or issuing an audit report or performing audit services and certain enterprise risk issues. Specific responsibilities of the audit committee include:

- evaluating the performance of and assessing the qualifications of the independent auditors;
- determining and approving the engagement and remuneration of the independent auditors;
- determining whether to retain or terminate the existing independent auditors or to appoint and engage new independent auditors;
- determining and approving the engagement of the independent auditors to perform any proposed permissible non-audit services;
- monitoring the rotation of partners of the independent auditors on our audit engagement team as required by applicable laws and rules;
- reviewing and advising on the selection and removal of the head of our internal audit function, the activities and organizational structure of the internal audit function and the results of internal audit activities;

- reviewing and approving the internal audit charter at least annually and the annual internal audit plan and budget;
- meeting to review our annual audited financial statements, our quarterly financial statements and our financial press releases with management and the independent auditors, including reviewing our disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our annual and quarterly reports filed with the SEC;
- reviewing, overseeing and approving transactions between our company and any related persons;
- conferring with management, the internal audit function and the independent auditors regarding the scope, adequacy and effectiveness of our internal control over financial reporting;
- reviewing with management, the internal audit function and the independent auditors, as appropriate, major financial risk exposures, including reviewing, evaluating and approving our hedging and other financial risk management policies, as well as the steps taken by management to monitor and control these exposures;
- establishing procedures, when and as required under applicable laws and rules, for the receipt, retention and treatment of any complaints received by our company regarding accounting, internal accounting controls or auditing matters and the confidential and anonymous submission by employees of concerns regarding questionable accounting or auditing matters; and
- reviewing with management our information security (including cybersecurity) risk exposures and the steps taken by management to monitor and mitigate these exposures.

The audit committee was during all of 2022 composed of Mr. Gray, Mr. Enright, Ms. McSharry, Mr. O'Keefe and Ms. O'Riordan. Our board of directors has determined that each of Mr. Gray, Mr. Enright, Ms. McSharry, Mr. O'Keefe and Ms. O'Riordan meets the independence requirements of Rule 10A-3 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the Nasdaq listing standards with respect to audit committee members. Our board of directors has also determined that each of Mr. Gray, Mr. Enright, Ms. McSharry and Mr. O'Keefe qualifies as an "audit committee financial expert" within the meaning of SEC regulations. In making this determination, our board of directors considered the overall knowledge, experience and familiarity of each with accounting matters, analyzing and evaluating financial statements, and, in the case of Mr. O'Keefe, managing private equity investments, and, in the case of Mr. Enright, managing venture capital investments. Mr. Gray serves as chair of the audit committee.

The audit committee met five times during 2022. The audit committee also had a number of informal discussions and consultations with one another, with our Chief Financial Officer, our Chief Accounting Officer and our Head of Internal Audit and with Mr. Cozadd during 2022.

Report of the Audit Committee of the Board of Directors[1]

The audit committee has reviewed and discussed the company's audited financial statements for the fiscal year ended December 31, 2022 with management of the company. The audit committee has discussed with KPMG, the independent registered public accounting firm that audited the company's financial statements for the fiscal year ended December 31, 2022, the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board, or PCAOB, and the SEC. The audit committee has also received the written disclosures and the letter from KPMG required by applicable requirements of the PCAOB regarding the independent accountants' communications with the audit committee concerning independence, and has discussed with KPMG that firm's independence. Based on the foregoing, the audit committee recommended to the board of directors that the audited financial statements be included in the 2022 Annual Report on Form 10-K filed with the SEC.

Respectfully submitted,
The Audit Committee of the Board of Directors

Mr. Peter Gray
Mr. Patrick Enright
Ms. Heather Ann McSharry
Mr. Kenneth W. O'Keefe
Ms. Anne O'Riordan

(1) The material under the heading "*Report of the Audit Committee of the Board of Directors*" in this proxy statement is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference in any filing of the company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Compensation Committee

The compensation committee of the board of directors reviews and oversees our compensation policies, plans and programs and reviews and generally determines the compensation to be paid to the executive officers and directors, and prepares and reviews the compensation committee report included in our annual proxy statement. Specific responsibilities and authority of our compensation committee include:

- reviewing, modifying (as needed) and approving overall compensation strategy and policies;
- recommending to our board of directors for determination and approval the compensation and other terms of employment of our Chief Executive Officer and evaluating our Chief Executive Officer's performance in light of relevant goals and objectives;
- reviewing and approving the goals and objectives of our other executive officers and determining and approving the compensation and other terms of employment of these executive officers, as appropriate;
- reviewing and recommending to our board of directors the type and amount of compensation to be paid or awarded to the members of our board of directors;
- having the full power and authority of our board of directors regarding the adoption, amendment and termination of our compensation plans and programs and administering these plans and programs;
- having direct responsibility for appointing, and providing compensation and oversight of the work of, any compensation consultants and other advisors retained by the compensation committee and considering the independence of each such advisor;
- reviewing our practices and policies of employee compensation as they relate to risk management and risk-taking incentives, to determine whether such compensation policies and practices are reasonably likely to have a material adverse effect on our company;
- periodically reviewing with our Chief Executive Officer the plans for succession to the offices of our executive officers and making recommendations to our board of directors with respect to the selection of appropriate individuals to succeed to these positions; and

- reviewing and discussing with management our disclosures contained under the caption "*Compensation Discussion and Analysis*" in our annual proxy statement.

The compensation committee was composed of four directors during 2022: Ms. Cook, Mr. Enright, Dr. Riedel and Dr. Sohn. Dr. Riedel served as the chair of the compensation committee until April 2022 at which time Ms. Cook was appointed chair of the compensation committee. Each member of the compensation committee meets the independence requirements of the Nasdaq listing standards with respect to compensation committee members. In determining whether Mr. Enright, Dr. Riedel, Dr. Sohn and Ms. Cook are independent within the meaning of the Nasdaq listing standards pertaining to compensation committee membership, our board of directors determined, based on its consideration of factors specifically relevant to determining whether any such director has a relationship to us that is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, that no member of the compensation committee has a relationship that would impair that member's ability to make independent judgments about compensation of our executive officers.

Compensation Committee Processes and Procedures

Our compensation committee meets as often as it determines necessary to carry out its duties and responsibilities through regularly scheduled meetings and, if necessary, special meetings. The agenda for each compensation committee meeting is usually developed by members of our human resources department and our Chief Executive Officer, with input from members of our legal department, and is reviewed and finalized with the chair of the compensation committee. Members of our human resources department also attend compensation committee meetings. From time to time, various other members of management and other employees as well as outside advisors or consultants may be invited by the compensation committee to make presentations, provide financial or other background information or advice or otherwise participate in the compensation committee meetings. The compensation committee met six times during 2022.

In making executive compensation determinations (other than for our Chief Executive Officer), the compensation committee considers recommendations from our Chief Executive Officer. In making his recommendations, our Chief Executive Officer receives input from our human resources department and from the individuals who manage or report directly to the other executive officers, and he reviews various third party compensation surveys and compensation data provided by the independent compensation consultant to the compensation committee, as described in the section of this proxy statement entitled "*Executive Compensation—Compensation Discussion and Analysis*." While our Chief Executive Officer discusses his recommendations for the other executive officers with the compensation committee, he does not participate in the deliberations and recommendations to our board of directors concerning, or our board of directors' determination of, his own compensation. The charter of the compensation committee grants the compensation committee full access to all books, records, facilities and personnel of the company, as well as authority to obtain, at our expense, advice and assistance from compensation consultants and internal and external legal, accounting or other advisors and consultants and other external resources that the compensation committee considers necessary or appropriate in the performance of its duties. In particular, the compensation committee has the authority, in its sole discretion, to retain or obtain, at the expense of the company, compensation consultants to assist in its evaluation of executive compensation, and is directly responsible for the appointment, compensation and oversight of the work of its compensation consultants. The compensation committee engages an independent compensation consultant each year to provide a competitive compensation assessment with respect to the executive officers to assist the compensation committee in making annual compensation decisions. Since 2010, Aon's Human Capital Solutions practice, a division of Aon plc, or Aon, has been engaged by the compensation committee each year to provide peer company and industry compensation data and provide the compensation committee with advice regarding executive officers' compensation, including base salaries, performance-based bonuses and long-term equity compensation, and similar advice regarding non-employee director compensation.

The charter of the compensation committee provides that the compensation committee may delegate any responsibility or authority of the compensation committee under its charter to the chair of the committee or to one or more committee members, including subcommittees, except to the extent inconsistent with any applicable laws

and rules, including the Nasdaq listing standards. Our compensation committee does not, however, delegate any of its functions to others in determining or recommending executive or director compensation.

For additional information regarding our processes and procedures for the consideration and determination of executive compensation, including the role of Radford in determining and recommending executive compensation, see the section of this proxy statement entitled "*Executive Compensation—Compensation Discussion and Analysis*." With respect to director compensation matters, our compensation committee recommends to our board of directors and our board of directors determines and sets non-employee director compensation. Our compensation arrangements for our non-employee directors are described under the section of this proxy statement entitled "*Director Compensation.*"

Compensation Committee Interlocks and Insider Participation

None of Ms. Cook, Dr. Riedel, Mr. Enright or Dr. Sohn was at any time our officer or employee during 2022. None of our executive officers serve, or in the past fiscal year served, as a member of the board of directors or the compensation committee of any entity that has one or more of its executive officers serving on our board of directors or compensation committee.

Compensation Consultant Fees

Since 2010, Aon has been engaged by the compensation committee each year to provide peer company and industry compensation data and provide the compensation committee with advice regarding executive officers' compensation, including base salaries, performance-based bonuses and long-term equity incentives, advice regarding directors' compensation as well as other matters under the compensation committee's charter. In 2022, the cost of Aon's consulting services directly related to compensation committee support was approximately $154,000.

Management also engaged with Aon for various insurance-related products and services, covering director and officer liability insurance, health and benefits, pension-related services, other insurance brokerage services and risk services to the business. The aggregate Aon revenue from these additional services in 2022 (not related to Aon's compensation committee consulting services) was approximately $5,900,000. Although the compensation committee was aware of the nature of the services performed by Aon affiliates and the non-executive employee compensation survey data provided by Aon, the compensation committee did not review and approve such services, surveys and insurance premiums and policies, as those were reviewed and approved by management in the ordinary course of business.

Aon maintains certain policies and practices to protect the independence of the executive compensation consultants engaged by the compensation committee. In particular, Aon provides an annual update to the compensation committee on the financial relationship between Aon and the company, and provides written assurances that, within Aon, the Aon consultants who perform executive compensation services for the compensation committee have compensation determined separately from Aon's other lines of business and from the other services it provides to the company. These safeguards were designed to help ensure that the compensation committee's executive compensation consultants continued to fulfill their role in providing independent, objective advice.

Compensation Committee Report[1]

The compensation committee has reviewed and discussed with management the Compensation Discussion and Analysis contained herein. Based on this review and discussion, the compensation committee has recommended to the board of directors that the Compensation Discussion and Analysis be included in our proxy statement for the 2023 annual general meeting of shareholders and be included in the company's Annual Report on Form 10-K we filed with the SEC for the fiscal year ended December 31, 2022.

Respectfully submitted,
The Compensation Committee of the Board of Directors

Ms. Jennifer E. Cook
Mr. Patrick G. Enright
Dr. Norbert G. Riedel, Ph.D.
Dr. Catherine A. Sohn, Pharm.D.

(1) The material under the heading "*Compensation Committee Report*" in this proxy statement is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference in any filing of the company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Science and Medicine Committee

The science and medicine committee of our board of directors was formed in April 2022. The science and medicine committee reviews research, development, and technology ("R&D") initiatives. Specific responsibilities of our science and medicine committee include:

- review and advise management and our board regarding the strategy, direction, value and progress of the company's R&D programs, pipeline and technology platforms;
- review and advise management and our board on pertinent scientific, technological and medical elements of the company's corporate development opportunities and transactions;
- review and advise management and our board on the company's R&D resource allocation strategy, including internal and external investments, investment allocation across R&D stages across franchises/therapeutic areas and technology platforms; and
- identify and discuss new and emerging trends in pharmaceutical and biotechnological science, technology, and regulation.

Our science and medicine committee was composed of the following six directors during 2022: Mr. Riedel, Ms. Cook, Mr. Mulligan, Dr. Smith, Dr. Sohn and Mr. Winningham. Mr. Riedel serves as chair of the science and medicine committee.

The science and medicine committee met twice during 2022.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee of our board of directors is responsible for, among other things:

- overseeing all aspects of our corporate governance functions on behalf of our board of directors;
- making recommendations to our board of directors regarding corporate governance issues;
- identifying, reviewing and evaluating candidates to serve on our board of directors, and reviewing and evaluating incumbent directors;

- reviewing, evaluating and considering the recommendation for nomination of incumbent members for reelection to our board of directors and monitoring the size of our board;
- recommending director candidates to our board of directors;
- overseeing on behalf of our board of directors the company's compliance with applicable laws and regulations, other than the financial compliance issues overseen by the audit committee;
- overseeing on behalf of our board of directors the company's risk management matters, other than with respect to risks that are financial or information security risks (as to which the audit committee has oversight responsibility on behalf of our board of directors) or risks related to compensation policies (as to which the compensation committee has oversight responsibility on behalf of our board of directors);
- evaluating director nominations and proposals by our shareholders and establishing policies, requirements, criteria and procedures in furtherance of the foregoing;
- assessing the effectiveness and performance of our board of directors and its committees, and recommending and implementing board of directors' self-evaluation process;
- overseeing the company's ESG strategy and practices and periodically reviewing and discussing with management the company's practices with respect to ESG matters that are expected to have a significant impact on the company's performance, business activities, or reputation; and
- reviewing, discussing and assessing the performance of our board of directors, including committees of our board of directors, seeking input from all board members, senior management and others.

The nominating and corporate governance committee believes that candidates for director should have certain minimum qualifications, including the ability to read and understand basic financial statements, being over 21 years of age, and the highest personal integrity and ethics. The nominating and corporate governance committee also intends to consider such factors as possessing relevant expertise upon which to be able to offer advice and guidance to management, having sufficient time to devote to our affairs, demonstrated excellence in his or her field, having the ability to exercise sound business judgment and having the commitment to rigorously represent the long-term interests of our shareholders. However, the nominating and corporate governance committee retains the right to modify these qualifications from time to time. Members of the nominating and corporate governance committee obtain recommendations for potential directors from their and other board members' contacts in our industry, and we or the nominating and corporate governance committee have in the past and may from time to time again in the future engage a search firm to assist in identifying potential directors.

Candidates for director nominees are reviewed in the context of the then current composition of the board of directors, the operating requirements of the company and the long-term interests of shareholders. In this regard, we examine the experience and expertise of our board as a whole to ensure alignment between the abilities and contributions of our board and our strategic priorities and long-range plan, emphasizing, among other things, expertise in global and U.S. sales and marketing, in product development, in financial management and in corporate development transactions. In addition, while we do not have specific numerical targets with respect to board diversity, our board believes it is important to consider diversity of race, ethnicity, gender, age, geographic residency, cultural background, and professional experiences in evaluating candidates. Accordingly, when undertaking a search for candidates for nomination as new directors, the nominating and corporate governance committee will consider (and will ask any search firm that it engages to provide) a set of candidates that includes both underrepresented people of color and different genders. The nominating and corporate governance committee assesses the effectiveness of its diversity policy through its periodic evaluation of the composition of the full board of directors. Recently, in recruiting and nominating candidates for our board of directors, our nominating and corporate governance committee has focused on increasing diversity overall, including with respect to gender, ethnicity, and geographic residency.

Of the director nominees and the continuing directors, our board of directors has four female directors, four Irish directors, one of whom is a non-resident, one director that identifies as LBGTQ and one person of color. In the case of incumbent directors whose terms of office are set to expire, the nominating and corporate governance committee reviews these directors' overall service to the company during their terms, including the number of meetings attended, level of participation, quality of performance and any other relationships and transactions that might impair the directors' independence, the importance of board refreshment, as well as the results of the board

of directors' self-evaluation, which is generally conducted annually, to determine whether to recommend them to the board of directors for nomination for a new term. In the case of new director candidates, the nominating and corporate governance committee also determines whether the nominee is "independent" based upon applicable Nasdaq listing standards, applicable SEC rules and regulations and the advice of counsel, if necessary. The nominating and corporate governance committee conducts appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the board of directors. The nominating and corporate governance committee meets to discuss and consider the candidates' qualifications and then selects a nominee for recommendation to the board of directors.

The nominating and corporate governance committee will consider director candidates recommended by shareholders on a case-by-case basis, as appropriate. Shareholders wishing to recommend individuals for consideration by the nominating and corporate governance committee may do so by delivering a written recommendation to our Company Secretary at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland with the candidate's name, biographical data and qualifications and a document indicating the candidate's willingness to serve if elected. The nominating and corporate governance committee does not intend to alter the manner in which it evaluates candidates based on whether the candidate was recommended by a shareholder or not.

To date, the nominating and corporate governance committee has not received any such nominations nor has it rejected a director nominee from a shareholder or shareholders.

Our nominating and corporate governance committee was composed of the following four directors during 2022: Ms. McSharry, Dr. Smith, Mr. Winningham, and Ms. O'Riordan, who was appointed as a member in April 2022, with Dr. Sohn ceasing to serve on the committee in April 2022. Ms. McSharry serves as chair of the nominating and corporate governance committee. Each member of the nominating and corporate governance committee meets (and Dr. Sohn met) the independence requirements of the Nasdaq listing standards.

The nominating and corporate governance committee met four times during 2022.

Corporate Governance Strengths

We are committed to exercising good corporate governance practices. We believe that good governance promotes the long-term interests of our shareholders and strengthens board and management accountability. The highlights of our corporate governance practices include the following:

- Of our director nominees and continuing directors, 11 out of 12 are independent
- Regular executive sessions of independent directors
- Audit, compensation and nominating and corporate governance committees are comprised solely of independent directors
- Diverse board in terms of tenure, residency, gender, race, ethnicity, sexual orientation, experience and skills
- Annual board self-evaluation
- Risk oversight by the full board and committees
- Board and committees may engage outside advisors independently of management
- Independent compensation consultant reporting directly to the compensation committee
- Limits for directors on other public company board service
- No poison pill in place
- Our Corporate Governance Guidelines incorporate a “Rooney Rule”-like policy with respect to new director searches
- Annual advisory approval of executive compensation Shareholders may call extraordinary meetings
- Proactive year-round, shareholder engagement program
- Regular meeting attendance and devote sufficient time and attention to board duties
- Director participation in continuing education and related reimbursement policy
- Lead Independent Director with clearly delineated duties
- Corporate Governance Guidelines
- Majority voting for elections of directors for a three-year term
- Share ownership guidelines for directors and executive officers
- Anti-hedging/pledging policy
- Code of Conduct

Other Corporate Governance Matters

Corporate Governance Guidelines. As a part of our board of directors’ commitment to enhancing shareholder value over the long term, our board of directors has adopted a set of Corporate Governance Guidelines to provide the framework for the governance of our company and to assist our board of directors in the exercise of its responsibilities. Our Corporate Governance Guidelines cover, among other topics, board composition, structure and functioning, director qualifications and board membership criteria, director independence, board and board committee annual self-evaluations, committees of the board, board access to management and outside advisors, board share ownership guidelines, and director orientation and education. Our Corporation Governance Guidelines are available on our website at *www.jazzpharmaceuticals.com* under the section entitled “About” under “Board of Directors.”

New Director Orientation. Jazz has a robust onboarding program for new directors, wherein all key Jazz materials and policies are shared with them, including comprehensive information and materials on our corporate, operational, financial and business activities/performance. Individual meetings for new directors are set up with members of the Jazz executive team and key leaders across the organization.

Anti-Hedging/Pledging Policy. Our insider trading policy prohibits directors, executive officers and other employees from engaging in speculative trading activities, including hedging transactions or other inherently speculative transactions with respect to our securities. Our insider trading policy also prohibits directors, executive officers and other employees from pledging our securities as collateral for any loans.

Clawback Policy. We maintain a clawback policy. The clawback policy provides that we may recover amounts of incentive compensation (including cash or equity compensation) under certain circumstances if we are required to restate our financial results due to material noncompliance with any financial requirement and the misconduct of an executive officer covered by the policy contributed to such noncompliance. The SEC has recently published finalized SEC Clawback Rules that required rulemaking by Nasdaq. The compensation committee will review and amend the clawback policy, as appropriate, to reflect the listing standards adopted by Nasdaq in 2023.

Share Ownership Guidelines for Directors and Executive Officers. We maintain and periodically review share ownership guidelines for our non-employee directors, Chief Executive Officer and certain other employees who serve on our executive committee. More information about our share ownership guidelines can be found under the sections of this proxy statement entitled "*Executive Compensation*—Compensation Discussion and Analysis—Additional Compensation Information—Ownership Guidelines for Executive Officers" and "*Director Compensation—Ownership Guidelines for Directors*."

Shareholder Ability to Call Extraordinary Meetings. Irish law provides that shareholders holding 10% or more of the total voting rights may at any time request that the directors call an extraordinary general meeting (*i.e.*, special meeting). The shareholders who wish to request an extraordinary general meeting must deliver to our principal executive office a written notice, signed by the shareholders requesting the meeting and stating the purposes of the meeting. If the directors do not, within 21 days of the date of delivery of the request, proceed to convene a meeting to be held within two months of that date, those shareholders (or any of them representing more than half of the total voting rights of all of them) may themselves convene a meeting within a specified period, but any meeting so convened cannot be held after the expiration of three months from the date of delivery of the request.

Shareholder Communications with the Board of Directors. Our board of directors believes that shareholders should have an opportunity to communicate with the board, and efforts have been made to ensure that the views of shareholders are heard by the board of directors or individual directors, as applicable, and that appropriate responses are provided to shareholders in a timely manner. We believe that our responsiveness to shareholder communications to the board of directors has been excellent. Shareholders interested in communicating with the board of directors or a particular director (including our Chairperson or our Lead Independent Director) may do so by sending written communication to: Jazz Pharmaceuticals plc, Attention: Company Secretary, Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland. Each communication should set forth the name and address of the shareholder as it appears on our records (and, if the shares are held by a nominee, the name and address of the beneficial owner of the shares), and the number of our ordinary shares that are owned of record by the record holder or beneficially by the beneficial owner, as applicable. The Company Secretary will, in his or her discretion, screen out communications from shareholders that are not related to the duties and responsibilities of the board of directors. The purpose of this screening is to allow the board of directors to avoid having to consider irrelevant or inappropriate communications (such as advertisements, solicitations and hostile communications). If deemed an appropriate communication, the Company Secretary will forward the communication, depending on the subject matter, to the Chairperson, the Lead Independent Director or the chair of the appropriate committee of the board of directors.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information regarding the ownership of our ordinary shares as of May 1, 2023 (except as noted) by: (i) each director; (ii) each of the executive officers named in the Summary Compensation Table under "*Executive Compensation*" below (referred to throughout this proxy statement as our NEOs); (iii) all of our executive officers and directors as a group; and (iv) all those known by us to be beneficial owners of more than five percent of our ordinary shares.

	Beneficial Ownership[2]	
Name and Address of Beneficial Owner[1]	Number of Shares	Percentage of Total
5% Shareholders:		
BlackRock, Inc.[3] 55 East 52nd Street New York, NY 10055	6,652,382	10.4%
The Vanguard Group[4] 100 Vanguard Blvd. Malvern, PA 19355	6,050,625	9.5%
Named Executive Officers and Directors:		
Bruce C. Cozadd[5]	907,976	1.4%
Daniel N. Swisher, Jr.[6]	82,174	*
Renée Galá[7]	44,908	*
Robert Iannone, M.D., M.S.C.E[8]	71,545	*
Kim Sablich[9]	35,700	*
Jennifer E. Cook[10]	7,443	*
Patrick G. Enright[11]	31,856	*
Peter Gray[12]	40,523	*
Heather Ann McSharry[13]	41,336	*
Seamus Mulligan[14]	1,195,589	1.9%
Kenneth W. O'Keefe[15]	53,623	*
Anne O'Riordan[16]	26,826	*
Norbert G. Riedel, Ph.D.[17]	38,160	*
Mark D. Smith, M.D.[18]	7,443	*
Catherine A. Sohn, Pharm.D.[19]	39,323	*
Rick E Winningham[20]	34,899	*
All directors and executive officers as a group (20 persons)[21]	2,797,753	4.4%

* Less than 1%.

(1) Unless otherwise provided in the table above or in the notes below, the address for each of the beneficial owners listed is c/o Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland.

(2) This table is based upon information supplied by officers and directors as well as Schedules 13G or 13G/A filed with the SEC by beneficial owners of more than five percent of our ordinary shares. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the shareholders named in this table has sole voting and investment power with respect to the ordinary shares indicated as beneficially owned. Applicable percentages are based on 64,002,906 ordinary shares outstanding on May 1, 2023, adjusted as required by rules promulgated by the SEC. The number of shares beneficially owned includes ordinary shares issuable pursuant to the exercise of stock options that are exercisable and RSUs that will vest within 60 days of May 1, 2023. Shares issuable pursuant to the exercise of stock options that are exercisable and RSUs that will vest within 60 days of May 1, 2023 are deemed to be outstanding and beneficially owned by the person to whom such shares are issuable for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

Security Ownership of Certain Beneficial Owners and Management (continued)

(3) This information is based on a Schedule 13G/A filed with the SEC on January 26, 2023 by BlackRock, Inc., or BlackRock. According to the Schedule 13G/A, as of December 31, 2022, BlackRock has sole power to vote or direct the vote of 6,169,462 ordinary shares and sole power to dispose or direct the disposition of 6,652,382 ordinary shares. The Schedule 13G/A also indicates that BlackRock is acting as a parent holding company for a number of entities that beneficially owned the ordinary shares being reported. The Schedule 13G/A provides information only as of December 31, 2022 and, consequently, the beneficial ownership of the above-mentioned entity may have changed between December 31, 2022 and May 1, 2023.

(4) This information is based on a Schedule 13G/A filed with the SEC on February 9, 2023 by The Vanguard Group, or Vanguard. According to the Schedule 13G/A, as of December 30, 2022, Vanguard has shared power to vote or direct the vote of 51,732 ordinary shares, sole power to dispose or direct the disposition of 5,911,765 ordinary shares, and shared power to dispose or direct the disposition of 138,860 shares. The Schedule 13G/A provides information only as of December 30, 2022 and, consequently, the beneficial ownership of the above-mentioned entity may have changed between December 30, 2022 and May 1, 2023.

(5) Includes 628,333 ordinary shares Mr. Cozadd has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(6) Includes 62,747 ordinary shares Mr. Swisher has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(7) Includes 33,718 ordinary shares Ms. Galá has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(8) Includes 53,000 ordinary shares Dr. Iannone has the right to acquire pursuant to options exercisable and 3,050 shares Dr. Iannone is expected to receive pursuant to RSUs scheduled to vest, in each case, within 60 days of May 1, 2023.

(9) Includes 31,500 ordinary shares Ms. Sablich has the right to acquire pursuant to options exercisable and 4,200 shares Ms. Sablich is expected to receive pursuant to RSUs scheduled to vest, in each case, within 60 days of May 1, 2023.

(10) Includes 5,396 ordinary shares Ms. Cook has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(11) Includes 15,305 ordinary shares Mr. Enright has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(12) Includes 28,850 ordinary shares Mr. Gray has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(13) Includes 28,850 ordinary shares Ms. McSharry has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(14) Includes 33,350 ordinary shares Mr. Mulligan has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(15) Includes 28,850 ordinary shares Mr. O'Keefe has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023. Includes 4,445 ordinary shares held by The Kenneth W. O'Keefe Trust U/A/D 2/12/1997, of which Mr. O'Keefe is the sole trustee and sole beneficiary.

(16) Includes 18,670 ordinary shares Ms. O'Riordan has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(17) Includes 28,850 ordinary shares Dr. Riedel has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(18) Includes 5,396 ordinary shares Dr. Smith has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(19) Includes 28,850 ordinary shares Dr. Sohn has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(20) Includes 28,850 ordinary shares Mr. Winningham has the right to acquire pursuant to options exercisable within 60 days of May 1, 2023.

(21) Includes 1,176,702 ordinary shares that our executive officers and non-employee directors have the right to acquire pursuant to options exercisable within 60 days of May 1, 2023 and 7,250 ordinary shares that our executive officers and non-employee directors are expected to receive pursuant to RSUs scheduled to vest within 60 days of May 1, 2023.

EXECUTIVE OFFICERS

The following table provides information regarding our executive officers as of June 1, 2023.

Name	Age	Position
Bruce C. Cozadd	59	Chairperson and Chief Executive Officer
Daniel N. Swisher, Jr.	60	President, Chief Operating Officer
Renée Galá	51	Executive Vice President and Chief Financial Officer
Robert Iannone, M.D., M.S.C.E	56	Executive Vice President, Global Head of Research and Development
Neena M. Patil	48	Executive Vice President and Chief Legal Officer
Kim Sablich	54	Executive Vice President and General Manager, US
Patricia Carr	52	Senior Vice President, Chief Accounting Officer
Finbar Larkin, Ph.D.	65	Senior Vice President, Technical Operations
Samantha Pearce	57	Senior Vice President, Europe and International

Bruce C. Cozadd. Biographical information regarding Mr. Cozadd is set forth above under "*Proposal 1 Election of Directors*."

Daniel N. Swisher, Jr. was appointed our President as of January 2018 and also served as our Chief Operating Officer from that date until May 2021 and from November 2022 to present. From December 2003 to December 2017, he was Chief Executive Officer and a member of the board of directors of Sunesis Pharmaceuticals, Inc., a biopharmaceutical company focused on the development of novel targeted cancer therapeutics in hematologic and solid tumor malignancies. He also served as Chief Business Officer and Chief Financial Officer of Sunesis from 2001 to 2003. Prior to 2001, Mr. Swisher served in various management roles, including Senior Vice President of Sales and Marketing, for ALZA Corporation from 1992 to 2001. He currently serves as Chairperson of the board of directors of Cerus Corporation, a biomedical products company focused on the field of blood transfusion safety, and as a member of the board of directors of Corcept Therapeutics Inc., a pharmaceutical company focused on cortisol-modulating therapeutics to address metabolic and other serious medical conditions. Mr. Swisher received a B.A. from Yale University and an M.B.A. from the Stanford Graduate School of Business.

Renée Galá was appointed our Executive Vice President and Chief Financial Officer as of March 2020. From January to June 2019, Ms. Galá served as the Chief Financial Officer of GRAIL, Inc., a private healthcare company focused on the early detection of cancer. Prior to that, from December 2014 to January 2019, she served as Senior Vice President and Chief Financial Officer of Theravance Biopharma, Inc., a biopharmaceutical company, following its spin-out from Innoviva, Inc. Ms. Galá joined Innoviva in 2006 and held various roles in the finance organization before leading the company's spin-out transaction. Prior to that, Ms. Galá served in various roles in global treasury, pharmaceutical sales and corporate strategy/business development at Eli Lilly and Company, from 2001 to 2006. Before joining Eli Lilly, Ms. Galá spent seven years in the energy industry in positions focused on corporate finance, project finance, and mergers and acquisitions. Ms. Galá serves on the board of directors of Gossamer Bio, Inc., a clinical-stage biopharmaceutical company, where she also chairs the audit committee. Ms. Galá previously served as a member of the board of Gyroscope Therapeutics (acquired by Novartis) and Corcept Therapeutics. Ms. Galá holds a B.S. in Mathematics from Vanderbilt University and an M.B.A. from Columbia Business School.

Robert Iannone, M.D., M.S.C.E. was appointed our Executive Vice President, Global Head of Research and Development as of May 2019. He also served as our Chief Medical Officer from December 2019 until October 2021. From April 2018 until May 2019, Dr. Iannone served as Head of Research and Development and Chief Medical Officer of Immunomedics, Inc., a biopharmaceutical company. Prior to that, from July 2014 to April 2018, Dr. Iannone served in the roles of Senior Vice President and Head of Immuno-oncology, Global Medicines Development and the Global Products Vice President at AstraZeneca plc, a global science-led biopharmaceutical

Executive Officers (continued)

company. From 2004 to 2014, Dr. Iannone served in management roles at Merck Co., Inc., a global biopharmaceutical company, culminating in his role as Executive Director and Section Head of Oncology Clinical Development. From 2001 to 2004, he served as Assistant Professor of Pediatrics and from 2004 to 2012 as Adjunct Assistant Professor of Pediatrics at the University of Pennsylvania School of Medicine. Dr. Iannone has been serving on the board of directors of iTeos Therapeutics, Inc., a clinical-stage biopharmaceutical company, since May 2021, and on the Cancer Steering Committee of the Foundation for the National Institutes of Health since 2011. Dr. Iannone previously served as director of Jounce Therapeutics, Inc., a clinical-stage immunotherapy company, from January 2020 to May 2023. Dr. Iannone received a B.S. from The Catholic University of America, an M.D. from Yale University and an M.S.C.E. from University of Pennsylvania and completed his residency in Pediatrics and fellowship in Pediatric Hematology-Oncology at Johns Hopkins University.

Neena M. Patil was appointed our Executive Vice President and Chief Legal Officer as of August 2022. Ms. Patil joined Jazz Pharmaceuticals as Senior Vice President and General Counsel in July 2019. From September 2018 to July 2019, Ms. Patil served as Senior Vice President, General Counsel and Corporate Secretary of Abeona Therapeutics Inc., a clinical-stage biopharmaceutical company. Prior to that, from May 2008 to October 2016, Ms. Patil served in management positions at Novo Nordisk Inc., culminating in her role as Vice President for Legal Affairs and Associate General Counsel. Prior to 2008, she worked for several other global biopharmaceutical companies including Pfizer, GPC Biotech and Sanofi. Ms. Patil serves on the board of directors of Teleflex, Inc., a global provider of medical technologies. Ms. Patil also serves on the U.S. Board of Mothers 2 Mothers, a global health care organization operating in Africa. Ms. Patil received a B.A. from Georgetown University and a J.D. and Master of Health Services Administration from the University of Michigan.

Kim Sablich was appointed our Executive Vice President and General Manager, North America, in June 2020 and has served as General Manager, US, since November 2022. Ms. Sablich previously served as the Chief Commercial Officer of Myovant Sciences, Inc., a clinical-stage biopharmaceutical company, from December 2018 to May 2020. Prior to that, she served in various executive roles at GlaxoSmithKline plc, a multinational pharmaceutical company, including as Vice President, U.S. Primary Care Marketing from May 2015 to May 2018, as Vice President, Global Medicines Commercialization from July 2013 to May 2015, and as Vice President, U.S. Vaccines Commercial Strategy from October 2010 to June 2013. Prior to 2010, Ms. Sablich served in various positions of increasing responsibility at Merck & Company, a global healthcare company, in its commercial organization across sales, product management, pricing/access, and customer insights, with a focus on the cardiovascular, respiratory, and vaccines business areas. She serves on the board of directors of Eiger BioPharmaceuticals, Inc., a commercial-stage biopharmaceutical company focused on rare diseases. Ms. Sablich previously served on the board of directors of AllerGenis, LLC, a food allergy diagnostic solutions company, from April 2018 to April 2021. Ms. Sablich holds a B.A. in Economics from Denison University and an M.B.A. from The Wharton School of the University of Pennsylvania.

Patricia Carr was appointed our Senior Vice President and Chief Accounting Officer as of August 2021. Ms. Carr joined Jazz Pharmaceuticals as Vice President, Finance in July 2012 and was appointed Principal Accounting Officer in August 2019. Prior to that, from September 2011 to July 2012, she served as Vice President, Finance of Alkermes plc, a global biopharmaceutical company. From June 2002 to September 2011, she served in a number of roles in Elan Corporation, a neuroscience-based biotechnology company, most recently as Vice President, Finance. Ms. Carr is a Fellow of the Institute of Chartered Accountants (Ireland) and received a Bachelor of Commerce from the University of Galway.

Finbar Larkin, Ph.D. was appointed our Senior Vice President, Technical Operations as of October 2019 and served as our Senior Vice President, Pharmaceutical Development & Manufacturing Science from September 2018 until October 2019, our Vice President, Technical Development from February 2014 until August 2018, and our Executive Director, Technical Operations from April 2013 until February 2014. Prior to that, from September 2009 until March 2013, Dr. Larkin served in management roles at Ipsen Pharma SAS, culminating in his role as Vice President, Engineering & Senior Specialist. From February 1997 until August 2009, he served as Vice President and Managing Director at Ipsen Manufacturing Ireland. From 1990 until 1997, he served in various project and operational management roles at Novartis. Prior to 1990, Dr. Larkin served in various roles in manufacturing science and technology, human resources and quality & analytical science at Lilly SA. Dr. Larkin received a B.Sc. and Ph.D. in Chemistry from University College Dublin.

Executive Officers (continued)

Samantha Pearce was appointed our Senior Vice President, Europe and International as of March 2020. From March 2010 to December 2019, Ms. Pearce held various global senior management positions with Celgene Corporation, most recently as Vice President and General Manager, International Markets. Prior to that, from August 2002 to March 2010, she served in management positions at AstraZeneca plc, culminating in her role as Director, Specialist Care. Prior to August 2002, she worked for DuPont Pharmaceuticals. Ms. Pearce received a B.Sc. from Birmingham University, U.K. and an M.B.A. from Cranfield University, U.K.

EXECUTIVE COMPENSATION

Compensation Discussion and Analysis

The following Compensation Discussion and Analysis describes the material elements of compensation for the following individuals who served as our principal executive officer, principal financial officer and three other most highly compensated executive officers as of December 31, 2022. These individuals are our named executive officers, or NEOs, for 2022.

Bruce C. Cozadd
Chairperson and Chief Executive Officer (CEO)

Daniel N. Swisher, Jr.
President, Chief Operating Officer (COO)

Renée Galá
Executive Vice President and Chief Financial Officer (CFO)

Robert Iannone
Executive Vice President, Global Head of Research and Development

Kim Sablich
Executive Vice President and General Manager, US

TABLE OF CONTENTS

Compensation Discussion and Analysis

Executive Summary

Our Business

We are 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.

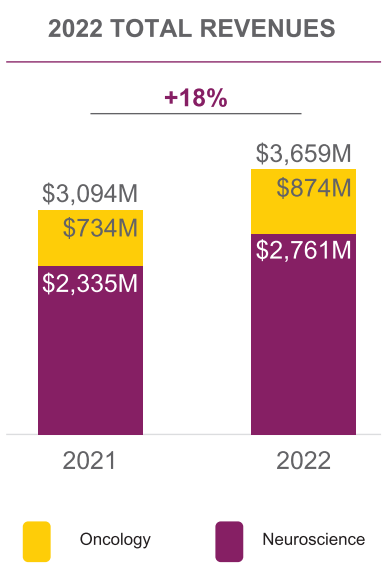
In 2022, consistent with our strategy, we continued to focus on R&D activities within our neuroscience and oncology therapeutic areas.

2022 Performance Highlights

2022 was a year of significant execution across our business that exemplified our purpose to innovate to transform the lives of patients and their families. Our total revenue growth was led by the strength of our commercial franchises, including the continued adoption of Xywav® across both narcolepsy and idiopathic hypersomnia (IH), meaningful Epidiolex® growth, robust demand for Rylaze®, driven by critical unmet patient need, and Zepzelca® remaining the treatment of choice in second-line small cell lung cancer, or SCLC. Building on several transformative years for R&D at Jazz, we have enhanced the breadth and depth of our pipeline, as well as our development capabilities.

Financial

- 2022 total revenues of $3,659 million increased 18% over 2021.
- 2022 GAAP[1] net loss of $(224.1) million, or $(3.58) per diluted share, compared to 2021 GAAP net loss of $(329.7) million, or $(5.52) per diluted share.
- 2022 non-GAAP adjusted net income[2] of $933.6 million, or $13.20 per diluted share, compared to $992.8 million, or $16.23 per diluted share, for 2021.



1 U.S. generally accepted accounting principles (GAAP).

2 Non-GAAP adjusted net income (and the related per share measure) are non-GAAP financial measures. See "*Reconciliations of Non-GAAP Adjusted Net Income*" below.

Commercial

Neuroscience

- Total oxybate product sales (Xywav and Xyrem) of $1,978.9 million in 2022 increased 10% over 2021.
- Xywav net product sales were $958.4 million in 2022, an increase of 79% over 2021. Exiting 2022, there were more narcolepsy patients taking Xywav than Xyrem. In the fourth quarter of 2022, Xywav became our largest product by net product sales.
- Epidiolex/Epidyolex® net product sales were $736.4 million in 2022, an increase of 12% on a pro-forma, basis over 2021. In the fourth quarter of 2022, we successfully completed the pricing and reimbursement process for Epidyolex in France. Epidyolex is now launched in all five key European markets: United Kingdom, Germany, Italy, Spain and France.

Oncology

- Zepzelca® net product sales were $269.9 million in 2022, an increase of 9% over 2021. Zepzelca continues to be the treatment of choice in second-line SCLC.
- Rylaze net product sales were $281.7 million in 2022, an increase of 229% over 2021. In November 2022, Rylaze received U.S. Food and Drug Administration (FDA) approval for a Monday/Wednesday/Friday (M/W/F) intramuscular (IM) dosing schedule.

Research & Development

Neuroscience

- FDA recognized seven years of Orphan Drug Exclusivity for Xywav in IH in January 2022, extending regulatory exclusivity to August 2028.
- We received Fast Track Designation for JZP150 development in post-traumatic stress disorder (PTSD) from FDA, underscoring the significant unmet medical needs of patients.
- In the fourth quarter of 2022, we enrolled the first patient in a pivotal Phase 3 trial of Epidyolex for Dravet syndrome, Lennox-Gastaut syndrome and tuberous sclerosis in Japan.
- In the fourth quarter of 2022, the first patient was enrolled in our Phase 2 trial of suvecaltamide (JZP385) in patients with Parkinson's disease tremor.
- In the fourth quarter of 2022, the first participant was enrolled into our Phase 1 development program to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of JZP441 in sleep-deprived healthy volunteers.

Oncology

- In May 2022, we completed the Marketing Authorization Application (MAA) submission to European Medicines Agency (EMA) for a M/W/F dosing schedule and IM and intravenous (IV) administration for JZP458 (approved as Rylaze in the U.S.) with potential for approval in 2023.
- Phase 3 trial in partnership with F. Hoffmann-La Roche Ltd (Roche) to evaluate 1L use of Zepzelca in combination with Tecentriq® (atezolizumab), compared to Tecentriq alone as maintenance therapy in patients with extensive-stage SCLC after induction chemotherapy, is ongoing. We expect to complete enrollment in the trial by the end of 2023.
- We enrolled the first patient in a Phase 1 trial evaluating JZP815 in patients with advanced or metastatic solid tumors with mitogen-activated protein kinase (MAPK) pathway alterations.

Corporate

- In October 2022, Jazz Pharmaceuticals and Zymeworks Inc. (Zymeworks) announced an exclusive licensing and collaboration agreement[3] and in December 2022, we and Zymeworks announced that we had exercised our option to continue with the exclusive development and commercialization rights to zanidatamab in key markets, including the U.S., Europe and Japan. On April 25, 2023, Jazz and Zymeworks entered into a Stock and Asset Purchase Agreement to, among other things, transfer to Jazz certain assets, contracts and employees associated with the development of zanidatamab.

[3] Exclusive development and commercialization rights to zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks.

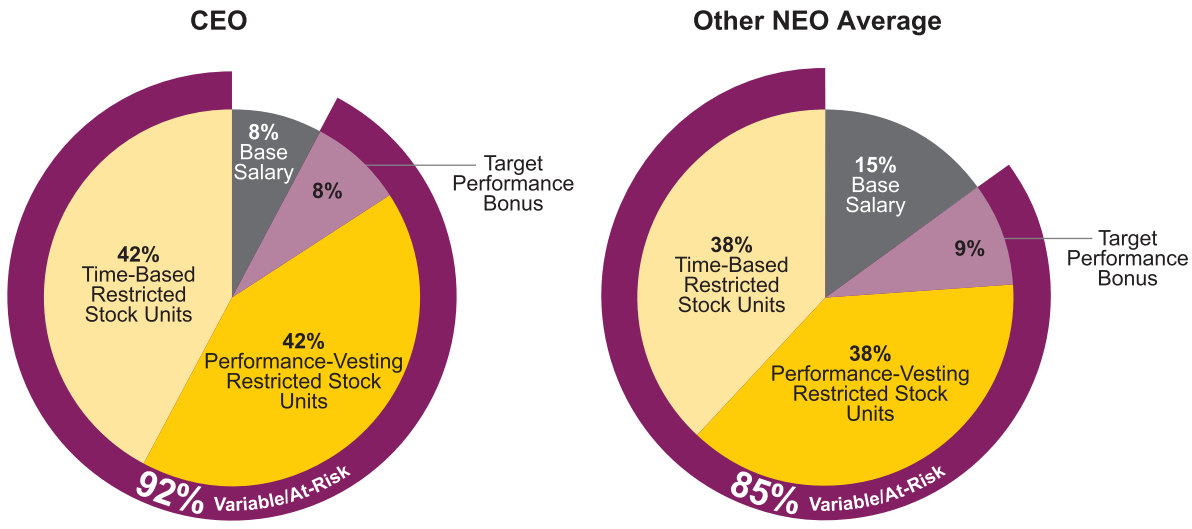
Key Features of Our Executive Compensation Program

What We Do	What We Don't Do
✓ Grant equity awards that vest based on performance goals over a multi-year performance period	✘ No excessive change in control or severance payments
✓ Maintain a clawback policy	✘ No "single-trigger" cash or equity change in control benefits
✓ Design executive compensation to align pay with performance	✘ No repricing of underwater stock options without prior shareholder approval
✓ Balance short-term and long-term incentive compensation, with a majority of executive compensation being "at-risk"	✘ No excessive perquisites
✓ Structure executive bonus opportunities to be dependent on achievement of rigorous corporate performance goals	✘ No tax gross ups on severance or change in control benefits
✓ Establish threshold and maximum levels of achievement for payouts under our annual performance bonus plan and our performance-vesting equity awards, including an overall cap on individual payout amounts	✘ No post-termination retirement or pension benefits that are not available to employees generally
✓ Maintain executive share ownership guidelines	✘ No guaranteed bonuses or base salary increases
✓ Provide "double-trigger" change in control benefits	
✓ Prohibit hedging and pledging by executive officers and directors	
✓ Have 100% independent directors on the compensation committee	
✓ Retain independent compensation consultant who reports directly to the compensation committee	
✓ Meet regularly in executive session without management present	

2022 Pay-for-Performance Overview

As illustrated in the charts below, a substantial majority of target total direct compensation (that is base salary, target annual bonus and target annual equity grant) for our CEO and other NEOs is structured in the form of variable or "at-risk" compensation that is dependent upon the performance of our share price and/or the achievement of financial and strategic objectives. This aligns our executives' interests with those of our shareholders for near- and long-term performance.

The pie charts below show the various recurring components of target total direct compensation for 2022 for our CEO and other NEOs. These components include the following: (i) annual base salary rate for 2022; (ii) annual target bonus opportunity for 2022; and (iii) the target value of equity awards granted in 2022. Target value of equity awards granted for purposes of the chart below means the target dollar value approved by the compensation committee and board of directors for each NEO's equity awards granted in 2022. This value differs from the value show in the Summary Compensation Table, as discussed further below under *"2022 Compensation Decisions for Our Named Executive Officers—Summary of 2022 Compensation Decisions—Long-Term Incentive Program*."



Compensation Philosophy and Objectives

Our executive compensation program is designed to support the following philosophy and objectives:

- **Attract, incentivize, reward and retain diverse, talented individuals with relevant experience in the life sciences industry through a competitive pay structure.** We reward individuals fairly over time and seek to retain those individuals who continue to meet our high expectations.
- **Deliver balanced total compensation packages to accomplish our business objectives and mission.** Our executive compensation program focuses on *target total direct compensation*, combining short-term and long-term components, cash and equity, and fixed and variable payments, in the proportions that we believe are the most appropriate to incentivize and reward our executive officers for achieving our corporate goals while minimizing incentives for excessive risk-taking or unethical conduct.
- **Align pay with our performance.** As described above, a substantial portion of our NEOs compensation opportunity is variable or "at-risk" and dependent upon our performance. Our annual performance bonus awards are not earned unless pre-determined levels of performance are achieved against annual corporate objectives approved by our board of directors at the beginning of the year. Likewise, our performance-vesting restricted stock unit awards ("PSUs") are not earned unless pre-determined levels of performance are achieved and our RSUs will not provide increased value unless there is an increase in the value of our shares, which benefits all shareholders. We also have executive share ownership guidelines to further support our ownership culture and align the interests of executive officers and shareholders.

How We Determine Executive Compensation

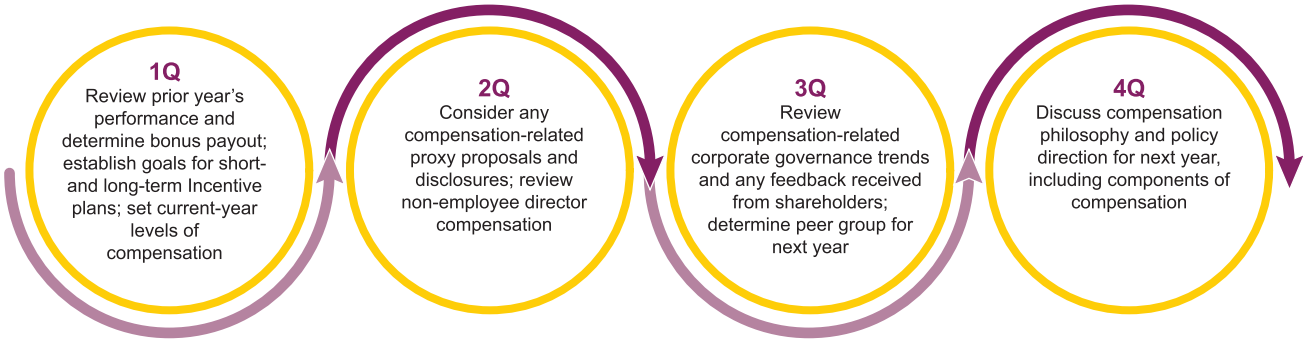
Role of Our Compensation & Management Development Committee and Executive Officers

We refer to the Compensation & Management Development Committee in this report as the compensation committee. The compensation committee is (and was at all times during 2022) composed entirely of independent directors, as defined by Rule 5605(a)(2) of the Nasdaq listing standards. Our compensation committee meets as often as it determines necessary to carry out its duties and responsibilities through regularly scheduled meetings and, if necessary, special meetings. Our compensation committee also has the authority to take certain actions by written consent of all members. The agenda for each compensation committee meeting is usually developed by members of our human resources department and our CEO, with input from members of our legal department, and is reviewed and finalized with the chairperson of the compensation committee.

The compensation committee reviews and oversees our compensation policies, plans and programs and reviews and generally determines the compensation to be paid to the executive officers, including the NEOs. Our CEO's compensation is approved by the compensation committee or the independent members of our board of directors, upon recommendation from the compensation committee, after considering advice from its independent compensation consultant. References in this Compensation Discussion and Analysis to our board of directors approving our CEO's compensation are to the independent members of our board of directors.

In making executive compensation determinations other than for our CEO, the compensation committee considers recommendations from our CEO. In making his recommendations, our CEO receives input from our human resources department and from the individuals who manage or report directly to the other executive officers, and he reviews various sources of market compensation data provided by the independent compensation consultant to the compensation committee, as described below. While our CEO discusses his recommendations for the other executive officers with the compensation committee, he does not participate in the deliberations and recommendations to our board of directors concerning, or our board of directors' determination of, his own compensation. Members of our human resources department also attend compensation committee meetings.

Below are the highlights of the annual cycle our compensation committee follows in reviewing and making decisions with respect to our executive compensation program.



Role of the Independent Compensation Consultant

The compensation committee engages an independent compensation consultant each year to provide a competitive compensation assessment with respect to the executive officers to assist the compensation committee in making annual compensation decisions. Since 2010, Aon's Human Capital Solutions practice, a division of Aon plc, or Aon, has been engaged by the compensation committee. Aon supports the compensation committee in addressing the design of the peer group, provides industry compensation data, when requested, provides the compensation committee with advice regarding executive officers' compensation, including base salaries, performance-based bonuses and long-term equity compensation, and similar advice regarding non-employee directors' compensation. The compensation committee has also consulted with Aon to update the peer company and industry compensation data on an annual basis, address specific questions that arise as the committee fulfills their responsibilities as outlined in the compensation committee charter. Aon provides support in

addressing changes in trends and best practices for executive compensation, incentive and equity and/or other best practices that are requested by the compensation committee, in order to help inform the compensation committee's decisions. Aon reports directly to the compensation committee, which maintains the authority to direct Aon's work and engagement. As requested, and under the purview of the compensation committee, Aon may advise the human resources department on projects from time to time. Aon interacts with management to gain access to company information that is required to perform services and to understand the culture and policies of the organization. Aon attends compensation committee meetings, and the compensation committee and Aon meet in executive session with no members of management present, as needed, to address various compensation matters, including deliberations regarding our CEO's compensation.

In assessing Aon's independence from management in providing executive compensation services to the compensation committee, the compensation committee considered that Aon is only engaged by, takes direction from, and reports to, the compensation committee for such services and, accordingly, only the compensation committee has the right to terminate or replace Aon as its compensation consultant at any time. The compensation committee also analyzed whether the work of Aon as a compensation consultant with respect to executive and director compensation raised any conflict of interest, taking into consideration the following factors:

- ✔ the provision of other services to our company by Aon and its affiliates;
- ✔ the amount of fees we paid to Aon and its affiliates as a percentage of Aon's total revenue;
- ✔ any business or personal relationship of Aon or the individual compensation advisors employed by it with any executive officer of our company;
- ✔ any business or personal relationship of the individual compensation advisors with any compensation committee member;
- ✔ Aon's policies and procedures that are designed to prevent conflicts of interest; and
- ✔ any ordinary shares of our company owned by Aon or the individual compensation advisors employed by it.

The compensation committee has determined, based on its analysis of the above factors, that the work of Aon and the individual compensation advisors employed by Aon as compensation consultants to our company has not created any conflict of interest.

Competitive Assessment of Compensation – Peer Companies and Market Data

Because we aim to attract and retain the most highly qualified executive officers in an extremely competitive market, the compensation committee believes that it is important when making its compensation decisions to be informed as to the current practices of comparable public companies with which we compete for top talent. To this end, the compensation committee reviews market data for each executive officer's position, compiled by Aon as described below, including information relating to the mix and levels of compensation for executive officers in the life sciences industry, with a focus on target total direct compensation in line with the compensation committee's holistic approach to executive compensation.

2022 Peer Group. The compensation committee uses a peer group and other market data to provide context for its executive compensation decision-making. Each year, Aon reviews the external market data and evaluates the composition of our peer group to ensure it appropriately reflects our growth, the increase in our revenues and market capitalization and the consolidation in our industry. In July 2021, with the assistance of Aon, the compensation committee considered companies:

- in the life sciences industry (specifically biotechnology and select bio/pharma companies) with commercial products on the market;
- with revenues of approximately one-fourth (0.25x) to three times (3x) our then-projected revenue (resulting in a range of $775 million to $9.3 billion in revenues);
- with market value of approximately one-fourth (0.25x) to four times (4x) our market capitalization at the time (resulting in a range of between $2.7 billion to $43.5 billion in market capitalization); and
- primarily located in the U.S. with a secondary focus on companies that are headquartered in Europe.

Executive Compensation (continued)

Based on the above criteria, the compensation committee approved the following changes to the executive compensation peer group for 2022:

- added Biogen Inc., and
- removed Endo International plc, Mallinckrodt plc, and Nektar Therapeutics.

The peer group used for our 2022 compensation decisions consisted of the 14 companies listed in the table below. At the time the compensation committee approved the peer group, we were at the 70th percentile for trailing 12 months revenue and the 41st percentile for market capitalization among the new peer group. The compensation committee considered this a reasonable balance and a good representation of companies that were of similar scope and complexity.

Alexion Pharmaceuticals, Inc.[1]	Exelixis, Inc.	Neurocrine Biosciences, Inc.	United Therapeutics Corporation
Alkermes plc	Horizon Therapeutics plc[2]	Regeneron Pharmaceuticals, Inc.	Vertex Pharmaceuticals Incorporated
Biogen Inc.	Incyte Corporation	Sarepta Therapeutics, Inc.	
BioMarin Pharmaceutical Inc.	Ionis Pharmaceuticals, Inc.	Seagen Inc.[3]	

1 Acquired by AstraZeneca plc in July 2021.

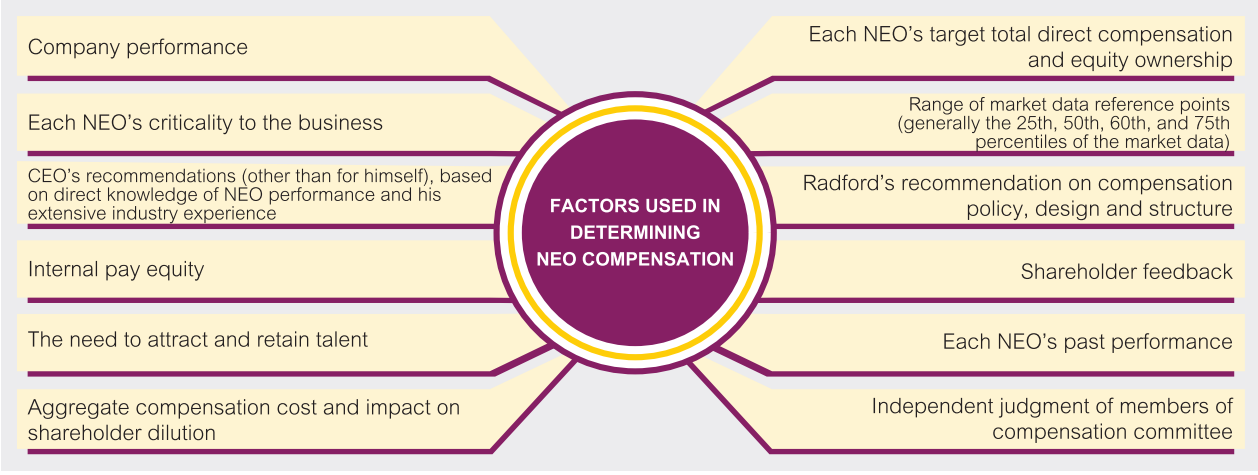
2 In December 2022, Amgen Inc. announced an agreement to acquire Horizon Therapeutics, plc.

3 In March 2023, Seagen announced a definitive merger agreement under which Pfizer Inc. will acquire Seagen.

2022 Market Data. In early 2022, Aon completed an assessment of executive compensation based on our 2022 peer group to inform the compensation committee's determinations of executive compensation for 2022. The compensation committee reviews target total direct compensation, consisting of target total cash compensation and equity compensation, against the market data provided by Aon primarily to ensure that our executive compensation program, as a whole, is positioned competitively to attract and retain the highest caliber of executive officers and to ensure that the total direct compensation opportunity for the executive officer group is aligned with our corporate objectives and strategic needs. The compensation committee does not target a specific percentile for setting the level of compensation for the NEOs and does not otherwise use a formulaic approach to setting pay against the market data. The compensation committee believes that over-reliance on benchmarking can result in compensation that is unrelated to the value delivered by our executive officers because compensation benchmarking does not consider company-to-company variations among actual roles with similar titles or the specific performance of the executive officers.

Factors Used in Determining Executive Compensation

Our compensation committee sets the compensation of our executive officers at levels that the compensation committee determines to be competitive and appropriate for each NEO, using the compensation committee's professional experience and judgment. The compensation committee's pay decisions are not driven by a particular target level of compensation based on market data, and the compensation committee does not otherwise use a formulaic approach to setting executive pay. Instead, the compensation committee believes that executive pay decisions require consideration of multiple relevant factors, which may vary from year to year. The figure below reflects the factors the compensation committee considers in determining and approving the amount, form and mix of pay for our NEOs.



2022 Advisory Vote on Executive Compensation and Shareholder Engagement

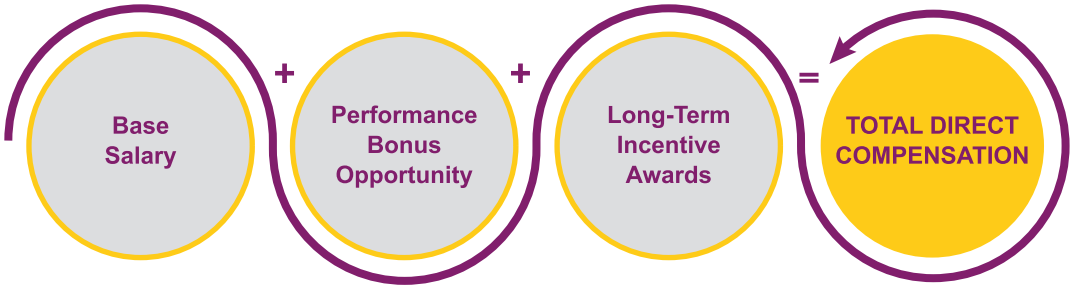
We hold a say-on-pay advisory vote on executive compensation annually. Accordingly, at our 2022 annual meeting, we provided shareholders with the opportunity to cast a non-binding vote on a proposal regarding the compensation of our named executive officers for the year ended December 31, 2021. Of the votes cast, approximately 94% were voted in favor of the proposal. We were pleased with these results and believe it reflects our continuous efforts to engage with shareholders and solicit their feedback on our executive compensation program.

The compensation committee reviewed the final vote results for the proposal and, given the significant level of shareholder support and positive feedback received on recent program and governance changes, concluded that our executive compensation program continues to provide a competitive pay-for-performance package that effectively incentivizes the NEOs and encourages long-term retention. The compensation committee and, with respect to our CEO's compensation, our board of directors, determined not to make any significant changes to our 2022 executive compensation policies or decisions as a result of the vote. Our compensation committee and, with respect to our CEO's compensation, our board of directors will continue to consider the outcome of our say-on-pay proposals and our shareholders' views when making future compensation decisions for the NEOs.

Key Components and Design of the Executive Compensation Program

Total Direct Compensation

Our compensation program focuses on target total direct compensation, which consists of base salary, target performance bonus opportunity (which, together with base salary, we refer to as target total cash compensation), and target long-term incentive opportunity.



The table below captioned "*Components of Total Direct Compensation*" describes key features of each primary component of our executive compensation program and explains why we provide a particular compensation component.

Because we believe it is important to our success to pursue both short- and long-term objectives that drive sustainable shareholder value creation, to avoid excessive risk-taking, and to preserve our cash resources, the majority of the NEOs' total direct compensation is comprised of variable, "at-risk" compensation, consisting of performance-based bonus opportunities and long-term incentives, in the form of PSUs and RSUs, which align the executive officers' incentives with the interests of our shareholders. This allocation between variable, "at-risk" and fixed compensation is consistent with our pay-for-performance philosophy.

The compensation committee takes a holistic approach to compensation and seeks to ensure that the aggregate level of pay, across all of the pay elements is meeting the company's desired objectives for each executive officer. The compensation committee does not have any formal policies for allocating compensation among base salary, target performance bonus opportunity and long-term incentive awards.

Instead, the compensation committee uses its experience and business judgment to establish a total compensation program for each NEO that is a mix of current, short-term and long-term incentive compensation, and cash and non-cash compensation, which it believes is appropriate to achieve the goals of our executive compensation program and our corporate goals.

Components of Total Direct Compensation

Component	Key Features	Purpose
Base Salary	♦ Fixed level of cash compensation ♦ No amount is contractually guaranteed ♦ Amounts reviewed and determined annually, and are generally effective on or around March 1 each year	♦ Provides fixed level of compensation that is competitive within our industry and reflective of the skills and experience required to be successful in fulfilling the role
Performance Bonus Award	♦ Cash compensation under the performance bonus plan, which is variable and "at-risk" because it is dependent upon achievement of pre-established financial and strategic objectives ♦ Target bonus opportunities reviewed and determined annually ♦ Actual bonuses paid shortly after the end of each year, based on the extent corporate goals are attained as determined by the compensation committee, and for executive officers other than our CEO and our President, their individual contributions toward such achievements ♦ Actual bonuses capped at 300% of executive officer's target award (other than for our CEO and President, whose actual bonuses are determined based solely on the achievement of corporate objectives and thus capped at 200% of target)	♦ Provides financial incentives to achieve key corporate objectives that are aligned with our business strategy ♦ Rewards NEOs (other than our CEO and President) for extraordinary individual contributions to our corporate achievements
Long-Term Incentive Compensation	♦ PSUs vest, if at all, at the end of a multi-year performance period and represent 50% of the NEO target annual equity grant. ♦ RSUs generally vest over a 4-year period subject to executive officer's continued service ♦ Awards reviewed and generally granted annually, in the first quarter, or at the time of hire or promotion	♦ Fosters ownership culture ♦ Links compensation to long-term success ♦ PSUs align compensation earned to the achievement of multi-year strategic objectives and share price performance versus peer companies. ♦ RSUs assist with managing dilution for our shareholders, while reinforcing the importance of shareholder value creation over time ♦ Executive share ownership guidelines to further support our ownership culture and align the interests of executive officers and shareholders

Other Benefits. We also offer our executive officers severance benefits upon certain types of involuntary terminations in connection with a change in control. Executive officers based in the United States are eligible to participate in all our benefit plans, such as the 401(k) Plan (see the section below titled "*Description of Compensation Arrangements–401(k) Plan*"), our medical, dental, vision, short-term disability, long-term disability, group life insurance plans and other tax qualified reimbursement plans, in each case on the same basis as other employees. Executive officers based in the United States and Ireland are eligible to participate in our 2007 Employee Stock Purchase Plan, or ESPP, on the same basis as other employees. We do not currently offer defined benefit pension or other retirement benefits in the United States; for executive officers based outside the U.S. we offer pension or other retirement benefits that are consistent with local regulations and on the same basis as other employees in such jurisdictions.

Severance Benefits upon Change in Control. Executive officers based in the United States are also eligible to participate in our Amended and Restated Executive Change in Control and Severance Benefit Plan, or the change in control plan, which is described below under the headings "*Additional Compensation Information—Change in Control Plan*" and "*Potential Payments upon Termination or Change in Control—Amended and Restated Executive Change in Control and Severance Benefit Plan*." The change in control plan provides certain severance benefits to participants, in connection with specified involuntary termination events, including termination without cause and constructive termination, following a change in control. Certain executive officers who are not employed by our U.S. affiliates receive comparable change in control benefits pursuant to their employment or service agreements.

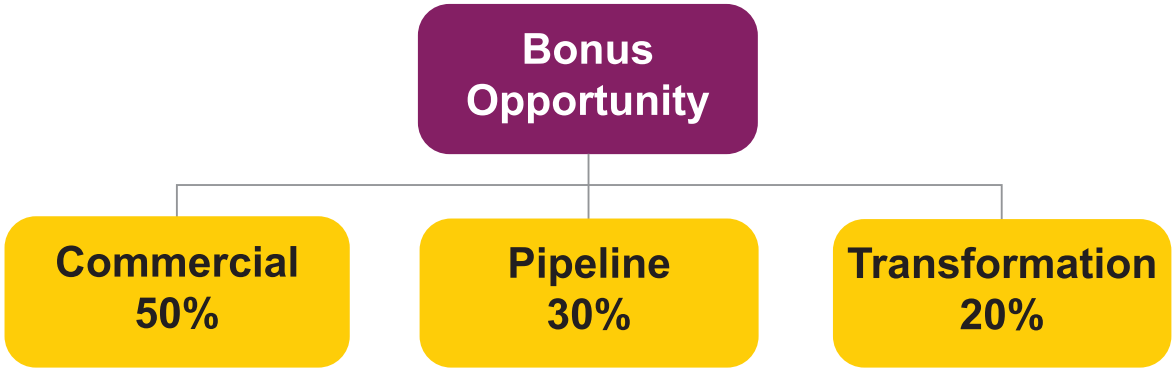
Given the frequency of consolidation in the biopharmaceutical industry, the compensation committee believes these severance benefits are important from a retention perspective to provide some level of protection to our executives who might be terminated following a change in control and that the amounts are reasonable and maintain the competitiveness of our executive compensation and retention program. The compensation committee believes this structure serves to mitigate the distraction and loss of key executive officers that may occur in connection with rumored or actual fundamental corporate changes. Such payments protect the interests of our shareholders by enhancing executive focus during rumored or actual change in control activity, retaining executives despite the uncertainty that generally exists while a transaction is under consideration and encouraging the executives responsible for negotiating potential transactions to do so with independence and objectivity. We do not provide any tax gross up payments on severance benefits.

Goals for and Achievement of 2022 Performance-Based Compensation

For 2022, our annual performance bonus opportunity and the PSUs granted were dependent on annual and long-term performance objectives and methodology established by our compensation committee. The following section describes the performance objectives, discrete goals, payout ranges, and, with respect to the annual bonus program, our actual performance achievement.

2022 Performance Bonus Program

The corporate objectives and relative weightings established by the board of directors for the 2022 performance bonus program that were communicated to the NEOs in early 2022 are described in the chart below. Each of the three corporate objectives consisted of multiple discrete goals. The commercial and pipeline objectives contained additional difficult-to-achieve stretch goals that provided the opportunity to earn up to 12.5% and 15% additional bonus pool funding, respectively. Achievement could range from 0% and 200% for each of the three corporate objectives, including the stretch objectives. However, total payout under the 2022 performance bonus program was capped at 300% of the NEO's target award (with the exception of our CEO and President, whose actual bonuses are determined based solely on the achievement of the corporate objectives and thus capped at 200% of target).



The compensation committee did not set specific objectives for individual executive officers based on the philosophy that each executive officer is responsible for contributing to the corporate objectives, individually and as part of the leadership team to collectively achieve the company's goals. In approving individual bonus awards, the compensation committee considered the individual contribution towards the company's achievement of the corporate objectives by each executive officer (other than our CEO and President). The actual bonus payments approved for each of the NEOs for 2022 are described below under "*2022 Compensation Decisions for Our Named Executive Officers.*"

No adjustments to the goals or to the assessment of their achievement were made in calculating the 2022 bonus pool. Individual bonus awards are determined in accordance with the following methodology:

Annual Base Salary	X	Target Bonus %	X	Company Performance %	X	Individual Performance % (if applicable)	=	Final Bonus Award

Objectives

Each of three objectives is described in the table and accompanying footnotes below, including the goals within each objective, each goal weighting, actual results and performance multipliers, as well as the total bonus pool funding percentage resulting from the level of achievement of the objectives.

The compensation committee approved, at the start of the performance year, an algorithm with respect to each of the three main objectives (as well as the difficult-to-achieve stretch goals) for calculating the bonus pool funding attributable to the extent of achievement for each such objective. The commercial objective, with a weighting of 50%, consisted of individual goals related to each of Xywav and Epidiolex/Epidyolex net product sales and oncology revenues, as well as stretch goals with an aggregate weighting of 12.5%, as described further in the chart below. The pipeline objective, with a weighting of 30%, consisted of goals associated with top priority programs, and other strategic objectives with a weighting of 15%, as described further in the chart below. The transformation objective, with a weighting of 20%, consisted of achieving a specified budgeted non-GAAP adjusted operating margin and included a discretionary segment, as described further below. The compensation committee set specific threshold and maximum levels of achievement for the commercial objective and the related stretch goals, as well as the transformation objective.

Objectives	Weighting	Actual Results	Multiplier	Bonus Pool Funding[12]
1. Commercial:				
• Achieve Xywav net product sales in 2022 of $994 million[1]	20%	Between threshold and target: net product sales of $958 million	82%	16%
• Achieve Epidiolex/Epidyolex net product sales in 2022 of $781 million[1]	18%	Between threshold and target: net product sales of $750 million[7]	80%	14%
• Achieve oncology revenues in 2022 of $885 million[1]	12%	Above target: revenues of $888 million[8]	102%	12%
• *Stretch goal:* Xywav achieves equal to or greater than 51% of oxybate narcolepsy market share by year-end 2022[2]	3%	Between threshold and maximum	80%	2%
• *Stretch goal:* Xywav idiopathic hypersomnia (IH) active patients of equal to or greater than 2,100 by year-end 2022[3]	3%	Below threshold	0%	0%
• *Stretch goal:* Achieve Epidiolex new patient starts in 2022 of equal to or greater than 10,819[4]	3.5%	Below threshold	0%	0%
• *Stretch goal:* Achieve Epidyolex new patient starts in 2022 of equal to or greater than 4,725[5]	2%	Below threshold	0%	0%
• *Stretch goal:* Zepzelca Second line (2L) small cell lung cancer (SCLC) market share metric by year-end 2022 of equal to or greater than 48%[6]	1%	Below threshold	0%	0%
2. Pipeline:				
• Top priority programs[9]	30%	Achieved at 17% level[9]	56%	17%
• Strategic add-ons[10]	15%	Achieved at 10% level[10]	67%	10%
3. Transformation:				
• Achieve budgeted non-GAAP adjusted operating margin[11]	20%	Achieved at 113% level[11]	190%	38%
Total				**110%**

Note: Amounts may not total due to rounding.

Executive Compensation (continued)

Following the end of the 2022 fiscal year, after summing the resulting bonus pool funding percentages for the commercial, pipeline and transformation objectives based on their relative weightings of 50%, 30% and 20%, respectively, and considering achievement of stretch goals, the compensation committee approved an overall bonus pool funding percentage of 110% of the target bonus pool for the 2022 plan year.

(1) If the specified threshold annual performance level was met (80% of target for the three commercial objectives), then a pre-established scaled performance multiplier (ranging from 0% to 175% of target) would be used to calculate the applicable bonus pool funding percentage attributable to such objective. The performance multiplier would be zero if performance was below the 80% threshold level, and if performance exceeded the threshold level, the performance multiplier scaled linearly up to the applicable maximum level. The performance multiplier was capped for performance above the specified maximum performance level (115% of target).

(2) With respect to this stretch goal, the performance threshold was set at 51% of oxybate narcolepsy market share by December 31, 2022. If performance was below 51%, no addition to the total bonus pool funding would be made. If performance was between 51% and 53% of narcolepsy market share on Xywav by December 31, 2022, the amount added to the total bonus pool funding percentage would increase from 1.5% to 3%. Actual achievement of 52.2% of total oxybate narcolepsy patients on Xywav by December 31, 2022, was between the threshold and maximum achievement levels.

(3) With respect to this stretch goal, the performance threshold was set at 2,100 Xywav active patients for IH by December 31, 2022. If performance was below the threshold no addition to the total bonus pool funding would be made. Performance between 2,100 and 2,200 Xywav active patients for IH by December 31, 2022, would have resulted in 1.5% to 3% (scaled linearly) being added to the total bonus pool funding percentage. This stretch goal was difficult to achieve from the outset given its ambition relative to historical actual active patient generation. Actual Xywav active patients for IH was below the threshold achievement level.

(4) With respect to this stretch goal, the performance threshold was set at 10,819 new patient starts on Epidiolex in 2022, below which no addition to the total bonus pool funding would be made. Between 10,819 and 11,334 new patient starts on Epidiolex in 2022, the amount added to the total bonus pool funding percentage would increase between 1.75% to 3.5%. This stretch goal was difficult to achieve from the outset given its ambition relative to historical new patient start trends. Actual achievement of new patient starts on Epidiolex in 2022 was below the threshold achievement level.

(5) With respect to this stretch goal, the performance threshold was set at 4,725 new patient starts on Epidyolex in 2022, below which no addition to the total bonus pool funding would be made. Between 4,725 and 4,950 of new patient starts on Epidyolex in 2022, the amount added to the total bonus pool funding percentage would increase between 1% to 2%. This stretch goal was difficult to achieve from the outset given its ambition relative to historical actual new patient start trends and impact of market access activities. Actual achievement of new patient starts on Epidyolex in 2022 was below the threshold achievement level.

(6) With respect to this stretch goal, the performance threshold was set at 48% 2L SCLC share by December 31, 2022, at or below which no addition to the total bonus pool funding would be made. Between 48% and 50% 2L SCLC share by December 31, 2022, the amount added to the total bonus pool funding percentage would increase between 0.5% to 1%. This stretch goal was difficult to achieve from the outset given its ambition relative to historical actual share trends, and timing of real world evidence publication. Actual achievement of 2L SCLC share by December 31, 2022, was below the threshold achievement level.

(7) To calculate the threshold performance achievement level and performance multiplier, the reported Epidiolex/Epidyolex net product sales of $736 million was increased by approximately $14 million to adjust for changes in foreign currency exchange rates.

(8) To calculate the threshold performance achievement level and performance multiplier, the reported oncology revenue (which includes net product sales and contract revenue) of $874 million was increased by approximately $14 million to adjust for changes in foreign currency exchange rate.

(9) Consisted of the following top-priority goals, to be achieved by year-end (except as noted): (i) completing Rylaze regulatory actions (FDA approval in IM MWF dosing and submission of MAA to the EMA) by mid-year 2022, (ii) JZP378 (nabiximols) multiple sclerosis related spasticity (MS-S) advancement, including clinical trial enrollment targets and trial readout (by mid-year) and a potential New Drug Application submission to FDA (by the fourth quarter), (iii) achieving JZP150 (Fatty acid amide hydrolase Inhibitor) enrollment targets (greater than or equal to 65%) for Phase 2 PTSD study and (iv) achieving JZP385 (suvecaltamide) patient enrollment targets (greater than 25%) for Phase 2b essential tremor (ET) study. In setting the objective, we incorporated key inflection points in 2022 and interim goals where programs were across multiple years, to incentivize in year performance. The compensation committee determined that we had substantially met both goals with respect to Rylaze, we had partially achieved our nabiximols goals as we had progressed against the goals up until the decision was made to discontinue the program, and we partially achieved the goals for JZP150 and JZP385. In light of these results, the compensation committee determined that the actual achievement of the goals was 56% in aggregate and therefore a 17% bonus pool funding percentage. The capped payout for top-priority goals was 150%.

(10) Consisted of the following stretch goals, to be achieved by year-end: (i) corporate development, which included further expanding our portfolio through potential acquisitions, in-licensing, partnering and collaborations; (ii) advancing the cannabinoid platform acquired in our acquisition of GW Pharmaceuticals plc (GW), (iii) drug development progress on a Redx acquired product candidate, and (iv) pipeline advancement to create meaningful value, as evaluated in the compensation committee's discretion. The compensation committee determined that goals (ii) and (iv) were below the threshold achievement levels and that goals (i) and (iii) were achieved in full. In particular, goal (i) outperformed expectations with the execution licenses for zanidatamab, JZP441 and JZP898. In aggregate, the compensation committee assessed the performance on the stretch goals of 67% and therefore a 10% bonus pool funding percentage. The capped payout for strategic add-on goals was 50%.

(11) The target threshold for non-GAAP adjusted operating margin was established at 43.4% and included the Sunosi divestiture, transformation efficiencies, and other initiatives. The multiplier applied to the non-GAAP adjusted operating margin ranged from 0-200% for adjusted operating margin between 40.5% and 46.5%. The compensation committee had the discretion to adjust the payout level or calculation if it determined appropriate. The actual year end non-GAAP adjusted operating margin achieved, as calculated for purposes of the performance bonus program, was 49.1%,(i) reflecting 113% achievement and a 40% payout threshold with a multiplier of 200%. However, the compensation committee used its discretion to reduce the payout from 40% to 38%, reflecting their view on overall performance on transformation initiatives completed in 2022.

(12) The percentages in this column represent, for each objective, the weight of the objective multiplied by the performance multiplier that corresponds to the actual achievement of such objective.

(i) Non-GAAP adjusted operating margin is a non-GAAP financial measure that is calculated as (a) total revenues less non-GAAP adjusted cost of product sales, SG&A expenses and R&D expenses divided by (b) total revenues. Non-GAAP adjusted cost of product sales, SG&A expenses and R&D expenses exclude from GAAP cost of product sales, SG&A expenses and R&D expenses, as applicable, share-based compensation expense, restructuring and other charges, transaction and integration related expenses, costs related to disposal of a business and acquisition accounting inventory fair value step-up expense. In addition, solely for purposes of calculating the target threshold and level of achievement, non-GAAP adjusted operating margin also excluded $44 million of operating expenses associated with three corporate development programs licensed in fiscal year 2022: zanidatamab, JZP898 (interferon alpha agonist) and JZP441 (Orexin-2 agonist).

2022 – 2024 PSU Program. The compensation committee designed the 2022 – 2024 PSU Program, or the 2022 PSUs, to align closely to Vision 2025, our previously announced strategy for long-term, sustainable top- and bottom-line growth and shareholder value creation. As described in more detail below, the performance goals and target performance levels were set by the compensation committee to align with our Vision 2025 by incentivizing and rewarding Jazz leaders for demonstrating strong progress towards the Vision 2025 objectives.

The 2022 PSUs are eligible to vest based on achievement of three objective performance goals over a three-year performance period, which performance payout is then adjusted based on our relative total shareholder return, or TSR, for the three-year performance period. Below is a summary of the performance metrics and associated weightings and targets applicable to the 2022 PSUs, as well as the TSR modifier. We chose the performance goals below given their alignment to Vision 2025.

Performance Goals	Target	Weighting
3-year Revenue Compound Annual Growth Rate (CAGR)(1)	11%	40%
Enhance Pipeline Value(2)	25 points	30%
Non-GAAP Adjusted Operating Margin(3)	47%	30%
TOTAL		100%

(1) The 3-year Revenue CAGR is the compound annual growth rate of our Revenue, calculated with a beginning value equal to fiscal 2021 Revenue and an ending value equal to fiscal 2024 Revenue. “Revenue” means our total consolidated revenues calculated in accordance with GAAP.

(2) Points are awarded for achievement of the following: successful investigational new drug applications, proof-of-concept studies, pivotal studies and product approvals by a regulatory authority occurring during the performance period.

(3) Non-GAAP Adjusted Operating Margin is a non-GAAP financial measure that is calculated as (a) Adjusted Income from Operations for fiscal 2024 divided by (b) total revenues for fiscal 2024. Adjusted Income from Operations means total revenues for fiscal 2024 less non-GAAP adjusted cost of product sales, SG&A expenses and R&D expenses for fiscal 2024. Non-GAAP adjusted cost of product sales, SG&A expenses and R&D expenses exclude from GAAP cost of product sales, SG&A expenses and R&D expenses, as applicable, share-based compensation expense, transaction and integration related expenses, acquisition accounting inventory fair value step-up expense, and other expenses deducted in arriving at non-GAAP adjusted net income.

The three performance goals described above can independently, and in the aggregate, be achieved at 50% of target at threshold performance levels up to 160% of target for stretch performance, with linear interpolation used between the performance levels.

Once the aggregate achievement percentage of the three performance goals is determined, that result is modified, from 75% to 125%, based on the performance of our share price relative to peers over the same three-year performance period, or what we refer to as a relative TSR modifier. The compensation committee believes that having a TSR modifier helps balance the importance of providing executives clearer line of sight to payout opportunities using financial and operational measures with the need to ensure that those payouts are aligned with shareholders’ experience during the performance period. The achievement percentage, as adjusted to reflect

the TSR modifier, will determine the number of shares underlying the PSUs that will be earned, vest and be issued to each NEO. Furthermore, the total payout percentage is capped at 100% in the event the TSR percentile rank is ≤ 25th percentile.

Percentile Rank vs. Comparator Group	Payout Modifier
≥ 75th percentile	125%
For every increase in percentile rank between 50th and 75th percentiles	Increase by 1%
50th percentile	100%
For every decrease in percentile rank between 50th and 25th percentiles	Decrease by 1%
≤ 25th percentile	75%

The compensation committee selected the constituents of the Russell 1000 pharmaceutical component companies as the comparator group for purposes of the relative TSR modifier for the following reasons:

- the number of companies is large enough to withstand any potential industry consolidation;
- the group includes all 14 of the companies in our executive compensation peer group (see page 54); and
- the revenue, market cap and volatility of these companies is more aligned with the company's profile.

The companies initially listed on the index are:

AbbVie Inc.	bluebird bio, Inc.	Incyte Corporation	Reata Pharmaceuticals, Inc.
ACADIA Pharmaceuticals Inc.	Bristol-Myers Squibb Company	Ionis Pharmaceuticals, Inc.	Regeneron Pharmaceuticals, Inc.
Acceleron Pharma Inc.	Catalent, Inc.	Iovance Biotherapeutics, Inc.	Sage Therapeutics, Inc.
Agios Pharmaceuticals, Inc.	Elanco Animal Health Incorporated.	Johnson & Johnson	Sarepta Therapeutics, Inc.
Alexion Pharmaceuticals, Inc.	Eli Lilly and Company	Merck & Co., Inc.	Seagen Inc.
Alkermes plc	Exact Sciences Corporation	Moderna, Inc.	United Therapeutics Corporation
Alnylam Pharmaceuticals, Inc.	Exelixis, Inc	Nektar Therapeutics	Vertex Pharmaceuticals Incorporated
Amgen Inc.	Gilead Sciences, Inc	Neurocrine Biosciences, Inc.	Zoetis Inc.
Biogen Inc.	Global Blood Therapeutics, Inc.	Perrigo Company plc	
BioMarin Pharmaceutical Inc.	Horizon Therapeutics plc	Pfizer Inc.	

Companies that are acquired during the performance period will be removed from the final calculation.

The 2022 PSUs are subject to potential vesting acceleration upon the NEO's termination in connection with a change in control, as well as upon death, disability or retirement, as described below under the heading, "*Potential Payments upon Termination or Change in Control—Treatment of 2021 and 2022 PSUs.*"

2022 Compensation Decisions for Our Named Executive Officers

General Approach

In making compensation decisions for 2022, the compensation committee considered the factors discussed in "*Factors Used in Determining Executive Compensation*" above and the compensation committee's specific compensation objectives for 2022. Our compensation committee did not use a formula or assign a particular weight to any one factor in determining each NEO's target total direct compensation. Rather, our compensation committee's determination of the target total direct compensation, mix of cash and equity and fixed and variable, "at-risk" pay opportunities was a subjective, individualized decision for each NEO. The compensation committee reviewed and considered each element of pay in the context of the overall target total direct compensation for each NEO. When the compensation committee made changes to one element of pay, those changes were made in the context of the levels of the other elements of pay, and the resulting target total direct compensation for each NEO. As a result, the 2022 pay decisions for each NEO are presented holistically in this section.

Summary of 2022 Compensation Decisions

Target Total Cash Compensation. The compensation committee (and board of directors, with respect to Mr. Cozadd) increased total target cash compensation by 3.7% for Mr. Cozadd and in varying amounts for our other NEOs (with all increases falling under 10%). Total target cash increases were a result of increases to base salary rates for 2022 in varying amounts based on each NEO's individual performance, responsibilities, market data reference points and total pay opportunities, which were effective in March 2022. The compensation committee did not increase target performance bonus percentages from 2021 because the compensation committee felt existing percentages (100% for our CEO, 75% for our President and 55% for each of our NEOs) remained aligned with the level of "at-risk" cash appropriate for the company.

Target Equity Compensation and Impact on Target Total Direct Compensation. In determining the appropriate size of 2022 equity award grants, at the time the compensation committee (and the board of directors, with respect to Mr. Cozadd) made its decisions, after careful consideration, it aimed to deliver equity awards to each executive officer to balance the need to maintain equity opportunities competitive with the market, serve the retention and incentive purposes of the awards, facilitate stock ownership and manage overall dilution to our shareholders. With the 2022 target equity compensation grant, the compensation committee (and the board of directors, with respect to Mr. Cozadd) approved total target direct compensation reflecting a 4.8% increase for Mr. Cozadd, with similarly sized increases for other NEOs, except for Mr. Iannone who received a larger increase to ensure his target equity opportunity was positioned competitively with the market.

Long-Term Incentive Program. In 2021, we redesigned our annual long-term incentive program to introduce PSUs, with 50% of each NEO's aggregate target annual long-term incentive compensation in the form of PSUs that vest based on achievement of performance goals and 50% in the form of time-vesting RSUs. The compensation committee believes this mix strikes the right balance between the variable nature of PSUs and the retentive nature of RSUs and accordingly, continued this same mix of PSUs and RSUs for our NEOs in 2022. The vesting terms and structure of our PSUs granted in 2022 is discussed in "*2022 – 2024 PSU Program"* above.

The share amounts underlying the PSUs and RSUs granted to each executive officer in 2022 were determined by dividing the target fair value of the award that the compensation committee and, in the case of Mr. Cozadd, the board of directors, intended to deliver, by the company's 30-day average share price immediately preceding the grant date. We used a 30-day average share price, rather than a single day share price, to provide a more stabilized share value less susceptible to possible swings in the market. The grant date fair value of the RSUs and PSUs, as reported in the Summary Compensation Table and Grants of Plan-Based Awards Table in accordance with SEC rules and FASB Accounting Standards Codification Topic 718, Compensation—Stock Compensation, or FASB ASC 718, is based on the closing price of our ordinary shares on the grant date (with respect to RSUs) and based on a Monte Carlo simulation model (with respect to PSUs). The values for the RSUs and PSUs shown in the Summary Compensation Table and Grants of Plan-Based Awards Table differ from the intended target values and do not fully reflect the considerations of, and decisions made by, the compensation committee and the board of directors in its determination of the equity grants in this respect.

Individual NEO Compensation Decisions

Below are summaries, for each NEO individually, of the compensation committee's (or, as applicable, the board of directors') decisions about 2022 target total direct compensation and the changes from each NEO's 2021 target total direct compensation. As described above, when making the 2022 compensation decisions, the compensation committee (or the board of directors, as applicable) focused primarily on the target total direct compensation for each NEO while considering the factors set forth in the section titled "*Factors Used in Determining Executive Compensation*" and the compensation committee's specific compensation objectives for 2022. The footnotes to the tables also include the actual performance bonus paid to each of the NEOs for 2022 and how that actual bonus compared to each NEO's target bonus. Additionally, for each NEO, the target equity compensation presented in the charts below reflect the target dollar value approved by the compensation committee (or, with respect to Mr. Cozadd, the board of directors), which is different from the grant date fair value as reported in the Summary Compensation Table and Grants of Plan-Based Awards Table, as further described under "*Long-Term Incentive Program*" above.

Bruce C. Cozadd, Chairperson and CEO

	2021 Pay ($)	2022 Pay ($)	Change (%)
Target Total Cash Compensation	**2,159,354**	**2,240,200**	3.7%
Base Salary[1]	1,082,100	1,120,100	
Target Performance Bonus[2]	1,077,254	1,120,100	
Target Equity Compensation[3]	**12,000,000**	**12,600,000**	5.0%
Target Total Direct Compensation[4]	**14,159,354**	**14,840,200**	4.8%

(1) Represents annual base salary rate for the applicable year. 2022 base salary became effective in March 2022.

(2) There was no change to the target bonus as a percentage of base salary for 2022. The 2022 amount reflects a target performance bonus of 100% of 2022 base salary rate as of December 31, 2022. The 2021 amount reflects a target performance bonus of 100% of base salary earned. The actual 2022 performance bonus paid was $1,232,000, reflecting 110% of the target performance bonus, based entirely on the overall 2022 bonus pool funding percentage of 110%. The compensation committee (with approval from the board of directors) determined that the overall 2022 bonus pool funding percentage of 110% was applicable to Mr. Cozadd, because, as CEO, Mr. Cozadd is responsible for the company meeting its objectives.

(3) The target equity compensation presented in the chart above reflects the target dollar value recommended by the compensation committee and approved by the board of directors; this value differs from the values required to be shown in the Summary Compensation Table and Grants of Plan-Based Awards Table for 2021 and 2022, as applicable as further described above in *"2022 Compensation Decisions for Our Named Executive Officers—Summary of 2022 Compensation Decisions—Long-Term Incentive Program."*

(4) The compensation committee and board of directors designed Mr. Cozadd's target total direct compensation to be competitive as compared to the market data, as described in more detail on pages 53-55, appropriate from an internal equity perspective and more heavily weighted towards equity compensation, in line with our pay-for-performance philosophy. The compensation committee believed it was appropriate to provide a modest increase to his base salary in 2022 in recognition of his individual performance, the performance of the company under his leadership and to remain in line with general market increases. Based on the compensation committee's and board of directors' professional experience and judgment, the compensation committee and board of directors determined Mr. Cozadd's target equity compensation to be competitive and appropriate.

Daniel N. Swisher, Jr., President, COO

	2021 Pay ($)	2022 Pay ($)	Change (%)
Target Total Cash Compensation	**1,248,365**	**1,356,250**	8.6%
Base Salary[1]	715,000	775,000	
Target Performance Bonus[2]	533,365	581,250	
Target Equity Compensation[3]	**3,700,000**	**3,800,000**	2.7%
Target Total Direct Compensation[4]	**4,948,365**	**5,156,250**	4.2%

(1) Represents annual base salary rate for the applicable year. 2022 base salary became effective March 2022.

(2) There was no change to the target bonus as a percentage of base salary for 2022. The 2022 amount reflects a target performance bonus of 75% of base salary rate as of December 31, 2022. The 2021 amount reflects a target performance bonus of 75% of base salary earned. The actual 2022 performance bonus paid was $639,000, reflecting 110% of target performance bonus, based entirely on the overall 2022 bonus pool funding percentage of 110%. Like Mr. Cozadd, the compensation committee determined that the overall 2022 bonus pool funding percentage of 110% was applicable to Mr. Swisher, because, as President, he is responsible for the company meeting its objectives.

(3) The target equity compensation presented in the chart above reflects the target dollar value approved by the compensation committee; this value differs from the values required to be shown in the Summary Compensation Table and Grants of Plan-Based Awards Table for 2021 and 2022, as applicable as further described above in *"2022 Compensation Decisions for Our Named Executive Officers—Summary of 2022 Compensation Decisions—Long-Term Incentive Program."*

(4) The compensation committee designed Mr. Swisher's target total direct compensation to be competitive as compared to the market data, as described in more detail on pages 53-55, appropriate from an internal equity perspective and more heavily weighted towards equity compensation, in line with our pay-for-performance philosophy. The compensation committee determined it was appropriate to increase Mr. Swisher's base salary in an amount necessary to reflect his scope of responsibility and oversight of significant functions within the organization, as well as to maintain competitive positioning relative to the market data and the other NEOs. Based on the compensation committee's professional experience and judgment, the compensation committee determined Mr. Swisher's target equity compensation to be competitive and appropriate.

Executive Compensation (continued)

Renée Galá, Executive Vice President and CFO

	2021 Pay ($)	2022 Pay ($)	Change (%)
Target Total Cash Compensation	**959,308**	**1,046,250**	9.1%
Base Salary[1]	620,000	675,000	
Target Performance Bonus[2]	339,308	371,250	
Target Equity Compensation[3]	**3,200,000**	**3,300,000**	3.1%
Target Total Direct Compensation[4]	**4,159,308**	**4,346,250**	4.5%

(1) Represents annual base salary rate for the applicable year. 2022 base salary became effective March 2022.

(2) There was no change to the target bonus as a percentage of base salary for 2022. The 2022 amount reflects a target performance bonus of 55% of base salary rate as of December 31, 2022. The 2021 amount reflects a target performance bonus of 55% of base salary earned. The actual 2022 performance bonus paid was $430,000, reflecting 116% of target performance bonus, based on the overall 2022 bonus pool funding percentage of 110% and Ms. Galá's significant individual contributions to such achievement. Specifically, the compensation committee considered Ms. Galá's oversight of complex strategic matters and corporate priorities, such as development of our long-term strategy, Vision 2025, her performance with respect to supporting the execution of corporate development priorities and her overall criticality to our business.

(3) The target equity compensation presented in the chart above reflects the target dollar value approved by the compensation committee; this value differs from the values required to be shown in the Summary Compensation Table and Grants of Plan-Based Awards Table for 2021 and 2022, as applicable as further described above in *"2022 Compensation Decisions for Our Named Executive Officers—Summary of 2022 Compensation Decisions—Long-Term Incentive Program*."

(4) The compensation committee designed Ms. Galá's target total direct compensation to be competitive as compared to the market data, as described in more detail on pages 53-55, appropriate from an internal equity perspective and more heavily weighted towards equity compensation, in line with our pay-for-performance philosophy. The compensation committee determined it was appropriate to increase Ms. Galá's base salary in an amount necessary to reflect her scope of responsibility and oversight of significant functions within the organization, as well as to maintain competitive positioning relative to the market data and the other NEOs. Based on the compensation committee's professional experience and judgment, the compensation committee determined Ms. Galá's target equity compensation to be competitive and appropriate.

Robert Iannone, Executive Vice President, Global Head of Research and Development

	2021 Pay ($)	2022 Pay ($)	Change (%)
Target Total Cash Compensation	**920,558**	**1,007,500**	9.4%
Base Salary(1)	595,000	650,000	
Target Performance Bonus(2)	325,558	357,500	
Target Equity Compensation(3)	**2,700,000**	**3,200,000**	18.5%
Target Total Direct Compensation(4)	**3,620,558**	**4,207,500**	16.2%

(1) Represents annual base salary rate for the applicable year. 2022 base salary became effective March 2022.

(2) There was no change to the target bonus as a percentage of base salary for 2022. The 2022 amount reflects a target performance bonus of 55% of base salary rate as of December 31, 2022. The 2021 amount reflects a target performance bonus of 55% of base salary earned. The actual 2022 performance bonus paid was $400,000, reflecting 112% of target performance bonus, based on the overall 2022 bonus pool funding percentage of 110% and Dr. Iannone's individual contributions and leadership of the research and development organization during 2022.

(3) The target equity compensation presented in the chart above reflects the target dollar value approved by the compensation committee; this value differs from the values required to be shown in the Summary Compensation Table and Grants of Plan-Based Awards Table for 2021 and 2022, as applicable as further described above in "2022 Compensation Decisions for Our Named Executive Officers—Summary of 2022 Compensation Decisions—Long-Term Incentive Program."

(4) The compensation committee designed Dr. Iannone's target total direct compensation to be competitive as compared to market data, as described in more detail on pages 53-55, appropriate from an internal equity perspective and more heavily weighted towards equity compensation, in line with our pay-for-performance philosophy. The compensation committee determined it was appropriate to increase Dr. Iannone's base salary in an amount necessary to reflect his scope of responsibility and oversight of significant functions within the organization, as well as to maintain competitive positioning relative to the market data and the other NEOs. Based on the compensation committee's professional experience and judgment, the compensation committee determined Dr. Iannone's target equity compensation to be competitive and appropriate.

Kim Sablich, Executive Vice President and General Manager, US

	2021 Pay($)	2022 Pay($)	Change (%)
Target Total Cash Compensation	**881,808**	**930,000**	5.5%
Base Salary(1)	570,000	600,000	
Target Performance Bonus(2)	311,808	330,000	
Target Equity Compensation(3)	**2,700,000**	**2,800,000**	3.7%
Target Total Direct Compensation(4)	**3,581,808**	**3,730,000**	4.1%

(1) Represents annual base salary rate for the applicable year. 2022 base salary became effective March 2022.

(2) There was no change to the target bonus as a percentage of base salary for 2022. The 2022 amount reflects a target performance bonus of 55% of base salary rate as of December 31, 2022. The 2021 amount reflects a target performance bonus of 55% of base salary earned. The actual 2022 performance bonus paid was $370,000, reflecting 112% of target performance bonus, based on the overall 2022 bonus pool funding percentage of 110% and Ms. Sablich's individual contributions and leadership of the North America commercial organization during 2022.

(3) The target equity compensation presented in the chart above reflects the target dollar value approved by the compensation committee; this value differs from the values required to be shown in the Summary Compensation Table and Grants of Plan-Based Awards Table for 2021 and 2022, as applicable as further described above in "*2022 Compensation Decisions for Our Named Executive Officers—Summary of 2022 Compensation Decisions—Long-Term Incentive Program*."

(4) The compensation committee designed Ms. Sablich's target total direct compensation to be competitive as compared to the market data, as described in more detail on pages 53-55, appropriate from an internal equity perspective and more heavily weighted towards equity compensation, in line with our pay-for-performance philosophy. The compensation committee determined it was appropriate to increase Ms. Sablich's base salary in an amount necessary to reflect her scope of responsibility and oversight of significant functions within the organization, as well as to maintain competitive positioning relative to the market data and the other NEOs. Based on the compensation committee's professional experience and judgment, the compensation committee determined Ms. Sablich's target equity compensation to be competitive and appropriate.

Additional Compensation Information

Ownership Guidelines for Executive Officers

We maintain share ownership guidelines for our CEO and certain other employees who serve on our executive committee, including our NEOs. Under the guidelines, these individuals are expected to own a number of the company's ordinary shares with a value equal to six times base salary for the company's Chief Executive Officer, two times base salary for each other member of the company's executive committee who is an officer for purposes of Section 16 of the Exchange Act, and one times base salary for each other member of the company's executive committee. The guidelines provide that the officers are expected to establish the minimum ownership levels within five years of first becoming subject to the guidelines. Messrs. Cozadd and Swisher were in compliance with the guidelines as of March 31, 2023. Each of our other continuing NEOs has five years from the date of his or her appointment to comply with the guidelines.

Shares that count toward satisfaction of these guidelines include: shares owned outright by the individual (including RSUs and/or PSUs that have vested or were earned but not yet settled, net of taxes); shares retained after an option exercise or issuance under another type of equity award granted under the company's equity incentive plans; shares retained after purchase under the ESPP; and shares held in trust for the benefit of the individual. The compensation committee has discretion to develop an alternative individual guideline or an alternative method of complying with the applicable individual guideline for an individual covered by the guidelines if compliance would place a significant hardship on such individual.

Clawback Policy

In April 2021, ahead of SEC final rulemaking implementing the provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act relating to recoupment of incentive-based compensation (the "SEC Clawback Rules"), our compensation committee adopted a policy for recoupment of incentive compensation, or a clawback policy. The clawback policy provides that we may recover amounts of incentive compensation (including cash or

equity compensation) under certain circumstances if we are required to restate our financial results due to material noncompliance with any financial requirement and the misconduct of an executive officer covered by the policy contributed to such noncompliance. The SEC has recently published finalized SEC Clawback Rules that required rulemaking by Nasdaq. The compensation committee will review and amend the clawback policy, as appropriate, to reflect the listing standards adopted by Nasdaq in 2023.

In addition, as a public company, if we are required to restate our financial results due to our material noncompliance with any financial reporting requirements under the federal securities laws as a result of misconduct, our CEO and CFO may be legally required to reimburse our company for any bonus or other incentive-based or equity-based compensation they receive in accordance with the provisions of section 304 of the Sarbanes-Oxley Act of 2002.

Change in Control Plan

Our compensation committee periodically reviews the terms of our change in control plan, including its "double-trigger" structure and benefits, against market data to ensure that the benefits we offer remain appropriate.

Only our executive officers who are employees of our U.S. affiliates are eligible to participate in the change in control plan, which includes all of our NEOs. Certain executive officers who are not employed by our U.S. affiliates receive comparable change in control benefits pursuant to their employment or service agreements. The compensation committee believes that the change in control benefits we provide are representative of market practice, both in terms of design and cost, and are sufficient to retain our current executive team and to recruit talented executive officers in the future.

Equity Grant Timing and Equity Plan Information

Our equity incentive grant policy generally provides that grants to executive officers occur on the second trading day following the filing date of our next quarterly or annual report filed under the Exchange Act that occurs after the date on which such grants are approved by our board of directors or compensation committee, as applicable. Accordingly, our equity incentive grant policy generally requires that grants to our executive officers are made shortly after we have released information about our financial performance to the public for the applicable annual period. As a result, the timing of equity awards is not coordinated in a manner that intentionally benefits our executive officers.

We currently grant equity awards to the NEOs, including PSUs and RSUs, under the 2011 Equity Incentive Plan, or the 2011 Plan. The 2011 Plan was adopted by Jazz Pharmaceuticals, Inc.'s board of directors and approved by Jazz Pharmaceuticals, Inc.'s stockholders in connection with their approval of the Azur Merger in December 2011 and was assumed by us upon the completion of the Azur Merger. Before the 2011 Plan was adopted, we granted stock options under our 2007 Equity Incentive Plan, or the 2007 Plan, which was adopted by Jazz Pharmaceuticals, Inc.'s board of directors and approved by Jazz Pharmaceuticals, Inc.'s stockholders in connection with Jazz Pharmaceuticals, Inc.'s initial public offering. The 2011 Plan affords the compensation committee the flexibility to utilize a broad array of equity incentives and performance cash incentives in order to secure and retain the services of employees of our company and its subsidiaries and to provide long-term incentives that align the interests of employees with the interests of our shareholders.

Additional long-term equity incentives are provided through the ESPP. Pursuant to the ESPP, all eligible employees, including the NEOs (if eligible), may allocate up to 15% of their base salary to purchase our stock at a 15% discount to the market price, subject to specified limits.

Accounting and Tax Considerations

Under FASB ASC 718, the company is required to estimate and record an expense for each award of equity compensation over the vesting period of the award. We record share-based compensation expense on an ongoing basis according to FASB ASC 718.

Under Section 162(m) of the Internal Revenue Code, or Section 162(m), compensation paid to each of the company's "covered employees" that exceeds $1 million per taxable year is generally non-deductible for tax purposes unless the compensation qualifies for certain grandfathered exceptions (including the "performance-based compensation" exception) for certain compensation paid pursuant to a written binding contract in effect on November 2, 2017, and not materially modified on or after such date.

Although the compensation committee will continue to consider tax implications as one factor in determining executive compensation, the compensation committee also looks at other factors in making its decisions and retains the flexibility to provide compensation for the company's named executive officers in a manner consistent with the goals of the company's executive compensation program and the best interests of the company and its stockholders, which may include providing for compensation that is not deductible by the company due to the deduction limit under Section 162(m). The compensation committee also retains the flexibility to modify compensation that was initially intended to be exempt from the deduction limit under Section 162(m) if it determines that such modifications are consistent with the company's business needs.

Risk Assessment Concerning Compensation Practices and Policies

The compensation committee periodically reviews the company's compensation policies and practices to assess whether they encourage employees to take inappropriate risks. The compensation committee has determined that any risks arising from our compensation policies and practices for our employees are not reasonably likely to have a material adverse effect on our company. The compensation committee continues to believe that the mix and design of the elements of executive compensation do not encourage management to assume excessive risks, and significant compensation decisions, as well as decisions concerning the compensation of the company's executive officers, include subjective considerations by the compensation committee or the board of directors, which restrain the influence of formulae or objective factors on excessive risk-taking. Additionally, significant weighting of long-term compensation (in the form of PSUs and RSUs) in each NEOs total compensation opportunity ensures greater focus on driving sustainable growth and shareholder value creation over the longer term, and the mix of short-term compensation (in the form of salary and annual bonus, if any), and long-term compensation (in the form of PSUs and RSUs) also minimizes undue focus on short-term results and helps align the interests of the company's executive officers with the interests of our shareholders. Finally, we maintain robust share ownership requirements, a formal incentive compensation clawback policy and a strict anti-hedging and pledging policy, which individually and collectively, act to minimize risk and ensure a long-term focus on our business.

Reconciliations of Non-GAAP Adjusted Net Income

In this Compensation Discussion and Analysis, we present non-GAAP adjusted net income (and the related per share measure), which are non-GAAP financial measures that exclude from reported GAAP net loss (and the related per share measure) certain items, as detailed in the reconciliation table that follows, adjust for the income tax effect of the non-GAAP adjustments and impact of the change in the statutory tax rate in the U.K.

We believe that each of these non-GAAP financial measures provides useful supplementary information to, and facilitates additional analysis by, investors and analysts. In particular, we believe that each of these non-GAAP financial measures, when considered together with our financial information prepared in accordance with GAAP, can enhance investors' and analysts' ability to meaningfully compare our results from period to period, and to identify operating trends in our business. In addition, these non-GAAP financial measures are regularly used by investors and analysts to model and track our financial performance. Our management team also regularly uses these non-GAAP financial measures internally to understand, manage and evaluate our business and to make operating decisions. Because these non-GAAP financial measures are important internal measurements for our management team, we also believe that these non-GAAP financial measures are useful to investors and analysts since these measures allow for greater transparency with respect to key financial metrics we use in assessing our own operating performance and making operating decisions.

These non-GAAP financial measures are not meant to be considered in isolation or as a substitute for comparable GAAP measures; should be read in conjunction with our consolidated financial statements prepared

in accordance with GAAP; have no standardized meaning prescribed by GAAP; and are not prepared under any comprehensive set of accounting rules or principles. In addition, from time to time in the future there may be other items that we may exclude for purposes of our non-GAAP financial measures; and we have ceased, and may in the future cease, to exclude items that we have historically excluded for purposes of our non-GAAP financial measures. Likewise, we may determine to modify the nature of our adjustments to arrive at our non-GAAP financial measures. Because of the non-standardized definitions of non-GAAP financial measures, the non-GAAP financial measures as used by us in this Compensation Discussion and Analysis have limits in their usefulness to investors and may be calculated differently from, and therefore may not be directly comparable to, similarly titled measures used by other companies.

Reconciliations of GAAP reported net loss to non-GAAP adjusted net income (and the related per share measures) for the 2021 and 2022 annual periods are as follows (in millions, except per share amounts):

	2021	2022
GAAP reported net loss	**$(329.7)**	**$(224.1)**
Intangible asset amortization	525.8	599.2
Impairment charge[1]	—	133.6
Share based compensation expense	169.9	218.2
Transaction and integration related expenses[2]	243.7	23.6
Non-cash interest expense[3]	92.7	38.0
Acquisition accounting inventory fair value step-up	223.1	273.4
Costs related to disposal of a business[4]	—	47.8
Restructuring and other costs[5]	—	77.3
Income tax effect of above adjustments	(192.5)	(253.3)
Impact of U.K. tax rate change	259.9	—
Non-GAAP adjusted net income	$ 992.8	$ 933.6
GAAP reported net loss per diluted share[6]	**$ (5.52)**	**$ (3.58)**
Non-GAAP adjusted net income per diluted share[6]	$ 16.23	$ 13.2
Weighted-average ordinary shares used in diluted per share calculations -GAAP	**59.7**	**62.5**
Weighted-average ordinary shares used in diluted per share calculations-non-GAAP	61.2	72.6

Note: Amounts may not total due to rounding.

Explanation of Adjustments and Certain Line Items:

(1) Impairment charge related to the impairment of our acquired in-process research and development asset as a result of the decision to discontinue our nabiximols program.

(2) Transaction and integration expenses related to our acquisition in May 2021 of GW Pharmaceuticals, plc, or the GW Acquisition.

(3) Non-cash interest expense associated with debt discount and debt issuance costs.

(4) Loss on disposal of the *Sunosi* U.S. business to Axsome Therapeutics, Inc. and associated costs.

(5) Includes restructuring costs and costs related to program terminations.

(6) GAAP reported net loss per diluted share for the year ended December 31, 2022 was calculated using the “if-converted” method in relation to our exchangeable senior notes. There was no impact on GAAP reported net loss per diluted share for the year ended December 31, 2022 as our exchangeable senior notes were anti-dilutive. Non-GAAP adjusted net income per diluted share for the year ended December 31, 2022 includes 9.0 million of our ordinary shares related to the assumed conversion of our exchangeable senior notes and the associated interest expense add-back to non-GAAP adjusted net income of $25.2 million.

Summary of Compensation

The following table sets forth certain summary information for the years indicated with respect to the compensation earned by the NEOs during fiscal years 2022, 2021 and 2020, as applicable.

Name and Principal Position	Year	Salary ($)[1]	Bonus ($)[2]	Stock Awards ($)[3]	Option Awards ($)[4]	Non-Equity Incentive Plan Compensation ($)[5]	All Other Compensation ($)[6]	Total ($)
Bruce C. Cozadd	2022	1,199,169	—	14,873,643	—	1,232,000	20,806	17,325,618
Chairperson and CEO	2021	1,077,254	—	13,414,116	—	1,163,400	24,541	15,679,311
	2020	1,085,123	—	5,881,195	4,210,661	1,381,400	14,921	12,573,300
Daniel N. Swisher, Jr.	2022	801,433	—	4,485,538	—	639,000	27,774	5,953,745
President, COO	2021	711,154	—	4,136,737	—	540,000	16,001	5,403,892
	2020	713,654	—	1,809,598	1,295,588	636,000	16,247	4,471,087
Renée Galá[7]	2022	690,357	—	3,895,415	—	430,000	13,664	5,029,436
Executive Vice President and CFO	2021	616,923	—	3,577,891	—	400,000	10,410	4,605,224
	2020	484,616	25,000	1,816,868	1,382,012	405,000	9,904	4,123,400
Robert Iannone, M.D., M.S.C.E	2022	663,672	—	3,777,191	—	400,000	14,791	4,855,654
	2021	591,923	—	3,018,091	—	380,000	11,322	4,001,336
Executive Vice President, Global Head of Research and Development	2020	592,308	—	1,221,479	874,522	450,000	11,172	3,149,481
Kim Sablich [8]	2022	606,146	—	3,305,291	—	370,000	21,763	4,303,200
Executive Vice President and General Manager, US	2021	566,923	—	3,018,091	—	340,000	22,495	3,947,509
	2020	327,885	300,000	2,134,774	1,616,987	235,000	6,598	4,621,245

Note: Amounts may not total due to rounding.

(1) The dollar amounts in this column represent base salary earned during the indicated fiscal year. 2022 base salary rates were effective March 2022. For more information on salaries in 2022, see "*Compensation Discussion and Analysis—2022 Compensation Decisions for Our Named Executive Officers—Individual NEO Compensation Decisions*" above.

(2) The dollar amounts in this column represent cash signing bonuses paid to each of Ms. Galá and Ms. Sablich in 2020.

(3) The dollar amounts in this column reflect the aggregate grant date fair value of all time-based RSU and performance-based PSU awards granted during the indicated fiscal year computed in accordance with FASB ASC 718, excluding the effect of estimated forfeitures. The grant date fair value for time-based RSUs is measured in accordance with FASB ASC 718 and based on the closing price of our ordinary shares on the date of grant. The grant date fair value for performance-based PSUs was calculated in accordance with FASB ASC 718 using a Monte-Carlo simulation model since the performance-based PSUs are subject to a market condition. These amounts do not necessarily correspond to the actual value recognized or that may be recognized by the NEOs. Assuming that maximum performance is achieved, the value of the performance-based PSU awards made to Messrs. Cozadd, Swisher and Dr. Iannone in 2022 at the date of grant under FASB ASC 718 would have been $16,051,123, $4,840,639 and $4,076,214 and for Ms. Gala and Ms. Sablich would have been $4,203,797 and $3,566,956, respectively. For additional information on the time-based RSUs and performance-based PSUs granted to our NEOs in 2022, see "*Compensation Discussion and Analysis—2022 Compensation Decisions of Our Named Executive Officers—Long-Term Incentive Program*" and *"Compensation Discussion and Analysis—Goals for and Achievement of 2022 Performance-Based Compensation—2022 – 2024 PSU Program*" above and footnote 2 to the table entitled "*Grants of Plan-Based Awards.*"

(4) The dollar amounts in this column reflect the aggregate grant date fair value of all stock option awards granted during the indicated fiscal year. These amounts have been calculated in accordance with FASB ASC 718, using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. Assumptions used in the calculation of these amounts are included in the notes to our audited consolidated financial statements included in the company's 2022 Annual Report on Form 10-K. These amounts do not necessarily correspond to the actual value recognized or that may be recognized by the NEOs upon the vesting of the stock options, the exercise of the stock options, or the sale of the ordinary shares underlying such stock options.

(5) The dollar amounts in this column represent the cash bonus awarded under the performance bonus plan for the indicated fiscal year. For more information on the cash bonus awards for 2022, see "*Compensation Discussion and Analysis—Goals for and Achievement of 2022 Performance-Based Compensation—2022 Performance Bonus Program" and "Compensation Discussion and Analysis—2022 Compensation Decisions for Our Named Executive Officers*" above.

(6) The dollar amounts in this column for 2022 consisted of group term life insurance premiums paid, matching contributions under our 401(k) Plan, work from home expenses, and expenses associated with an annual conference for Messrs. Cozadd and Swisher, of $5,923 and $12,009, respectively, and for Ms. Sablich of $9,161.

(7) Ms. Galá was appointed our Executive Vice President and CFO as of March 16, 2020.

(8) Ms. Sablich was appointed our Executive Vice President and General Manager, North America as of June 1, 2020 and became Executive Vice President and General Manager, US in November 2022.

Grants of Plan-Based Awards

The following table shows, for the fiscal year ended December 31, 2022, certain information regarding grants of plan-based awards to the NEOs.

GRANTS OF PLAN-BASED AWARDS IN FISCAL 2022

Name	Award Type	Grant Date	Approval Date	Estimated Future Payouts Under Non-Equity Incentive Plan Awards[1] Threshold ($)	Target ($)	Maximum ($)	Estimated Future Payouts Under Equity Incentive Plan Awards[2] Threshold (#)	Target (#)	Maximum (#)	All Other Stock Awards: Number of Shares of Stock or Units (#)[3]	Grant Date Fair Value of Stock Awards ($)[4]
Bruce C. Cozadd	Annual Cash	—	—	—	1,120,100	2,240,200					
	PSU	3/3/2022	2/9/2022				16,795	44,788	89,576		8,025,562
	RSU	3/3/2022	2/9/2022							44,788	6,848,081
Daniel N. Swisher, Jr.	Annual Cash	—	—	—	581,250	1,162,500					
	PSU	3/3/2022	2/9/2022				5,065	13,507	27,014		2,420,319
	RSU	3/3/2022	2/9/2022							13,507	2,065,219
Renée Galá	Annual Cash	—	—	—	371,250	1,113,750					
	PSU	3/3/2022	2/9/2022				4,398	11,730	23,460		2,101,899
	RSU	3/3/2022	2/9/2022							11,730	1,793,516
Robert Iannone, M.D., M.S.C.E	Annual Cash	—	—	—	357,500	1,072,500					
	PSU	3/3/2022	2/14/2022				4,265	11,374	22,748		2,038,107
	RSU	3/3/2022	2/14/2022							11,374	1,739,084
Kim Sablich	Annual Cash	—	—	—	330,000	990,000					
	PSU	3/3/2022	2/9/2022				3,732	9,953	19,906		1,783,478
	RSU	3/3/2022	2/9/2022							9,953	1,521,813

(1) This column sets forth the target and maximum bonus amount for each NEO for the year ended December 31, 2022 under our performance bonus plan. There are no thresholds amounts for each individual officer established under our performance bonus plan. The amounts shown under "Target" reflect the applicable target payment under the performance bonus plan if (i) we achieved 100% of the pre-determined 2022 corporate goals established by our compensation committee, and (ii) as applicable, each NEO's individual performance percentage was assessed at 100% by our compensation committee with respect to his or her contributions toward the achievement of our corporate goals. The amounts shown under "Maximum" reflect the applicable maximum payment under our performance bonus plan if (i) we achieved maximum pre-determined 2022 corporate goals established by our compensation committee, and (ii) as applicable, each NEO achieved maximum individual performance as assessed by the compensation committee with respect to his or her contributions toward the achievement of our corporate goals; provided, however, that the 2022 bonus payable under the performance bonus plan may not exceed 200% of the officer's target bonus in the case of the CEO and President (whose bonuses are determined solely based on corporate objective achievement) and 300% for each other NEO. Target bonuses were set as a percentage of each NEO's base salary rate as of December 31, 2022 and were 100% for Mr. Cozadd, 75% for Mr. Swisher, and 55% for each of Ms. Galá, Dr. Iannone and Ms. Sablich. The dollar value of the actual bonus award earned for the year ended December 31, 2022 for each NEO is set forth in the Summary Compensation Table above. As such, the amounts set forth in this column do not represent either additional or actual compensation earned by the NEOs for the year ended December 31, 2022. For a description of the performance bonus plan, see "*Compensation Discussion and Analysis—Goals for and Achievement of 2022 Performance-Based Compensation—2022 Performance Bonus Program*" above.

(2) Performance-based PSU awards were granted to our NEO's on March 3, 2022 pursuant to the 2011 Plan. Each of the PSU awards vests depending on the achievement of certain performance criteria to be assessed over a performance period of January 1, 2022 to December 31, 2024. Following the determination of the company's achievement with respect to the performance criteria, the amount of shares awarded will be subject to adjustment based on the application of a TSR modifier, which depends on the company's relative TSR performance against the constituents of the Russell 1000 pharmaceutical component companies over the same three-year performance period. The number of shares that may be earned ranges between 37.5% of target for threshold performance and 200% of target for maximum performance based on the degree of achievement of the applicable performance metric and the application of the relative TSR modifier. For additional information on performance-based PSUs granted to our NEOs in 2022, see "*Compensation Discussion and Analysis—2022 Compensation Decisions of our Named Executive Officers—Long-Term Incentive Program*" and "*Compensation*

Discussion and Analysis—Goals for and Achievement of 2022 Performance-Based Compensation—2022 – 2024 PSU Program" above. The PSU awards are subject to potential vesting acceleration as described below under the heading "*Potential Payments upon Termination or Change in Control—Treatment of 2021 and 2022 PSUs* and "*Description of Compensation Arrangements—Equity Compensation Arrangements—2011 Equity Incentive Plan*" See also "*Description of Compensation Arrangements—Equity Compensation Arrangements—2011 Equity Incentive Plan*" below for a general description of the material terms of the 2011 Plan.

(3) Each of the annual time-based RSU awards vest in four equal annual installments on the anniversary of the vesting commencement date of March 5, 2022. As a general matter, time-based RSUs will cease vesting upon each NEO's last day of service. Time-based RSU awards are subject to potential vesting acceleration as described below under the headings "*Description of Compensation Arrangements—Equity Compensation Arrangements—2011 Equity Incentive Plan*" and "*Potential Payments upon Termination or Change in Control—Amended and Restated Executive Change in Control Plan and Severance Benefit Plan*" below.

(4) The dollar amounts in this column represent the grant date fair value of each PSU and RSU award, as applicable, granted to the NEOs in 2022. These amounts have been calculated in accordance with FASB ASC 718. The grant date fair value for time-based RSUs is based on the closing price of our ordinary shares on the date of grant. The grant date fair value for performance-based PSUs is calculated using a Monte-Carlo simulation model. These amounts do not necessarily correspond to the actual value recognized or that may be recognized by the NEOs. The fair value for each award may differ based on the applicable data, assumptions, and estimates used in the model.

Description of Compensation Arrangements

Executive Employment and Severance Agreements

We do not have employment agreements currently in effect with any of our NEOs. Like other employees, such executive officers are eligible for annual salary increases, participation in the performance bonus plan and discretionary equity grants. From time to time, we have provided an offer letter in connection with the commencement of employment of an executive officer based in the United States, which describes such executive officer's initial terms of employment. We do not have agreements currently in effect with any of our NEOs entitling such individuals to severance benefits (other than in connection with a change in control pursuant to our change in control plan described below).

Amended and Restated Executive Change in Control and Severance Benefit Plan

Each of the continuing NEOs is a participant in the change in control plan, a description of which is included below under the heading "*Potential Payments upon Termination or Change in Control—Amended and Restated Executive Change in Control and Severance Benefit Plan*."

Equity Compensation Arrangements

Since the Azur Merger, we have granted equity awards to employees, including the NEOs, under the 2011 Plan. From the initial public offering of Jazz Pharmaceuticals, Inc. until the Azur Merger, we granted equity awards to our employees, including some of the NEOs, under the 2007 Plan. As a result of the GW Acquisition, we assumed the GW 2020 Long-Term Incentive Plan. For more information on our current equity compensation program and decisions regarding the grants of equity awards in 2022 for our NEOs, see "*Compensation Discussion and Analysis—2022 Compensation Decisions for Our Named Executive Officers*" above. The following is a brief summary of the material terms of each of our equity compensation plans.

2011 Equity Incentive Plan

The following is a brief summary of the material terms of the 2011 Plan, as amended and restated.

Types of Awards. The 2011 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, RSU awards, other stock awards, and performance awards (including PSU awards) that may be settled in cash, shares, or other property, which may be granted to employees, including officers.

Corporate Transactions. In the event of certain significant corporate transactions (as defined in the 2011 Plan and described below), our board of directors will have the discretion to take one or more of the following actions with respect to outstanding stock awards (contingent upon the closing or completion of such corporate transaction),

unless otherwise provided in the stock award agreement or other written agreement with the participant or unless otherwise provided by our board of directors at the time of grant:

- arrange for assumption, continuation, or substitution of a stock award by a surviving or acquiring corporation (or its parent company);
- arrange for the assignment of any reacquisition or repurchase rights applicable to any shares issued pursuant to a stock award to the surviving or acquiring corporation (or its parent company);
- accelerate the vesting, in whole or in part, and exercisability of a stock award and provide for its termination if it is not exercised at or prior to the corporate transaction;
- arrange for the lapse of any reacquisition or repurchase rights applicable to any shares issued pursuant to a stock award;
- cancel or arrange for the cancellation of a stock award, to the extent not vested or exercised prior to the effective time of the corporate transaction, in exchange for such cash consideration, if any, as the board of directors may consider appropriate; or
- make a payment equal to the excess, if any, of (a) the value of the property that the participant would have received upon the exercise of the stock award over (b) any exercise price payable in connection with such exercise.

Our board of directors need not take the same action for each stock award or with regard to all participants.

For purposes of the 2011 Plan, a "corporate transaction" generally means (i) a sale or disposition of all or substantially all our assets or a sale or disposition of at least 90% of our outstanding securities; (ii) a merger, consolidation or similar transaction after which we are not the surviving corporation; or (iii) a merger, consolidation or similar transaction after which we are the surviving corporation but our ordinary shares are converted or exchanged into other property.

Change in Control. The board of directors has the discretion to provide additional acceleration of vesting and exercisability upon or after a change in control (as defined in the 2011 Plan and described below) as may be provided in a stock award agreement or any other written agreement between us or any of our affiliates and a participant. The forms of stock option agreement and RSU award agreement adopted by the board of directors under the 2011 Plan provide that in the event a participant's service relationship with us or a successor entity is terminated due to an involuntary termination without cause (as defined in the stock award agreement and as described below) within 12 months following, or one month prior to, the effective date of a change in control, the vesting (and in the case of stock options, exercisability) of the stock award will accelerate in full. The treatment of the 2022 PSUs in the event of a change in control is described below under the heading, "*Potential Payments upon Termination or Change in Control—Treatment of 2021 and 2022 PSUs*."

For purposes of the 2011 Plan and the forms of award agreements issued thereunder, a "change in control" generally means (i) a person or group acquires ownership of more than 30% of the combined voting power of our outstanding securities (other than directly from our company); (ii) certain compromises or arrangements sanctioned by the Irish courts, certain schemes, contracts or offers that have become binding on all of our shareholders, certain takeover bids, certain offers or reverse takeover transactions or a reorganization, merger, statutory share exchange, consolidation or similar transaction involving us, and (A) after which our shareholders do not own more than 50% of the combined voting power of the surviving entity or its parent in substantially the same proportion as their ownership of our outstanding voting securities immediately before the transaction, (B) a person or group acquires ownership of more than 30% of the combined voting power of the surviving entity or its parent, or (C) at least a majority of the members of the board of directors of the parent (or the surviving entity, if there is no parent) following such transaction are not incumbent board members (as defined in (v) below) at the time our board of directors approves the transaction; (iii) our shareholders or our board of directors approves a complete dissolution or liquidation of our company, or a complete dissolution or liquidation of our company otherwise occurs (except for a liquidation into a parent company); (iv) a sale, lease, exclusive license or other disposition of all or substantially all of our assets, other than to certain entities; or (v) individuals who were members of our board of directors on the date of adoption of the 2011 Plan (or members of our board of directors

approved or recommended by a majority vote of such members still in office), referred to as "incumbent board members," cease to constitute at least a majority of our board of directors.

An "involuntary termination without cause" generally means that a participant's service relationship with us is terminated for any reason other than for the following reasons (and not upon a participant's death or disability): (i) participant's commission of any felony or crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof (with respect to Irish participants, the participant's conviction for any criminal offense (other than an offense under any road traffic legislation in Ireland, the United Kingdom or elsewhere for which a fine or non-custodial penalty is imposed) or any offense under any regulation or legislation relating to insider dealing, fraud or dishonesty); (ii) participant's attempted commission of or participation in a fraud or act of dishonesty against us; (iii) participant's intentional, material violation of any contract or agreement with us or of any statutory duty owed to us; (iv) participant's unauthorized use or disclosure of our confidential information or trade secrets; or (v) participant's gross misconduct.

GW 2020 Long-Term Incentive Plan

The terms of the GW 2020 Long-Term Incentive 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. 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.

2007 Employee Stock Purchase Plan

Additional long-term equity incentives are provided through the ESPP. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of section 423 of the Internal Revenue Code, or the Code. Under the ESPP, all of our regular employees and employees of any of our parent or subsidiary companies designated by the board of directors as eligible to participate may participate and may contribute, normally through payroll deductions, up to 15% of their earnings up to a total of $15,000 per purchase period for the purchase of our ordinary shares under the ESPP. The ESPP is currently offered to our regular employees in Ireland, Canada and the United States, including the NEOs. The ESPP is implemented through a series of offerings of purchase rights to eligible employees. Under the ESPP, we may specify offerings with a duration of not more than 27 months and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which our ordinary shares will be purchased for employees participating in the offering. Unless otherwise determined by the board of directors, ordinary shares are purchased for accounts of employees participating in the ESPP at a price per share equal to the lower of (a) 85% of the fair market value of an ordinary share on the first date of an offering or (b) 85% of the fair market value of an ordinary share on the date of purchase.

Performance Bonus Plan

We maintain a performance bonus plan to reward executive officers and other employees for successful achievement of company-wide performance objectives and individual contributions toward those objectives on an annual basis. More information regarding the performance bonus plan is provided above under the headings "*Compensation Discussion and Analysis—Goals for and Achievement of 2022 Performance-Based Compensation—2022 Performance Bonus Program*" and "*Compensation Discussion and Analysis—2022 Compensation Decisions for Our Named Executive Officers*."

401(k) Plan

Our employees based in the United States are eligible to participate in the 401(k) Plan. The 401(k) Plan is intended to qualify as a tax-qualified plan under section 401 of the Code. Employee contributions are held and invested by the 401(k) Plan's trustee. The 401(k) Plan provides that each participant may contribute a portion of his or her pre-tax compensation, up to a statutory annual limit, which was $20,500 for employees under age 50,

and $27,000 for employees age 50 and over in 2022. The 401(k) Plan also permits us to make discretionary contributions and matching contributions, subject to established limits and a vesting schedule. In 2013, we began making discretionary matching contributions, which for 2022, consisted of a match of 50% of up to the first 6% of eligible compensation contributed by each employee toward his or her 401(k) plan.

Additional Benefits

The NEOs are eligible to participate in our benefit plans generally available to all employees, as described in "*Compensation Discussion and Analysis—Key Components and Design of the Executive Compensation Program*."

Pension Benefits

Other than with respect to tax-qualified defined contribution plans such as the 401(k) Plan, the NEOs do not participate in any plan that provides for retirement payments and benefits, or payments and benefits that will be provided primarily following retirement.

Nonqualified Deferred Compensation

During the year ended December 31, 2022, the NEOs did not contribute to, or earn any amounts with respect to, any defined contribution or other plan sponsored by us that provides for the deferral of compensation on a basis that is not tax-qualified.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth, for the fiscal year ended December 31, 2022, certain information regarding outstanding equity awards held at fiscal year-end for the NEOs.

OUTSTANDING EQUITY AWARDS AT 2022 FISCAL YEAR-END TABLE

	Options[1]				Stock Awards[1]			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date[2]	Number of Shares or Units of Stock That Have Not Vested (#)[3]	Market Value of Shares or Units of Stock That Have Not Vested ($)[4]	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)[5]	Equity Incentive Plan Awards: Market Value or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)[6]
Bruce C. Cozadd	92,083	37,917[8]	113.10	2/26/2030	44,788[10]	7,135,176	89,576	14,270,353
	119,791	5,209[9]	140.03	2/27/2029	28,443[11]	4,531,254	36,365	5,793,308
	92,500	—	140.67	2/29/2028	26,000[12]	4,142,060	—	—
	86,500	—	136.18	3/1/2027	12,500[13]	1,991,375	—	—
	77,500	—	123.36	2/24/2026	—	—	—	—
	72,500	—	175.19	2/25/2025	—	—	—	—
	48,784[7]	—	166.62	2/26/2024	—	—	—	—
Daniel N. Swisher, Jr.[14]	16,723	9,386[8]	113.10	2/26/2030	13,507[10]	2,151,800	27,014	4,303,600
	18,338	1,028[9]	140.03	2/27/2029	8,232[11]	1,311,440	10,891	1,735,045
	22,731	—	140.67	2/29/2028	6,446[12]	1,026,912		—
					2,481[13]	395,248		
Renée Galá	28,531	12,969[15]	109.45	5/6/2030	11,730[10]	1,868,706	23,460	3,737,413
	—	—	—	—	7,586[11]	1,208,526	9,700	1,545,307
	—	—	—	—	8,300[16]	1,322,273	—	—
Robert Iannone, M.D.,M.S.C.E.	19,125	7,875[8]	113.10	2/26/2030	11,374[10]	1,811,992	22,748	3,623,984
	27,322	3,178[17]	137.12	8/7/2029	6,401[11]	1,019,743	8,180	1,303,156
	—	—	—	—	5,400[12]	860,274	—	—
	—	—	—	—	3,050[18]	485,896	—	—
Kim Sablich	26,250	15,750[19]	127.07	8/5/2030	9,953[10]	1,585,612	19,906	3,171,255
			—	—	6,401[11]	1,019,743	8,180	1,303,156
			—	—	8,400[20]	1,338,204	—	—

(1) In addition to the specific vesting schedule for each stock award, each unvested stock award is subject to the general terms of the 2011 Plan, as applicable, including the potential for future vesting acceleration described above under the heading "*Description of Compensation Arrangements—Equity Compensation Arrangements*" as well as the potential vesting acceleration (i) under the terms of the change in control plan described below under the heading "*Potential Payments upon Termination or Change in Control—Amended and Restated Executive Change in Control and Severance Benefit Plan*" and (ii) pursuant to the 2021 and 2022 RSU and PSU award agreements described under, *"Potential Payments upon Termination or Change in Control—Treatment of 2021 and 2022 RSUs and—Treatment of 2021 and 2022 PSUs."*

(2) As a general matter, stock options granted to NEOs expire on the day before the tenth anniversary of their grant date, or earlier in the event of an NEO's termination of service. In the event of an NEO's termination of service, stock options generally expire three months after such termination of service, subject to extension under limited circumstances such as if the sale of shares during such time was prohibited by our insider trading policy or if exercise would result in violation of securities registration requirements. For more information, see description under the heading "*Potential Payments upon Termination or Change in Control—Equity Compensation Plans*."

(3) Subject to the terms of the award agreement, each time-based RSU award listed in this column represents an RSU award that vests in four equal annual installments on the anniversary of the applicable vesting commencement date.

Executive Compensation (continued)

(4) The market values of the time-based RSU awards that have not vested are calculated by multiplying the number of shares underlying the RSU awards shown in the table by $159.31, the closing price of our ordinary shares on December 30, 2022.

(5) In accordance with SEC rules, (i) with respect to the 2021 PSUs, amounts reported represent target achievement of performance criteria and (ii) with respect to the 2022 PSUs, amounts reported represent maximum achievement of performance criteria. For the PSUs granted in 2021, the actual number of PSUs that could be earned is between 0% and 200% of the target number of PSUs, which vest depending on the company's achievement with respect to certain performance criteria and our relative TSR compared to the constituents of the Russell 1000 pharmaceutical and biotechnology component companies over the 2.66-year performance period. For the PSUs granted in 2022, the actual number of PSUs that could be earned is between 0% and 200% of the target number of PSUs, which vest depending on the company's achievement with respect to certain performance criteria and our relative TSR compared to the constituents of the Russell 1000 pharmaceutical and biotechnology component companies over a three-year performance period. For additional information on the 2022 PSUs, see "*Compensation Discussion and Analysis—2022 Compensation Decisions of Our Named Executive Officers—Long-Term Incentive Program*" and *"Compensation Discussion and Analysis—Goals for and Achievement of 2022 Performance-Based Compensation—2022 – 2024 PSU Program* above.

(6) The market values of the PSU awards that have not vested are calculated by multiplying the number of shares underlying the PSU awards shown in the table by $159.31, the closing price of our ordinary shares on December 30, 2022.

(7) The number of shares reported reflects the transfer of beneficial ownership of a portion of the indicated stock option awards in 2015 to Mr. Cozadd's former spouse pursuant to a domestic relations order.

(8) The unexercisable shares subject to this stock option award as of December 31, 2022 vest monthly from January 27, 2023 to February 27, 2024.

(9) The unexercisable shares subject to this stock option award as of December 31, 2022 vest monthly from January 28, 2023 to February 28, 2023.

(10) Time-based RSUs awarded on March 3, 2022, vesting in equal annual installments over four years measured from the vesting commencement date of March 5, 2022.

(11) Time-based RSUs awarded on February 25, 2021, vesting in equal annual installments over four years measured from the vesting commencement date of March 5, 2021.

(12) Time-based RSUs awarded on February 27, 2020, vesting in equal annual installments over four years measured from the vesting commencement date of March 5, 2020.

(13) Time-based RSUs awarded on February 28, 2019, vesting in equal annual installments over four years measured from the vesting commencement date of March 5, 2019.

(14) The number of shares reported reflects the transfer of a portion of the awards in 2022 to Mr. Swisher's former spouse pursuant to a qualified domestic relations order.

(15) The unexercisable shares subject to this stock option award as of December 31, 2022 vest monthly from January 16, 2023 to March 16, 2024.

(16) Time-based RSUs awarded on May 7, 2020, vesting in equal annual installments over four years measured from the vesting commencement date of April 5, 2020.

(17) The unexercisable shares subject to this stock option award as of December 31, 2022 vest monthly from January 29, 2023 to May 29, 2023.

(18) Time-based RSUs awarded on August 8, 2019, vesting in equal annual installments over four years measured from the vesting commencement date of June 5, 2019.

(19) The unexercisable shares subject to this stock option award as of December 31, 2022 vest monthly from January 1, 2023 to June 1, 2024.

(20) Time-based RSUs awarded on August 6, 2020, vesting in equal annual installments over four years measured from the vesting commencement date of June 5, 2020.

Option Exercises and Stock Vested

The following table provides information on stock awards vested and stock options exercised, including the number of shares acquired upon exercise and the value realized, determined as described below, for the NEOs in the year ended December 31, 2022.

	Option Awards		Stock Awards	
Name	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise ($)[1]	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting ($)[2]
Bruce C. Cozadd	151,493	13,656,638	44,232	6,809,954
Daniel N. Swisher, Jr.[3]	—	—	14,924	2,194,423
Renée Galá	—	—	6,679	1,065,316
Robert Iannone, M.D., M.S.C.E	—	—	7,884	1,199,454
Kim Sablich	—	—	6,334	955,400

(1) The value realized on exercise is based on the difference between the closing price of our ordinary shares on the date of exercise and the applicable exercise price of those options and does not represent actual amounts received by the NEOs as a result of the option exercises.

(2) The value realized on vesting is based on the number of shares underlying the RSUs that vested and the closing price of our ordinary shares on the vesting date.

(3) In addition to the information provided in the table above with respect to stock awards vested and stock options exercised, PSUs covering 324 ordinary shares, RSUs covering 3,112 ordinary shares and stock options covering 51,794 ordinary shares were transferred to Mr. Swisher's former spouse pursuant to a qualified domestic relations order. Mr. Swisher did not realize a specific dollar amount upon this transfer, as the transfer was made in connection with a mutually agreed allocation of and release of claims with respect to marital property.

Potential Payments upon Termination or Change in Control

Amended and Restated Executive Change in Control and Severance Benefit Plan

All of our continuing NEOs are eligible for certain severance and change in control benefits under our change in control plan. The change in control plan applies to eligible executive employees of U.S. affiliates of Jazz and provides that, in the event that an executive's employment terminates due to an involuntary termination without cause or a constructive termination, in each case upon or within 12 months following a change in control (as such terms are defined in the change in control plan and described generally below), and assuming all of the other conditions of the change in control plan are met, each executive who is a participant in the change in control plan (including each of our NEOs) would be entitled to the following benefits under the change in control plan:

- A single, lump sum cash severance payment equal to the sum of: (i) the applicable base salary described below, multiplied by the applicable percentage set forth below; *plus* (ii) the product of (A) the applicable base salary, (B) the applicable bonus percentage described below and (C) the applicable percentage set forth below; *plus* (iii) the product of (A) the applicable base salary, (B) the applicable bonus percentage and the quotient obtained by dividing the number of full months that an executive is employed in the year of the termination by 12.
    - The "applicable base salary" is the higher of the executive's base salary in effect (i) on the date of termination (without giving effect to any reduction in base salary that would constitute grounds for a constructive termination) or (ii) immediately prior to the change in control, without giving effect to any voluntary pay reduction taken by the executive during the 12 months preceding the date of termination or the change in control.
    - The "applicable percentage" is 200% for our CEO, executive chairperson or president, 150% for senior vice presidents and above and 100% for vice presidents.
    - The "applicable bonus percentage" is the greater of (i) the highest amount of any annual bonus paid to the executive for either of the last two calendar years prior to (A) the date of termination or (B) the change in control, in each case expressed as a percentage of the executive's base salary for the applicable year,

and (ii) the higher of the executive's target bonus for the calendar year in which (A) the termination occurs or (B) the change in control occurs, in each case expressed as a percentage of the executive's base salary for such year.

- Full payment of all of the applicable COBRA premiums for any health, dental or vision plan sponsored by us for a period of up to (i) 24 months for our CEO, executive chairperson or president, (ii) 18 months for executive vice presidents and senior vice presidents, and (iii) 12 months for vice presidents, provided that the executive timely elects continued coverage.
- Acceleration in full of the vesting and exercisability, as applicable, of outstanding stock options and other equity awards held by the executive.

The following key terms are defined in the change in control plan:

- A "change in control" generally means: (i) a person or group acquires ownership of more than 30% of the combined voting power of our outstanding securities (other than directly from our company); (ii) certain compromises or arrangements sanctioned by the Irish courts, certain schemes, contracts or offers that have become binding on all of our shareholders, certain takeover bids, certain offers or reverse takeover transactions, or a reorganization, merger, statutory share exchange, consolidation or similar transaction involving us, after which our shareholders do not own more than 50% of the combined voting power of the surviving entity or its parent in substantially the same proportion as their ownership of our outstanding voting securities immediately before the transaction, or a person or group acquires ownership of more than 30% of the combined voting power of the surviving entity or its parent, or at least a majority of the members of the board of directors of the parent (or the surviving entity, if there is no parent) following such transaction are not incumbent board members (as defined in (v) below) at the time our board of directors approves the transaction; (iii) our shareholders or our board of directors approves a complete dissolution or liquidation of our company, or a complete dissolution or liquidation of our company otherwise occurs (except for a liquidation into a parent company); (iv) a sale, lease, exclusive license or other disposition of all or substantially all of our assets, other than to certain entities; or (v) individuals who were members of our board of directors as of February 10, 2016 (or members of our board of directors approved or recommended by a majority vote of such members still in office), referred to as "incumbent board members," cease to constitute at least a majority of the board of directors.
- An "involuntary termination without cause" generally means an executive's employment is terminated for any reason other than for the following reasons: (i) the executive's unauthorized use or disclosure of confidential information or trade secrets which causes material harm to us; (ii) the executive's material breach of any agreement with us (or the executive's material violation of any statutory duty owed to us) after an opportunity to cure; (iii) the executive's material failure to comply with our written policies or rules after an opportunity to cure; (iv) the executive's conviction or plea of guilty or no contest to any crime involving fraud, dishonesty or moral turpitude; (v) the executive's gross misconduct; (vi) the executive's continued failure to perform his or her assigned duties after notification; or (vii) the executive's failure to reasonably cooperate in good faith with any governmental or internal investigation of us or our directors, officers or employees. An "involuntary termination without cause" also includes an executive's termination of employment due to death or disability.
- A "constructive termination" generally means an executive resigns employment after any of the following actions are taken or events occur without the executive's written consent: (i) one or more reductions in the executive's base salary that results in a total reduction in the executive's base salary, as in effect immediately prior to the change in control or any higher base salary in effect following the change in control, by more than 10%; (ii) a relocation of the executive's principal place of employment that increases the executive's one-way commute by more than 35 miles; (iii) a substantial reduction in the executive's authority, duties or responsibilities that are in effect immediately prior to the change in control, provided that if the executive holds the same position but the size of the executive's employing entity or business unit has decreased significantly or our company or the executive's employing entity ceases to be a publicly-traded corporation, the executive's authority, duties and responsibilities will be considered to be substantially reduced; (iv) a reduction in the executive's title; or (v) a substantial increase in executive's required business travel as compared with the executive's required business travel prior to the change in control.

We benefit by requiring the executive to execute an effective general waiver and release of claims in order to be eligible to receive benefits under the change in control plan. All other benefits (such as life insurance, disability coverage and 401(k) Plan eligibility) will terminate as of the executive's termination date.

The change in control plan does not provide for the gross up of any excise taxes imposed by section 4999 of the Code. If any of the severance benefits payable under the change in control plan would constitute a "parachute payment" within the meaning of section 280G of the Code, subject to the excise tax imposed by section 4999 of the Code, the change in control plan provides for a best after-tax analysis with respect to such payments, under which the executive will receive whichever of the following two alternative forms of payment would result in executive's receipt, on an after-tax basis, of the greater amount of the transaction payment notwithstanding that all or some portion of the transaction payment may be subject to the excise tax: (i) payment in full of the entire amount of the transaction payment, or (ii) payment of only a part of the transaction payment so that the executive receives the largest payment possible without the imposition of the excise tax.

The executive would not receive benefits under the change in control plan in certain circumstances, including if (i) the executive voluntarily terminates employment with us to accept employment with another entity that is controlled, directly or indirectly, by us or is otherwise affiliated with us; (ii) the executive does not confirm in writing that he or she is subject to agreements with us relating to proprietary and confidential information and our code of conduct; or (iii) the executive does not return all company property. In addition, benefits would be terminated under the change in control plan if the executive willfully breaches his or her agreements with us relating to proprietary and confidential information or our code of conduct.

The structure and amount of benefits provided under the change in control plan are intended to balance our goals of attracting and retaining highly qualified individuals, providing the appropriate incentive for such individuals to perform in the best interests of our shareholders and maintaining responsible pay practices. Our compensation committee periodically reviews market data to gain a general understanding of the change in control benefits offered by our competitors and reviews the benefits offered under the change in control plan against such market data to ensure that the benefits under the change in control plan remain appropriate.

Equity Compensation Plans

The 2011 Plan and award agreements thereunder provide for potential vesting acceleration upon an executive's termination in connection with a change in control and, at the discretion of the board of directors, upon certain change in control events, as further described above under the heading "*Description of Compensation Arrangements—Equity Compensation Arrangements*." In addition, under the terms of the 2011 Plan and the option award agreements thereunder, the vested portion of stock options granted to the NEOs will generally expire three months after the applicable NEO's termination of service, subject to extension under limited circumstances such as if the sale of shares during such time was prohibited by our insider trading policy or if exercise would result in violation of securities registration requirements. We refer to the period following the NEO's termination during which he or she can continue to exercise his or her vested stock options as the post-termination exercise period. However, in termination situations involving the death or disability of an NEO, the post-termination exercise period is generally extended up to 12 months in connection with a termination due to disability and up to 18 months in connection with a termination due to death. As the value of such extended post-termination exercise periods is not quantifiable, such value is not included in the table below.

Treatment of 2021 and 2022 RSUs

The RSU award agreements applicable to the RSUs granted in 2021 and 2022 provide for vesting continuation or potential vesting acceleration upon an executive's death, disability or retirement. If an NEO's continuous service terminates due to death, such vesting of the RSUs will be accelerated in full, effective as of the date of such termination. If an NEO's continuous service terminates due to disability, the NEO's unvested RSUs will continue to vest pursuant to the original vesting schedule as provided in the RSU award grant notice. If, on or after the first anniversary of the date of grant of such RSUs, the NEO's continuous service terminates due to the NEO's Regular Retirement or NEO's Long-Service Retirement (each as defined below), then provided that (i) the NEO has given the company at least four months advance written notice of the NEO's intention to terminate her/his continuous service and (ii) the NEO executes and delivers a non-solicitation agreement satisfactory to the

company that will apply for a period of 12 months after the termination date, then the RSUs will be treated as follows: (1) In the case of an NEO's Regular Retirement, a pro-rata portion of each unvested tranche of RSUs will continue to vest pursuant to the original vesting schedule as provided in the grant notice. For each such unvested tranche of the RSUs, such pro-rata portion will be determined by reference to the number of RSUs in such unvested tranche of the award multiplied by the ratio of (x) the number of calendar days that have elapsed from the vesting commencement date through the date of an NEO's termination of continuous service divided by (y) the total number of calendar days in such vesting tranche (which, for clarity, will be equal to the number of calendar days that have elapsed from the vesting commencement date through the vesting date for such tranche), and rounded down to the nearest whole RSU. For purposes of the foregoing, "Regular Retirement" means an NEO's voluntary termination of continuous service, unless circumstances exist at the time of such termination that would constitute cause, following: (a) the NEO's completion of five years of continuous service and (b) the NEO's attainment of age 55. (2) In the case of the NEO's Long-Service Retirement, all of the NEO's unvested RSUs will continue to vest pursuant to the original vesting schedule as provided in the grant notice. For purposes of the Award, "Long-Service Retirement" means an NEO's voluntary termination of continuous service, unless circumstances exist at the time of such termination that would constitute cause, following: (a) the NEO's completion of 10 years of continuous service and (b) the NEO's attainment of age 55.

Treatment of 2021 and 2022 PSUs

The PSU award agreements applicable to the PSUs granted in 2021 and 2022 provide for vesting schedule adjustments or vesting acceleration benefits upon certain termination and change in control events. If a change in control occurs prior to the last day of the performance period and if the award is assumed or continued or substituted with a similar stock award in connection with such change in control, then the vesting schedule of the award will be revised in a manner as though the greater of (i) the number of target PSUs and (ii) the number of certified PSUs (as determined in accordance with the award agreement), or the CIC PSUs, had been subject solely to a vesting schedule pursuant to which the CIC PSUs would have vested on the last day of the performance period, subject to the NEO's continuous service through such date. In the event an NEO's service relationship with us or a successor entity is terminated due to an involuntary termination without cause (and other than due to death or disability) within 12 months following, or one month prior to, the effective date of a change in control (and in each case prior to the last day of the performance period), the CIC PSUs will become vested. If the NEO experiences an involuntary termination without cause or a constructive termination pursuant to the change in control plan prior to the last day of the performance period, the CIC PSUs will become vested.

In addition, if the NEO's continuous service terminates prior to the last day of the performance period due to death, then a number of PSUs will become vested in an amount equal to (i) the number of target PSUs, multiplied by (ii) a ratio, the numerator of which is the number of calendar days during the performance period that the NEO was in continuous service and the denominator of which is the total number of calendar days in the performance period, with the resulting number rounded up to the nearest whole PSU. If the NEO's continuous service terminates prior to the last day of the performance period due to the NEO's disability or retirement (as defined in the PSU award agreement), then effective as of the vesting date, a number of PSUs will become vested in an amount equal to (i) the number of certified PSUs determined in accordance with the award agreement, multiplied by (ii) a ratio, the numerator of which is the number of calendar days during the performance period that the NEO was in continuous service and the denominator of which is the total number of calendar days in the performance period, with the resulting number rounded up to the nearest whole PSU. With respect to the 2022 PSUs, the performance period for purposes of determining the prorated number of PSUs that will vest upon death, disability or retirement as described in this paragraph means the period commencing on (and including) the date of grant and ending on (and including) December 31, 2024.

Potential Payments upon Termination or Change in Control Table

The following table estimates the potential severance payments and benefits under the change in control plan to which the NEOs would have been entitled in connection with specified termination events, calculated as if each NEO's employment had terminated as of December 31, 2022. In addition, the table sets forth the amounts to which the NEOs would have been entitled under the 2011 Plan, if, upon a corporate transaction or change in control transaction, the board of directors had exercised its discretion to accelerate the vesting and exercisability

of stock options and the vesting of PSU awards and RSU awards, and such event had occurred on December 31, 2022. The table also reflects amounts relating to potential vesting acceleration of the 2021 and 2022 PSU awards and RSU awards, as described above.

There are no other agreements, arrangements or plans that entitle any NEOs to severance, perquisites or other benefits upon termination of employment or a change in control. For purposes of the table below, we have assumed that none of the potential severance benefits payable under the change in control plan would be subject to the excise tax imposed by section 4999 of the Code and therefore would not be reduced in accordance with the terms of the change in control plan.

POTENTIAL PAYMENTS UPON TERMINATION OR CHANGE IN CONTROL AS OF DECEMBER 31, 2022

Name	Benefit	Involuntary Termination Without Cause or Constructive Termination in Connection with a Change of Control($)[1][8]	Certain Corporate Transactions($)[2]	Death (No Change of Control) ($)[3]	Disability or Retirement (No Change of Control) ($)[4]
Bruce C. Cozadd	Lump Sum Cash Severance Payment	5,936,200	—	—	—
	COBRA Payments	85,732	—	—	—
	Vesting Acceleration[5]	32,580,905	32,580,905	17,370,651	11,666,431
	Benefit Total	38,602,837	32,580,905	17,370,651	11,666,431
Daniel N. Swisher, Jr.	Lump Sum Cash Severance Payment	3,467,000	—	—	—
	COBRA Payments	85,732	—	—	—
	Vesting Acceleration[5]	9,225,787	9,225,787	5,175,964	3,463,240
	Benefit Total	12,778,519	9,225,787	5,175,964	3,463,240
Renée Galá	Lump Sum Cash Severance Payment	2,101,210	—	—	—
	COBRA Payments	64,299	—	—	—
	Vesting Acceleration[5]	8,460,147	8,460,148	4,588,657	3,077,232
	Benefit Total	10,625,656	8,460,148	4,588,657	3,077,232
Robert Iannone, M.D., M.S.C.E	Lump Sum Cash Severance Payment	2,012,815	—	—	—
	COBRA Payments	61,170	—	—	—
	Vesting Acceleration[5]	7,727,471	7,727,471	4,175,509	2,831,735
	Benefit Total	9,801,456	7,727,471	4,175,509	2,831,735
Kim Sablich	Lump Sum Cash Severance Payment	1,825,000	—	—	—
	Cobra Payments	61,170	—	—	—
	Vesting Acceleration[5]	7,340,103	7,340,104	3,882,792	2,605,356
	Benefit Total	9,226,273	7,340,104	3,882,792	2,605,356

(1) These benefits would be payable under the change in control plan if the involuntary termination without cause or constructive termination occurred upon or within 12 months following a change in control and assuming such termination took place on December 31, 2022. The

forms of equity grant agreements under the 2011 Plan provide for the same vesting acceleration benefit as shown here under the change in control plan (except as otherwise described above under the heading, "Potential Payments upon Termination or Change in Control—Treatment of 2021 and 2022 PSUs"), therefore no separate vesting acceleration benefit is listed. Pursuant to the change in control plan, an involuntary termination without cause also includes an individual's death or disability.

(2) These benefits would be payable under the 2011 Plan, if, upon a corporate transaction event, including a change of control, the board of directors exercised its discretion to accelerate the vesting and exercisability of outstanding equity grant agreements, assuming the vesting acceleration took place on December 31, 2022. For a description of the potential vesting acceleration provisions in the 2011 Plan, see *"Description of Compensation Arrangements—Equity Compensation Arrangements*" above. As described above under "*Potential Payments upon Termination or Change in Control—Treatment of 2021 and 2022 PSUs*," the terms of the 2021 and 2022 PSUs provide for a vesting schedule adjustment if a change in control occurs prior to the last day of the performance period and if the award is assumed or continued or substituted with a similar stock award in connection with such change in control, Since this value of this vesting schedule adjustment is based on future events, including with respect to PSU award certification, no separate quantification of this benefit is shown. However, the value of the 2021 and 2022 PSU full vesting acceleration is included in the table.

(3) Represents the value of the 2021 and 2022 RSU vesting acceleration and pro-rated portion of 2021 and 2022 PSU vesting benefit upon death. Since the value of the extended post-termination option exercise period in this termination scenario is not quantifiable, such value is not included in the table.

(4) Represents the value of 2021 and 2022 RSU vesting continuation upon a termination due to disability as well as the value of 2021 RSU vesting continuation upon retirement. The value of 2022 RSU vesting continuation upon retirement is not included because the vesting continuation benefit in this termination scenario under the 2021 and 2022 RSUs does not arise until one year from the date of grant. The value of the 2021 and 2022 PSU vesting benefit upon retirement or a termination due to disability is not included because no PSUs were earned as of December 31, 2022. In addition, since the value of the extended post-termination option exercise period in this termination scenario is not quantifiable, such value is not included in the table.

(5) The value of equity grants vesting acceleration or continuation, as applicable, is based on the closing price of $159.31 per ordinary share on December 30, 2022, minus, in the case of stock options, the exercise price of the unvested stock option shares subject to acceleration.

Pay Ratio Disclosure

Under SEC rules, we are required to calculate and disclose the annual total compensation of our median employee, as well as the ratio of the annual total compensation of our median employee as compared to the annual total compensation of our CEO, or our CEO pay ratio. For 2022, to identify our median employee, we used the following methodology:

- To determine our total population of employees, we included all full-time, part-time, regular and temporary employees as of October 1, 2022.
- To identify our median employee from our employee population, we calculated the annual target amount of each employee's 2022 base salary (using a reasonable estimate of the hours worked and no overtime for hourly employees) and bonus or commission, as applicable, and added the estimated value of all equity awards granted during 2022. For purposes of base salaries, bonuses and commissions, we used an estimate based on the rates in effect on October 1, 2022. The value of equity awards was not included in the calculation of the median of the annual total compensation of our employees for 2022.
- In making this determination, we annualized the base salaries, bonuses and commissions of employees who were employed by us for less than the entire calendar year.
- Compensation paid in foreign currencies was converted to U.S. dollars based on the average daily exchange rates for the year-to-date period ending on October 1, 2022.

Using this approach, we determined our median employee and then calculated the annual total compensation of this employee for 2022 in accordance with the requirements of the Summary Compensation Table.

For 2022, the median of the annual total compensation of our employees (other than our CEO) was $236,307 and the annual total compensation of our CEO, as reported in our Summary Compensation Table, was $17,325,618. Based on this information, the ratio of the annual total compensation of our CEO to the median of the annual total compensation of all employees was 73 to 1.

The CEO pay ratio above represents our reasonable estimate calculated in a manner consistent with SEC rules and applicable guidance. SEC rules and guidance provide significant flexibility in how companies identify the median employee, and each company may use a different methodology and make different assumptions

particular to that company. As a result, and as explained by the SEC when it adopted these rules, in considering the pay ratio disclosure, shareholders should keep in mind that the rule was not designed to facilitate comparisons of pay ratios among different companies, even companies within the same industry, but rather to allow shareholders to better understand and assess each company's compensation practices and pay ratio disclosures.

Neither the compensation committee nor our management team used our CEO pay ratio measure in making compensation decisions.

Item 402(v) Pay versus Performance

The disclosure included in this section is prescribed by SEC rules and does not necessarily align with how the company or the compensation committee view the link between the company's performance and NEO pay. For additional information about our pay-for-performance philosophy and how we align executive compensation with company performance, refer to "*Executive Compensation—Compensation Discussion and Analysis"* section above.

Required Tabular Disclosure of Pay versus Performance

The table below reflects information regarding the compensation of our NEOs for fiscal years 2022, 2021 and 2020, as well as our financial performance for each of these fiscal years in accordance with SEC rules. The amounts set forth below under the headings "Compensation Actually Paid to PEO" and "Average Compensation Actually Paid for Non-PEO NEOs" have been calculated in a manner consistent with Item 402(v) of Regulation S-K. Use of the term "compensation actually paid" is required by the SEC's rules and as a result of the calculation methodology required by the SEC, such amounts differ from compensation actually received by the individuals and the compensation decisions described in "*Executive Compensation—Compensation Discussion and Analysis*" section above.

Year	Summary Compensation Table Total for PEO ($)[1]	Compensation Actually Paid to PEO($)[2]	Average Summary Compensation Table Total for Non-PEO NEOs($)[1]	Average Compensation Actually Paid to Non-PEO NEOs($)[2]	Value of Initial Fixed $100 Investment Based On:		GAAP Net Income/ (Loss) ($) (in thousands)[4]	Total Revenues($) (in thousands)[5]
					Total Shareholder Return ($)[3]	Peer Group Total Shareholder Return($)[3]		
2022	17,325,618	26,315,005	5,035,509	7,254,180	107	114	(224,060)	3,659,374
2021	15,679,311	4,921,238	4,544,613	2,655,063	85	126	(329,668)	3,094,238
2020	12,573,300	19,597,659	4,091,303	6,145,655	111	126	238,616	2,363,567

(1) For each fiscal year, represents amount reported for our principal executive officer (PEO) and average amount reported for our non-PEO NEOs, in each case in the Total column of the Summary Compensation Table. Our PEO for each of the applicable years is Bruce C. Cozadd. The non-PEO NEOs for 2022 were Daniel N. Swisher, Jr. Renee Gala, Robert Iannone and Kim Sablich; the non-PEO NEOs 2021 were Daniel N. Swisher, Jr. Renee Gala, Robert Iannone, and Chris Tovey; and the non-PEO NEOs for 2020 were Daniel N. Swisher, Jr. Renee Gala, Robert Iannone, and Kim Sablich.

(2) Amounts represent Compensation Actually Paid to our PEO and the average Compensation Actually Paid to our non-PEO NEOs for the relevant fiscal year. Compensation Actually Paid represents the amount reported in the Total column of the Summary Compensation Table for the applicable fiscal year, adjusted as shown below. Fair value or change in fair value, as applicable, of equity awards in the Compensation Actually Paid columns was determined as follows: (i) for RSUs, the closing price of our ordinary shares on the applicable fiscal year-end date, or, in the case of vesting RSUs, the closing price of our ordinary shares on the applicable vesting date; (ii) for PSUs, the closing fair value of the awards using a Monte-Carlo simulation method, multiplied by a factor reflecting achievement of the probable outcome of the cumulative performance objective as of the measurement date; and (iii) for stock options, the closing fair value of the stock

options based on a Black-Scholes option pricing model on the applicable fiscal year-end date, or, in the case of vesting stock options, the closing fair value on the applicable vesting date. Details of the adjustments made to the Summary Compensation Table are as follows:

Adjustments	2022		2021		2020	
	PEO ($)	Average Non-PEO NEOs ($)	PEO ($)	Average Non-PEO NEOs ($)	PEO ($)	Average Non-PEO NEOs ($)
Total compensation as reported in the Summary Compensation Table (SCT)	17,325,618	5,035,509	15,679,311	4,544,613	12,573,300	4,091,303
(Deduct): Grant date fair value of awards as reported in the Stock Awards and Option Awards columns in the SCT for applicable fiscal year (FY)	(14,873,643)	(3,865,859)	(13,414,116)	(3,505,027)	(10,091,856)	(3,037,957)
Add: ASC 718 fair value of awards granted during applicable FY that remain unvested as of applicable FY-end, determined as of applicable FY-end	18,049,908	4,691,422	9,742,948	2,802,063	17,526,705	5,048,743
Add/(deduct): ASC 718 fair value of awards granted during prior FYs that were outstanding and unvested as of applicable FY-end, determined based on change in ASC 718 fair value from prior FY-end to applicable FY-end	3,823,712	996,931	(6,252,113)	(1,092,121)	1,921,083	221,269
Add/(deduct): ASC 718 fair value of awards granted during prior FYs that vested during applicable FY, determined based on change in ASC 718 fair value from prior FY-end to vesting date	1,989,410	396,177	(834,792)	(94,465)	(2,331,573)	(177,703)
Total adjustments	8,989,387	2,218,671	(10,758,073)	(1,889,550)	7,024,359	2,054,352
Compensation actually paid	**26,315,005**	**7,254,180**	**4,921,238**	**2,655,063**	**19,597,659**	**6,145,655**

(3) For the relevant fiscal year, represents the cumulative Total Shareholder Return of our ordinary shares and the NASDAQ Biotechnology Index at the end of each fiscal year. In each case, assume an initial investment of $100 on December 31, 2019, and reinvestment of dividends, if any.

(4) The amounts represent the GAAP net income (loss) as reported in the company's audited financial statements for the applicable fiscal year.

(5) As required by Item 402(v) of Regulation S-K, we have determined that the Company-Selected Measure is total revenues as reported in the company's audited financial statements for the applicable fiscal year.

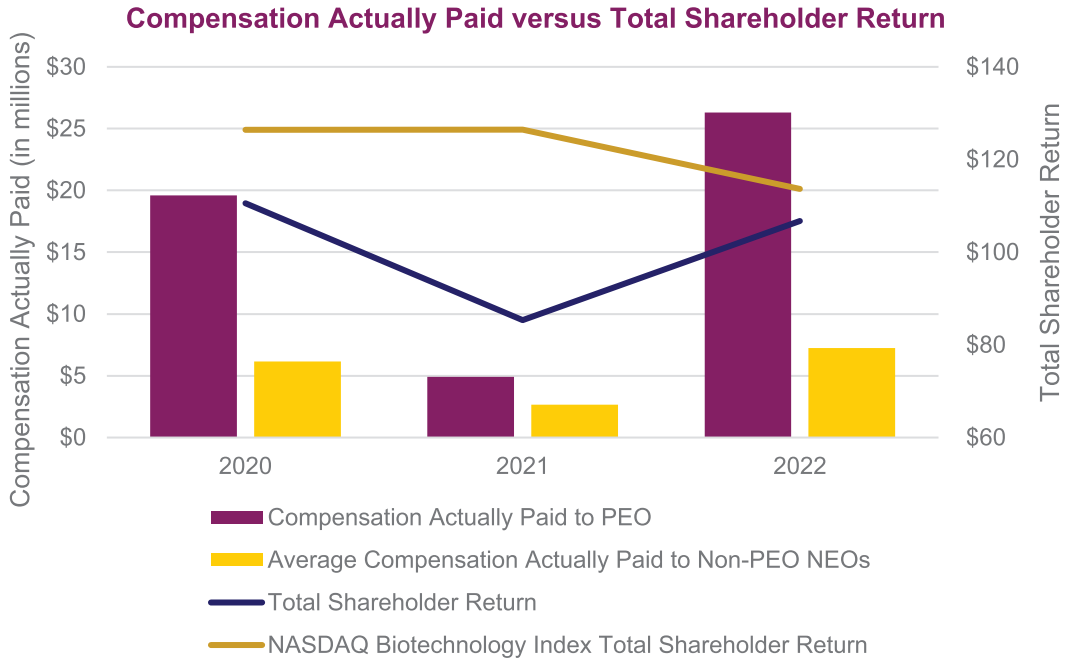
Required Tabular Disclosure of Most Important Measures

The most important financial and non-financial performance measures used by the company to link compensation actually paid to the company's NEOs for the most recently completed fiscal year to the company's performance are set forth below. For further information regarding these performance metrics and their function in our executive compensation program, please see *"Executive Compensation—Compensation Discussion and Analysis"* above.

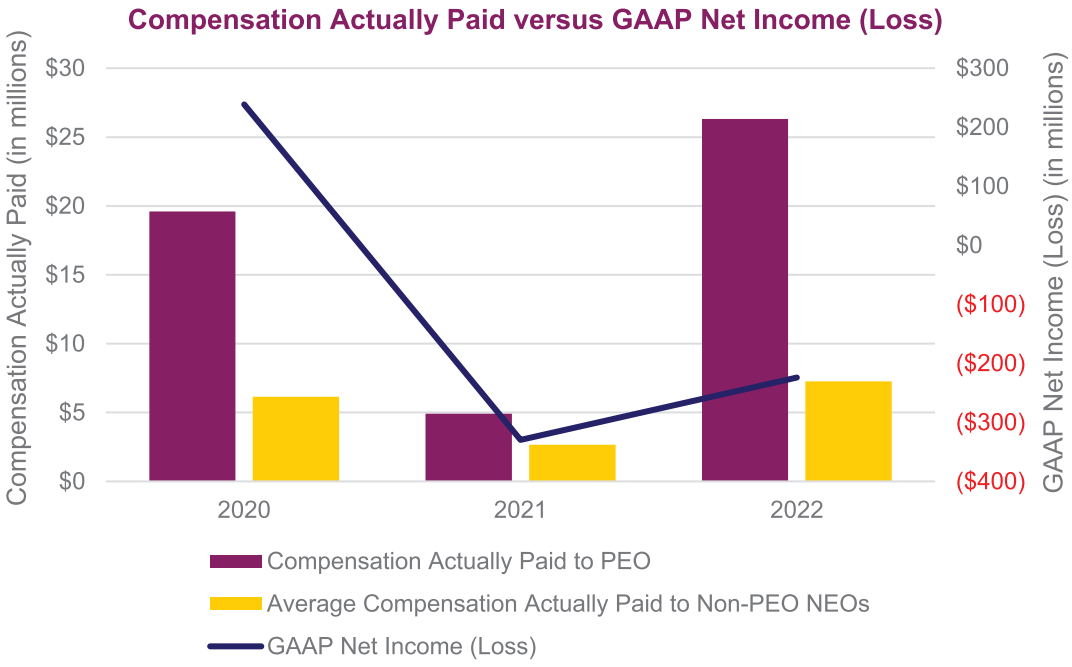
- Total Revenues
- Revenue (product- / therapeutic area-specific)
- Non-GAAP Adjusted Operating Margin
- Relative TSR
- 3 Year Revenue Compound Annual Growth Rate
- Pipeline Progression
- Regulatory Advancement

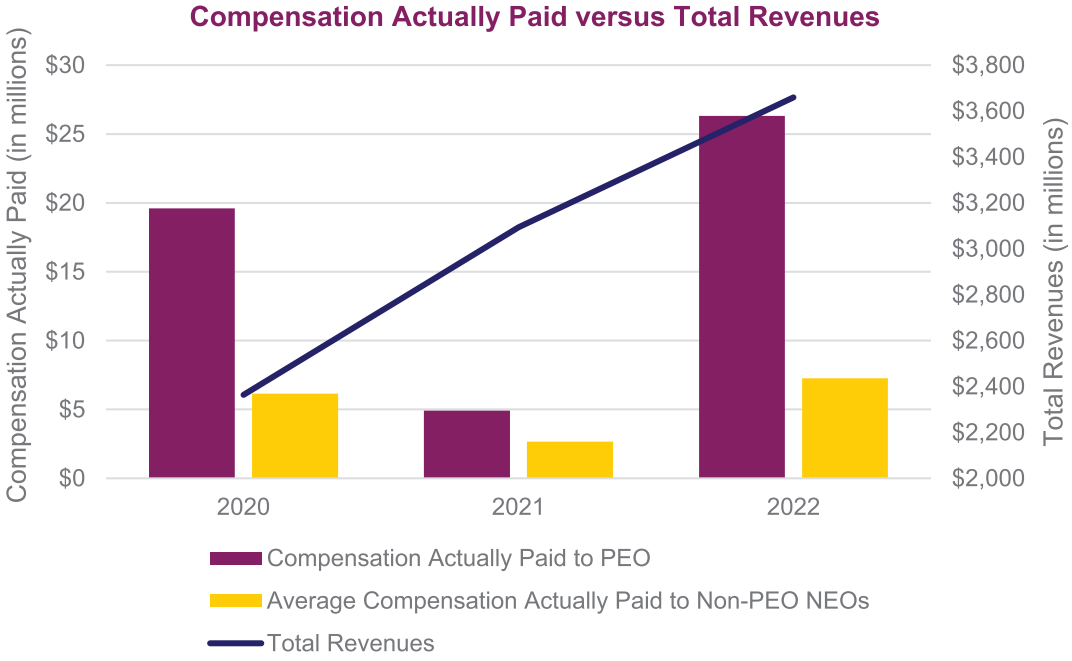
Disclosure of the Relationship Between Compensation Actually Paid and Financial Performance Measures

As required by Item 402(v) of Regulation S-K, we are providing the following graphs to illustrate the relationship between the pay and performance figures that are included in the pay versus performance tabular disclosure above. In addition, the first graph below further illustrates the relationship between company total shareholder return and that of the NASDAQ Biotechnology Index. As noted above, compensation actually paid for purposes of the tabular disclosure and the following graphs were calculated in accordance with SEC rules and do not fully represent the actual final amount of compensation earned by or actually paid to our NEOs during the applicable years.



Executive Compensation (continued)





All information provided above under the "Item 402(v) Pay Versus Performance" heading will not be deemed to be incorporated by reference into any filing of the company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing, except to the extent the company specifically incorporates such information by reference.

DIRECTOR COMPENSATION

Non-Employee Director Compensation Policy

Overview of Director Compensation. Our non-employee directors receive cash compensation and equity compensation for their service on the board of directors. The compensation committee reviews the compensation of our non-employee directors periodically and recommends changes to the board of directors when it deems appropriate. To assist with the compensation committee's and the board of directors' review, the compensation committee's external compensation consultant prepares a comprehensive annual assessment of our non-employee director compensation program. The assessment includes benchmarking director compensation against the same peer group used for executive compensation decision-making, an update in recent trends in director compensation and a review of related corporate governance best practices. We target compensation for service on our board of directors and committees generally at the 50th percentile for board service at companies in our peer group of companies.

Non-Employee Director Compensation Policy. Our non-employee director compensation policy, or director compensation policy, was originally approved by our board of directors in 2013 and has subsequently been amended, most recently in 2022 to add cash compensation for service on the recently formed science & medicine committee and to adjust cash compensation for service on the transaction committee. The equity grants made pursuant to the director compensation policy are granted under the Amended and Restated 2007 Non-Employee Directors Stock Award Plan, or 2007 Directors Plan.

Limit on Director Compensation. In any case, the aggregate value of all compensation granted or paid, as applicable, to any non-employee director with respect to any period commencing on the date of the annual general meeting of our shareholders for a particular year and ending on the day immediately prior to the date of the annual general meeting of our shareholders for the subsequent year, including equity awards granted and cash fees paid by us to the non-employee director, will not exceed (i) $750,000 in total value or (ii) in the event such non-employee director is first appointed or elected to the board of directors during that same period, $1,350,000 in total value.

Cash Compensation. Pursuant to our director compensation policy, each non-employee director was entitled to receive the following cash compensation for board services, as applicable, for 2022:

- $60,000 per year for service as a member of our board of directors;
- additional $50,000 per year for service as the Lead Independent Director;
- supplemental amounts for the chairs of the following board committees in the following amounts: $25,000 per year for the chairperson of the audit committee, $22,500 per year for the chairperson of the compensation committee, $20,000 per year for the chairperson of the nominating and corporate governance committee, $22,500 per year for the chairperson of the science & medicine committee and $5,000 per meeting, up to $20,000 per year, for the chairperson of the transaction committee (prior to April 2022, the chair of the transaction committee received $22,500 per year); and
- supplemental amounts for each member of the following board committees other than the chairs, in the following amounts: $15,000 per year for service as a member of the audit committee, $12,500 per year for service as a member of the compensation committee, $10,000 per year for service as a member of the nominating and corporate governance committee, $12,500 per year for service as a member of the science & medicine committee and $2,500 per meeting, up to $10,000 per year, for service as a member of the transaction committee (prior to April 2022, each member of the transaction committee received $12,500 per year).

The additional cash compensation described above for the non-employee director's service on the committees other than the transaction committee is paid in four equal quarterly installments, earned upon the completion of service each calendar quarter. The additional cash compensation for the non-employee director's service on the transaction committee is paid in four quarterly installments, earned upon the completion of services each calendar quarter.

Director Compensation (continued)

Equity Compensation—Size of Annual Grants. Each individual who is a non-employee director on the date of an annual general meeting of shareholders and continuing as a non-employee director following such meeting will receive an automatic annual grant in the form of an RSU having a target grant date value of $400,000, or an automatic continuing annual grant. Each person who is elected or appointed to be a non-employee director for the first time other than at an annual general meeting and is entitled to receive an automatic annual grant in the form of an RSU having a target grant date value of $400,000, prorated based on the number of days from the date of election or appointment until the date of the first anniversary of the prior annual general meeting of shareholders, or an automatic prorated annual grant. The actual share amounts underlying each annual grant are determined by dividing the target grant date value by the company's 30-day average share price ending on the grant date.

Equity Compensation—Terms of Annual Grants. The grant date of automatic continuing annual grants is the date of our annual general meeting and the grant date of automatic prorated annual grants is the second trading day following the filing date of our next quarterly or annual report filed under the Exchange Act that occurs after the date the director first joined our board of directors. Each automatic continuing annual grant vests in full on the first anniversary of the annual general meeting of our shareholders in the year an award is granted and each automatic prorated annual grant vests in full on the first anniversary of the annual general meeting of our shareholders held prior to the director's initial election or appointment, subject in each case to the non-employee director's continuous service through such dates. However, if a non-employee director does not stand for reelection at an annual general meeting of our shareholders in the year in which his or her term expires or otherwise resigns effective at an annual general meeting of our shareholders and, in either case, the non-employee director's continuous service terminates at such meeting, then effective as of the date of such meeting, any unvested portion of the annual grant will become vested in full. The other terms and conditions applicable to equity awards made to our non-employee directors are included below under the heading "*Equity Compensation Plans*."

Travel and Other Reasonable Expenses. In addition, our non-employee directors are reimbursed for travel and other reasonable expenses incurred in attending board or committee meetings, as are our employees who serve as directors. If any reimbursement payment is subject to tax imposed by the Irish Revenue Commissioners, each non-employee director is also entitled to a tax equalization payment in order to allow them to retain the full reimbursement payment. There were no such tax equalization payments made to any of our non-employee directors with respect to any reimbursement payments in 2022.

Directors Continuing Education

In furtherance of our ongoing commitment to the continuing education of our directors, our nominating and corporate governance committee adopted a policy for the reimbursement of director continuing education. Under this policy, we will pay or reimburse each director for enrollment fees and reasonable expenses incurred in connection with attending and participating each year in one director continuing education program and in one healthcare industry continuing education program, each sponsored by an outside provider.

Ownership Guidelines for Directors

We maintain share ownership guidelines for our non-employee directors which require each non-employee director to own a number of the company's ordinary shares with a value equal to five times his or her annual cash retainer within five years of first becoming subject to the guidelines. As of March 31, 2023, each non-employee director was in compliance with his or her share ownership requirement under the applicable guidelines, except for Ms. Cook and Dr. Smith who joined our board of directors in December 2020 and, accordingly, have five years from their appointment, or until 2025, to comply with the guidelines.

Equity Compensation Plans

The 2007 Directors 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. Equity awards under our director compensation policy described above are granted under the 2007 Directors Plan.

Director Compensation (continued)

With respect to options granted under the 2007 Directors Plan, if a non-employee director's service relationship with us or any of our affiliates, whether as a non-employee director or subsequently as our employee, director or consultant or that of any of our affiliates, ceases for any reason other than disability or death, or after any 12-month period following a change in control, the optionee may exercise any vested options for a period of three months following the cessation of service. If such optionee's service relationship with us, or any of our affiliates, ceases due to disability or death (or an optionee dies within a certain period following cessation of service), the optionee or a beneficiary may exercise the option for a period of 12 months in the event of disability, and 18 months in the event of death. With respect to options granted under the 2007 Directors Plan, if such optionee's service terminates within 12 months following a specified change in control transaction, the optionee may exercise any vested portion of the option for a period of 12 months following the effective date of such a transaction. The option term may be extended in the event that exercise of the option following termination of service is prohibited by applicable securities laws. In no event, however, may an option be exercised beyond the expiration of its term.

With respect to RSU awards granted under the 2007 Directors Plan, if a non-employee director's service relationship with us or any of our affiliates, whether as a non-employee director or subsequently as our employee, director or consultant or that of any of our affiliates, ceases for any reason, any RSU awards that were unvested as of the date of such termination will be forfeited. RSU awards granted pursuant to the director compensation policy are also subject to potential acceleration, as described above under the heading, "*Equity Compensation—Terms of Annual Grants.*"

In the event of certain significant corporate transactions (which generally have a meaning similar to "corporate transaction" under the 2011 Plan), all outstanding awards under the 2007 Directors Plan may be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue or substitute for such awards, then (a) with respect to any such awards that are held by participants then performing services for us or our affiliates, the vesting and exercisability of such awards will be accelerated in full and such awards will be terminated if not exercised (if applicable) prior to the effective date of the corporate transaction and (b) all other outstanding awards will terminate if not exercised prior to the effective date of the corporate transaction. The board of directors may also provide that the holder of an outstanding award not assumed in the corporate transaction will surrender such award in exchange for a payment equal to the excess of (i) the value of the property that the holder would have received upon exercise of the award, over (ii) the exercise price otherwise payable in connection with the exercise. In addition, the vesting and exercisability of awards under the 2007 Directors Plan held by non-employee directors who are either required to resign their position as a condition of a specified change in control transaction (which generally has a similar meaning as a "change in control" under the 2011 Plan) or are removed from their position in connection with such a change in control will be accelerated in full.

2022 Equity Grants

In accordance with our non-employee director compensation policy described above, we made automatic continuing annual grants to each of our non-employee directors as a result of their continuing on the board of directors through our annual general meeting in July 2022, which grants consisted of an RSU award covering 2,561 ordinary shares. All RSUs granted to non-employee directors during 2022 were granted under the 2007 Directors Plan.

Director Compensation Table

The following table sets forth certain information with respect to the compensation of all of our non-employee directors for the fiscal year ended December 31, 2022.

Mr. Cozadd, our Chairperson and CEO, is not listed in the following table because he is our employee. Mr. Cozadd's compensation is described under "*Executive Compensation*." Mr. Cozadd received no additional compensation for serving on our board of directors in 2022.

Director Compensation (continued)

DIRECTOR COMPENSATION FOR FISCAL 2022

Name	Fees Earned Or Paid in Cash ($)[1]	Stock Awards ($)[2][3]	Total ($)
Jennifer E. Cook	87,641	393,677	481,318
Patrick G. Enright	87,500	393,677	481,177
Peter Gray	95,782	393,677	489,459
Heather Ann McSharry	105,782	393,677	499,459
Seamus Mulligan	89,186	393,677	482,863
Kenneth W. O'Keefe	75,000	393,677	468,677
Anne O'Riordan	81,744	393,677	475,421
Norbert G. Riedel, Ph.D.	94,910	393,677	488,587
Mark D. Smith, M.D.	78,429	393,677	472,106
Catherine A. Sohn, Pharm.D.	84,160	393,677	477,837
Rick E Winningham	128,429	393,677	522,106

Note: Amounts may not total due to rounding.

(1) The dollar amounts in this column represent each non-employee director's actual cash compensation earned for board services in 2022, which is equal to the aggregate of $60,000 per year for service as a member of the board plus supplemental amounts for his or her service on one or more board committees, and for Mr. Winningham, for service as Lead Independent Director. Each non-employee director's cash compensation was earned and payable in four quarterly installments, as further described above. Fees paid to each of Ms. McSharry, Ms. O'Riordan and Messrs. Gray and Mulligan were paid in Euro. The conversion to U.S. dollars was calculated based on the average exchange rate for each quarter as reported by the OANDA Corporation.

(2) The dollar amounts in this column reflect the aggregate grant date fair value of RSU awards computed in accordance with FASB ASC 718. The grant date fair value of each RSU award is measured based on the closing price of our ordinary shares on the date of grant. These amounts do not necessarily correspond to the actual value recognized or that may be recognized by the non-employee directors.

(3) The aggregate number of shares subject to outstanding stock options and RSU awards held by the non-employee directors listed in the table above as of December 31, 2022 was as follows: 37,850 shares subject to outstanding stock options and 2,561 shares subject to outstanding RSUs for Mr. Mulligan; 15,305 shares subject to outstanding stock options and 2,561 shares subject to outstanding RSUs for Mr. Enright; 33,350 shares subject to outstanding stock options and 2,561 shares subject to outstanding RSUs for Mr. O'Keefe; 28,850 shares subject to outstanding stock options and 2,561 shares subject to outstanding RSUs for each of Dr. Sohn, Mr. Winningham, Ms. McSharry, Mr. Gray and Dr. Riedel; 6,475 shares subject to outstanding stock options and 3,424 shares subject to outstanding RSUs for each of Ms. Cook and Dr. Smith; and 18,670 shares subject to outstanding stock options and 2,561 shares subject to outstanding RSUs for Ms. O'Riordan.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Policy and Procedures for Review of Related Party Transactions

We have adopted a Related Party Transaction Policy that sets forth our procedures for the identification, review, consideration and approval or ratification of "related-person transactions." For purposes of our policy, a "related-person transaction" is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we are, were or will be a participant, and the amount involved exceeds $120,000, and any "related person" had, has or will have a direct or indirect material interest. Transactions involving compensation for services provided to us as an employee or director are not covered by this policy. A related person who has a position or relationship with a firm, corporation or other entity that engages in a transaction with us will not be deemed to have an indirect material interest in such transaction under this policy where the interest arises solely where: (i) if such entity is not a partnership, such related person's position as a director of such entity and/or the direct or indirect ownership by such related person and all other related persons,

in the aggregate, of less than a 10% equity interest in such entity; or (ii) if such entity is a partnership, from such related person's position as a limited partner in such entity and such related person's and all other related persons have an interest in such entity of less than 10% in the aggregate, and the related person is not a general partner of and does not hold another position in such entity. A "related person" is any executive officer, director or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related-person transaction (including any transaction that was not a related-person transaction when originally consummated or any transaction that was not initially identified as a related-person transaction prior to consummation), our management team must present information regarding the related-person transaction to our audit committee (or, if audit committee approval would be inappropriate, to another independent body of our board of directors) for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related person(s), the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will, on an annual basis, collect information that our Chief Legal Officer, or CLO, deems reasonably necessary from each director, executive officer and (to the extent feasible) significant shareholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy. In addition, under our code of conduct, our employees and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest. In considering related-person transactions, our audit committee (or other independent body of our board of directors) will take into account the relevant available facts and circumstances including, but not limited to, the risks, costs and benefits to us, the terms of the transaction, the availability of other sources for comparable services or products and, if applicable, the impact on a director's independence in the event that the related person is a director, immediate family member of a director or an entity with which a director is affiliated.

The policy requires that, in determining whether to approve, ratify or reject a related-person transaction, our audit committee (or other independent body of our board of directors) must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our shareholders, as our audit committee (or other independent body of our board of directors) determines in the good faith exercise of its discretion. The policy also requires that directors interested in a related-person transaction will recuse themselves from any discussion or vote on a related-person transaction in which they have an interest.

Transactions with Related Persons; Indemnification

Transactions with Related Persons. Except as described under "*Executive Compensation*" and "*Director Compensation*" above except as would not be reportable in this proxy statement under SEC rules, since January 1, 2022, we have not engaged in any transactions, nor are any such transactions currently proposed, in which we were a participant and the amount involved exceeded $120,000, and in which any related person had or will have a direct or indirect material interest.

Indemnification Agreements. We have entered into indemnification agreements with our directors, executive officers and certain other of our officers and employees. These indemnification agreements require us, under the circumstances and to the extent provided for therein, to indemnify such persons to the fullest extent permitted by applicable law against certain expenses and other amounts incurred by any such person as a result of such person being made a party to certain actions, suits, proceedings and other actions by reason of the fact that such person is or was a director, officer, employee, consultant, agent or fiduciary of our company or any of our subsidiaries or other affiliated enterprises. The rights of each person who is a party to an indemnification agreement are in addition to any other rights such person may have under our Amended and Restated Memorandum and Articles of Association, the Irish Companies Act 2014, any other agreement, a vote of the shareholders of our company, a resolution of directors of our company or otherwise. We believe that these agreements are necessary to attract and retain qualified persons as our officers and directors. We also maintain directors' and officers' liability insurance.

PROPOSAL 2
RATIFY, ON A NON-BINDING ADVISORY BASIS, THE APPOINTMENT OF INDEPENDENT AUDITORS AND AUTHORIZE, IN A BINDING VOTE, THE BOARD OF DIRECTORS, ACTING THROUGH THE AUDIT COMMITTEE, TO DETERMINE THE INDEPENDENT AUDITORS' REMUNERATION

Pursuant to authority delegated by the board of directors, the audit committee of the board of directors is responsible for the appointment, remuneration and retention of our independent auditors. The audit committee has selected and appointed KPMG, a registered public accounting firm, as our independent auditors to audit our consolidated financial statements for the year ending December 31, 2023. Under Irish law, KPMG will be deemed to be reappointed as our independent auditors at the annual meeting without the necessity of a shareholder vote. However, our shareholders are being asked in this proposal to ratify such appointment on a non-binding advisory basis because we value our shareholders' views on the company's independent auditors. The board of directors and the audit committee intend to consider the results of this vote in making determinations in the future regarding the appointment of the company's independent auditors. In addition, our shareholders are being asked to authorize the board of directors, acting through the audit committee, to determine KPMG's remuneration. This authorization is required by Irish law.

KPMG has been engaged to audit our financial statements, beginning with our consolidated financial statements for the fiscal year ended December 31, 2012, since the consummation of the Azur Merger. Representatives of KPMG are expected to attend the annual meeting, will have an opportunity to make a statement if they so desire, and will be available to respond to appropriate questions.

Proposal 2 is an ordinary resolution and must receive the affirmative vote of a majority of the votes cast in person or by proxy at the annual meeting (including any adjournment thereof) in order to be approved.

Independent Registered Public Accounting Firm Fees and Services

In connection with the audit of our 2022 financial statements, we entered into an engagement agreement with KPMG (KPMG, Dublin, Ireland, Auditor Firm ID: 1116) which sets forth the terms under which KPMG performed audit and tax services for the company.

The following table represents aggregate fees billed to us for the years ended December 31, 2022 and 2021 by KPMG, our independent registered public accounting firm (in thousands):

	Year Ended December 31,	
	2022	2021
Audit Fees	$3,453	$4,039
Audit-Related Fees	109	176
Tax Fees	1,098	1,029
Tax compliance services	*1,056*	*881*
Tax advisory services	*42*	*148*
All Other Fees	3	3
Total Fees	$4,663	$5,247

Audit Fees: Consist of fees and expenses for professional services in respect of the audit of the company's consolidated financial statements and of our internal control over financial reporting, the review of quarterly consolidated financial statements and statutory audits.

Audit-Related Fees: Consist of fees for assurance and related services (e.g., due diligence services) that traditionally are performed by the independent accountant. More specifically, these services included: due diligence in connection with divestiture and consultation concerning financial accounting and reporting standards.

Tax Fees: Consist of fees and expenses for professional services for tax compliance, tax advice and tax planning. Tax compliance services consist of professional services related to domestic and international tax compliance, and assistance with domestic and international tax return preparation. Tax advisory service fees relate to tax advice and planning services provided to us in connection with certain transactions undertaken by the company in 2022 and 2021. During the year ended December 31, 2022, fees and expenses of approximately $1,056,000 were billed in connection with tax compliance services, and fees and expenses of approximately $42,000 were billed in connection with tax advice and planning services. During the year ended December 31, 2021, fees and expenses of approximately $881,000 were billed in connection with tax compliance services, and fees and expenses of approximately $148,000 were billed in connection with tax advice and planning services.

All Other Fees: Consist of fees for products and services other than the services described above. For the years ended December 31, 2022 and December 31, 2021, these fees were paid in connection with access to the online accounting and tax research tool of KPMG.

All of the services and fees described above were approved by our audit committee.

As shown in the table above, less than 1% of the total fees that KPMG billed us for in 2022 were for services other than audit, audit-related and tax compliance services.

Pre-Approval Policies and Procedures

Our audit committee has a policy and procedures for the pre-approval of audit and non-audit services rendered by our independent registered public accounting firm. Our policy generally requires the pre-approval of specified services in the defined categories of audit services, audit-related services, and tax services up to specified amounts. Pre-approval may also be given as part of the audit committee's approval of the scope of the engagement of the independent auditor or on an individual explicit case-by-case basis before the independent auditor is engaged to provide each service. The pre-approval of services may be delegated to one or more of the audit committee's members, but the decision must be reported to the full audit committee at its next scheduled meeting.

Independence

Our audit committee determined that the rendering of the services other than audit services by our independent registered public accounting firm is compatible with maintaining the principal accountant's independence.

The board of directors recommends a vote "FOR" Proposal 2.

PROPOSAL 3
NON-BINDING ADVISORY VOTE ON EXECUTIVE COMPENSATION

Overview

Under the Dodd-Frank Act and Section 14A of the Exchange Act, our shareholders are entitled to vote to approve, on a non-binding advisory basis, the compensation of our named executive officers, or NEOs, as disclosed in this proxy statement in accordance with the compensation disclosure rules of the SEC. This non-binding advisory vote is commonly referred to as a "say-on-pay" vote.

At our 2022 annual meeting of shareholders, our shareholders indicated their preference that we hold a non-binding say-on-pay vote every year and our board of directors has adopted a policy that is consistent with that preference. At our 2022 annual meeting of shareholders, the shareholders also overwhelmingly approved our say-on-pay proposal, with approximately 94% of the total votes cast voting in favor of the proposal.

This year, we are again asking our shareholders to vote "FOR" the advisory approval of the compensation of our NEOs as disclosed in the "*Compensation Discussion and Analysis*," the compensation tables and the related narrative disclosure contained in this proxy statement beginning on page 47. As discussed in those disclosures, our compensation committee designs our executive compensation program with the following objectives and philosophy:

- **Attract, incentivize, reward and retain diverse, talented individuals with relevant experience in the life sciences industry through a competitive pay structure.** We reward individuals fairly over time and seek to retain those individuals who continue to meet our high expectations.
- **Deliver balanced total compensation packages to accomplish our business objectives and mission.** Our executive compensation program focuses on *target total direct compensation*, combining short-term and long-term components, cash and equity, and fixed and variable payments, in the proportions that we believe are the most appropriate to incentivize and reward our executive officers for achieving our corporate goals while minimizing incentives for excessive risk-taking or unethical conduct.
- **Align pay with our performance.** Our annual performance bonus awards are not earned unless pre-determined levels of performance are achieved against annual corporate objectives approved by our board of directors at the beginning of the year. Likewise, our stock option awards will not provide realizable value and our restricted stock unit awards will not provide increased value unless there is an increase in the value of our shares, which benefits all shareholders. We also have executive share ownership guidelines to further support our ownership culture and align the interests of executive officers and shareholders. Further, beginning in 2021 we implemented a new performance-based equity program tied to the achievement of critical multi-year financial and other strategic objectives as well as relative total shareholder return goals, with performance-based restricted stock unit awards making up approximately 50% of each NEO's target annual equity grant, and time-vested restricted stock unit awards making up the other approximately 50%.

The compensation committee will continue to monitor our business and the design of our executive compensation program.

Say-on-Pay Vote

This vote is not intended to address any specific item of compensation, but rather the overall compensation of our NEOs and the philosophy, policies and practices described in this proxy statement. The board of directors is asking our shareholders to indicate their support for the compensation of our NEOs as described in this proxy statement by casting a non-binding advisory vote "FOR" the following resolution:

"**RESOLVED**, that the compensation paid to Jazz Pharmaceuticals' NEOs, as disclosed pursuant to Item 402 of Regulation S-K of the Exchange Act, including the Compensation Discussion and Analysis, compensation tables and narrative discussion, is hereby APPROVED."

Proposal 3 (continued)

Because the vote is advisory, it is not binding on the board of directors or the company. Nevertheless, the views expressed by our shareholders, whether through this vote or otherwise, are important to management and the board of directors and, accordingly, the board of directors and the compensation committee intend to consider the results of this vote in making determinations in the future regarding executive compensation arrangements.

Proposal 3 is an ordinary resolution and must receive the affirmative vote of a majority of the votes cast in person or by proxy at the annual meeting (including any adjournment thereof) in order to be approved.

Unless our board of directors changes the frequency of future advisory votes on the compensation of our NEOs, the next advisory vote on the compensation of our NEOs will be held at the 2024 annual meeting of shareholders.

The board of directors recommends a vote "FOR" Proposal 3.

PROPOSAL 4
BOARD AUTHORITY TO ISSUE SHARES FOR CASH WITHOUT FIRST OFFERING SHARES TO EXISTING SHAREHOLDERS

Background

As a matter of Irish law, when an Irish public limited company issues shares for cash (including rights to subscribe for, convert into or otherwise acquire any shares), unless otherwise authorized by shareholders, it is required first to offer those shares on the same or more favorable terms to existing shareholders of the company on a pro-rata basis (commonly referred to as the pre-emption right). Under Irish law, the authority to opt-out of the pre-emption right, which we call the pre-emption opt-out authority, can be granted by shareholders covering up to the maximum of a company's authorized but unissued ordinary share capital for a maximum period of five years, at which point it lapses unless renewed by shareholders.

At our 2022 AGM, our shareholders approved our board of director's authority to opt out of the pre-emption rights provision in the event of an issuance of shares for cash, up to the amount of 20% of our issued ordinary share capital in the aggregate, for a period of 18 months from the date of the 2022 AGM. Accordingly, our current pre-emption opt-out authority will expire on January 28, 2024, unless otherwise varied, renewed or revoked. The statutory pre-emption rights do not apply where shares are issued for non-cash consideration or pursuant to employee equity plans.

Renewal Request

Pursuant to this Proposal 4, we are seeking a renewal of our existing authority to opt out of the pre-emption rights provision in the event of an issuance of ordinary shares for cash, if the issuances are limited to up to 20% of our issued ordinary share capital in the aggregate, for a period expiring on the date being 18 months from the passing of the below resolution, unless otherwise varied, renewed or revoked.

Accordingly, Proposal 4 is much more limited than Irish law maximally allows for in terms of both amount and duration as it relates to pre-emption opt-out authorities. We expect to next propose renewal of the Board's pre-emption opt-out authority at our 2024 AGM.

We are not asking you to approve an increase in our authorized share capital or to approve a specific issuance of shares. Rather, approval of this Proposal 4 will simply provide our Board with certain continued flexibility to issue shares (subject to the board of directors' authority to allot and issue such shares approved by shareholders at our 2021 annual general meeting of shareholders) that are already within our authorized share capital for cash on a non-pre-emptive basis, in accordance with the terms described herein, to advance our business and drive shareholder value, including, if applicable, in connection with potential capital-raising and corporate development transactions.

Why Our Shareholders Should Approve this Proposal 4

Granting our board of directors the pre-emption opt-out authority on the terms set forth in this Proposal 4 is vital to the way we intend to advance our business. In this regard, our strategy for sustainable growth is rooted in executing commercial launches and ongoing commercialization initiatives; advancing robust research and development 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. 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. In this regard, strategic capital allocation will continue to be an important driver of our growth, including investing in our current pipeline and facilitating our ability to continue corporate development.

In any event, our strategy for growth depends in part on our ability to quickly take advantage of strategic opportunities, including potential acquisitions and other capital-intensive transactions that we believe would increase shareholder value. Many of these opportunities are highly competitive, with multiple parties often offering comparable or even the same economics.

If Proposal 4 is not approved, in each case where we propose to issue shares for cash consideration after January 28, 2024 and/or beyond the limits of our current pre-emption opt-out authority, we would first have to offer those shares on the same or more favorable terms to our existing shareholders pro-rata to their existing shareholdings following a specific Irish statutory procedure and timeline in the absence of a new shareholder approval to dis-apply the pre-emption rights provision to the issuance of those shares. This could put us at a distinct disadvantage vis-à-vis many of our peers in competing for acquisitions and similar transactions (particularly since many of the companies with which we compete strategically are listed and incorporated in the U.S. and are not subject to similar pre-emption right restrictions), and might make it difficult for us to complete such transactions in a timely manner or at all, thus potentially limiting our ability to further our strategy for growth by deploying capital to meet strategic goals that are in the best interests of our shareholders. Furthermore, we note that this pre-emption opt-out authorization is required as a matter of Irish law and is not otherwise required for U.S.-incorporated companies listed on Nasdaq or NYSE. And importantly, Jazz remains, like all U.S.-incorporated companies listed on Nasdaq, subject to compliance with Nasdaq listing rules, including the Nasdaq shareholder approval requirements related to equity issuances.

Supermajority Vote Standard; Special Resolution

As required under Irish law, Proposal 4 is a special resolution that requires the affirmative vote of at least 75% of the votes cast in person or by proxy at the AGM (including any adjournment thereof) in order to be approved. If Proposal 4 is approved, our current pre-emption opt-out authority approved at the 2022 AGM will be revoked effective upon the passing of the resolution set out below. If Proposal 4 is not approved, our current pre-emption opt-out authority approved at the 2022 AGM will continue to apply until January 28, 2024 unless otherwise varied, renewed or revoked following the AGM.

The board of directors is asking our shareholders to vote “FOR” the following special resolution:

“RESOLVED that the directors be and are hereby empowered pursuant to section 1023 of the Companies Act 2014 of Ireland (the 2014 Act) to allot equity securities (as defined in section 1023 of the 2014 Act) for cash, pursuant to the authority conferred by shareholders at Jazz Pharmaceuticals’ annual general meeting on July 29, 2021 in accordance with section 1021 of the 2014 Act, as if sub-section (1) of section 1022 of the 2014 Act did not apply to any such allotment, provided that this power shall be limited to the allotment of equity securities up to an aggregate nominal value of US$1,282.85 (12,828,534 shares) (being equivalent to approximately 20% of the aggregate nominal value of Jazz Pharmaceuticals’ issued ordinary share capital as at the last practicable date prior to the issue of the notice of this meeting), and the authority conferred by this resolution shall expire 18 months from the passing of this resolution, unless previously renewed, varied or revoked; provided that Jazz Pharmaceuticals may make an offer or agreement before the expiry of this authority, which would or might require any such securities to be allotted after this authority has expired, and in that case, the directors may allot equity securities in pursuance of any such offer or agreement as if the authority conferred hereby had not expired.”

The board of directors recommends a vote “FOR” Proposal 4.

PROPOSAL 5
ADJOURNMENT PROPOSAL

You are being asked to consider and vote upon an adjournment proposal.

This resolution proposes to approve any motion to adjourn the annual meeting, or any adjournments thereof, to another time and place to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4.

Proposal 4 is subject to the Irish law super majority voting regime of voting by special resolution, which requires no less than 75% of the votes of shareholders cast (in person or by proxy) at a general meeting to be voted "FOR" the proposal in order to be passed. Given the high vote threshold associated with Proposal 4, we are seeking your authority to adjourn the meeting to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4.

The board of directors is asking our shareholders to vote "FOR" the following ordinary resolution:

"**RESOLVED**, that any motion to adjourn the annual meeting, or any adjournments thereof, to another time and place to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4 set forth in this proxy statement, be approved."

Proposal 5 is an ordinary resolution and must receive the affirmative vote of a majority of the votes cast in person or by proxy at the annual meeting (including any adjournment thereof) in order to be approved.

The board of directors recommends a vote "FOR" Proposal 5.

QUESTIONS AND ANSWERS ABOUT THESE PROXY MATERIALS AND VOTING

Q: Why am I receiving these materials?

A: Our board of directors is soliciting your proxy to vote at the annual meeting, including at any adjournments or postponements of the annual meeting. This proxy statement contains important information regarding the annual meeting, the proposals on which you are being asked to vote, information you may find useful in determining how to vote and voting procedures.

Q: Why did I receive a notice in the mail regarding the internet availability of proxy materials instead of a full set of proxy materials?

A: We are pleased to take advantage of SEC rules that allow companies to furnish their proxy materials over the internet. Most of our shareholders will not receive paper copies of our proxy materials (unless requested), and will instead be sent a Notice of Internet Availability of Proxy Materials, or Notice. All shareholders receiving a Notice will have the ability to access the proxy materials on the website referred to in the Notice and to request a printed set of the proxy materials. Instructions on how to access the proxy materials via the internet or to request a printed set of the proxy materials may be found in the Notice.

Q: Why did I receive a full set of proxy materials in the mail instead of a notice regarding the internet availability of proxy materials?

A: We are providing shareholders who have previously requested a printed set of our proxy materials with paper copies of our proxy materials instead of a Notice.

Q: What is the annual report included in the proxy materials?

A: Under applicable U.S. securities laws, we are required to provide an annual report to security holders along with this proxy statement. We intend to satisfy this annual report requirement by providing the 2022 Annual Report on Form 10-K together with this proxy statement.

Q: How do I attend the annual meeting?

A: The annual meeting will be held on Thursday, August 3, 2023, at 9:45 a.m. local time at our corporate headquarters located at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland. For directions to attend the annual meeting in person, please contact our Investor Relations department at +353.1.634.7892 (Ireland) or +1.650.496.2800 (United States) or by email at investorinfo@jazzpharma.com. Information on how to vote in person at the annual meeting is discussed below. However, you do not need to attend the annual meeting to vote your shares and, as noted in the next question, we strongly recommend that you vote your shares in advance of the meeting as instructed below.

Q: Who can vote at the annual meeting?

A: Only shareholders of record at the close of business on June 7, 2023, the record date for the annual meeting, will be entitled to vote at the annual meeting.

Shareholders of Record: Shares registered in your name

If, at the close of business on June 7, 2023, your shares were registered directly in your name with our transfer agent, Computershare Trust Company, N.A., then you are a shareholder of record. As a shareholder of record, you may vote in person at the annual meeting or vote by proxy. Whether or not you plan to attend the annual meeting, we urge you to vote by proxy over the telephone or via the internet as instructed below, or, for those shareholders who receive a paper proxy card in the mail, by mailing a completed proxy card.

Beneficial Owners: Shares registered in the name of a broker, bank or other agent

If, at the close of business on June 7, 2023, your shares were held not in your name, but rather in an account at a brokerage firm, bank or other agent, then you are the beneficial owner of shares held in "street name" and a Notice is being sent to you by that broker, bank or other agent. The broker, bank or other agent holding your account is considered to be the shareholder of record for purposes of voting at the annual meeting. As a beneficial owner, you have the right to direct your broker, bank or other agent regarding how to vote the shares in your account as set forth in the voting instructions in the Notice from your broker, bank or other agent. You are also invited to attend the annual meeting. However, since you are not the shareholder of record, you may not vote your shares in person at the annual meeting unless you request and obtain a valid proxy from your broker, bank or other agent.

Q: What am I voting on?

A: There are five matters scheduled for a vote at the annual meeting:

- Election by separate resolutions of the four named nominees for director to hold office until the 2026 annual meeting of shareholders (*Proposal 1*).
- Ratification, on a non-binding advisory basis, of the appointment of KPMG as the independent auditors of the company for the fiscal year ending December 31, 2023 and the authorization, in a binding vote, of the board of directors, acting through the audit committee, to determine the independent auditors' remuneration (*Proposal 2*).
- Approval, on a non-binding advisory basis, of the compensation of our NEOs as disclosed in this proxy statement (*Proposal 3*).
- Granting to the board of directors authority under Irish law to allot and issue ordinary shares for cash without first offering those ordinary shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply (*Proposal 4*).
- Approval of any motion to adjourn the annual meeting, or any adjournments thereof, to another time and place to solicit additional proxies if there are insufficient votes at the time of the annual meeting to approve Proposal 4 (Proposal 5).

Q: What are the board's voting recommendations?

A: The board of directors recommends that you vote your shares "FOR" each of the director nominees named in this proxy statement to hold office until the 2026 annual meeting of shareholders, and "FOR" each of the other four proposals.

Q: What if another matter is properly brought before the annual meeting?

A: The board of directors knows of no other matters that will be presented for consideration at the annual meeting. If any other matters are properly brought before the annual meeting, it is the intention of the persons named in the accompanying proxy, referred to in this proxy statement as the "proxy holders," to vote on those matters in accordance with their best judgment.

Q: How do I vote?

A: For the election of directors (*Proposal 1*), you may vote "FOR" or "AGAINST" each nominee, or you may abstain from voting for all or any of the nominees. For each of the other four proposals, you may vote "FOR" or "AGAINST" or abstain from voting.

Shareholders of Record: Shares registered in your name

If you are a shareholder of record, you may vote in person at the annual meeting, you may vote by electronic proxy over the telephone or via the internet as instructed below, or, for those shareholders who receive a paper proxy card in the mail, by mailing a completed proxy card. Whether or not you plan to attend the

annual meeting, we urge you to vote by proxy to ensure your vote is counted. You may still attend the annual meeting and vote in person even if you have already voted by proxy. **However, as noted above, we recommend that you vote your shares by proxy in advance of the meeting**.

- To vote in person, come to the annual meeting and we will give you a ballot when you arrive. Please bring your admission ticket or proof of ownership, as further discussed under "*Do I need a ticket to attend the annual meeting?*" below.
- To vote using a proxy card, simply complete, sign and date the proxy card that was mailed to you and return it promptly in the envelope provided. Proxy cards must be received by August 2, 2023. If you return your signed proxy card before this time, we will forward it to the company's registered office electronically in accordance with Irish law and we will vote your shares as you direct.
- To vote by telephone, dial toll-free +1.800.690.6903 within the United States, U.S. territories and Canada using a touch-tone phone and follow the recorded instructions to submit an electronic proxy card. You will be asked to provide the company number and control number from the enclosed proxy card. Your vote must be received by 11:59 p.m., U.S. Eastern Time, on August 2, 2023 to be counted.
- To vote via the internet, go to www.proxyvote.com to complete an electronic proxy card. You will be asked to provide the company number and control number from the enclosed proxy card. Your vote must be received by 11:59 p.m., U.S. Eastern Time, on August 2, 2023 to be counted.

Beneficial Owners: Shares registered in the name of a broker, bank or other agent

If you are a beneficial owner of shares registered in the name of your broker, bank or other agent, you should have received a Notice or the full set of proxy materials containing voting instructions from that broker, bank or other agent rather than from us. Simply follow the voting instructions in the Notice or the full set of proxy materials to ensure that your vote is counted. Alternatively, you may vote by telephone or via the internet as instructed by your broker, bank or other agent. To vote in person at the annual meeting, you must request and obtain a valid proxy from your broker, bank, or other agent. Follow the voting instructions from your broker, bank or other agent, or contact your broker, bank or other agent to request a proxy form.

We provide internet proxy voting to allow you to vote your shares online, with procedures designed to ensure the authenticity and correctness of your proxy vote instructions. However, please be aware that you must bear any costs associated with your internet access, such as usage charges from internet access providers and telephone companies.

Q: How many votes do I have?

A: On each matter to be voted upon, you have one vote for each ordinary share you owned as of the close of business on June 7, 2023.

Q: If I am a shareholder of record and I do not vote, or if I return a proxy card or otherwise vote without giving specific voting instructions, what happens?

A: If you are a shareholder of record and you do not vote by completing your proxy card, vote by proxy via the internet or by telephone, or vote in person at the annual meeting, your shares will not be voted.

If you are a shareholder of record and you do not specify your vote on each proposal individually when voting by proxy via the internet or by telephone, or if you sign and return a proxy card without giving specific voting instructions, then the proxy holders will vote your shares in the manner recommended by the board of directors on all matters presented in this proxy statement and as the proxy holders may determine in their discretion with respect to any other matters properly presented for a vote at the annual meeting. The voting recommendations of the board of directors are set forth under "*What are the board's voting recommendations?*" above.

Q: If I am a beneficial owner of shares held in street name and I do not provide my broker or bank with voting instructions, what happens?

A: If you are a beneficial owner of shares held in street name and you do not instruct your broker, bank or other agent how to vote your shares, your broker, bank or other agent may still be able to vote your shares in its discretion. In this regard, under the rules of the New York Stock Exchange (NYSE), brokers, banks and other securities intermediaries that are subject to NYSE rules may use their discretion to vote your "uninstructed" shares with respect to matters considered to be "routine" under NYSE rules, but not with respect to "non-routine" matters. In this regard, we have been advised by the NYSE that Proposals 1 and 3 are considered to be "non-routine" under NYSE rules meaning that your broker may not vote your shares on those proposals in the absence of your voting instructions. We have also been advised by the NYSE that Proposals 2, 4 and 5 are considered to be "routine" matters under NYSE rules meaning that if you do not return voting instructions to your broker by its deadline, your shares may be voted by your broker in its discretion on Proposals 2, 4 and 5.

If you are a beneficial owner of shares held in street name, in order to ensure your shares are voted in the way you would prefer, you must provide voting instructions to your broker, bank or other agent by the deadline provided in the materials you receive from your broker, bank or other agent.

Q: What does it mean if I receive more than one set of proxy materials, more than one Notice, or a combination thereof?

A: If you receive more than one set of proxy materials, more than one Notice, or a combination thereof, your shares may be registered in more than one name or are registered in different accounts. Please follow the voting instructions on each set of proxy materials or Notices to ensure that all of your shares are voted.

Q: Can I change my vote after submitting my proxy?

A: Yes. You can revoke your proxy at any time before the commencement of the annual meeting. If you are the record holder of your shares, you may revoke your proxy in any one of the following ways:

- You may submit another properly completed proxy card with a later date.
- You may grant a subsequent proxy by telephone or via the internet.
- You may send a timely written notice that you are revoking your proxy to our Company Secretary at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland.
- You may attend the annual meeting and vote in person. Simply attending the annual meeting will not, by itself, revoke your proxy.

Your most recent proxy card or telephone or internet proxy is the one that is counted. If your shares are held by your broker, bank or other agent as a nominee or agent, you should follow the instructions provided by your broker, bank or other agent.

Q: Do I need a ticket to attend the annual meeting?

A: Yes, you will need an admission ticket or proof of ownership of ordinary shares to enter the annual meeting. If you are a shareholder of record and you received a full set of proxy materials in the mail, your admission ticket is attached to the proxy card sent to you. If you plan to attend the annual meeting, please so indicate when you vote and bring the ticket and valid photo identification with you to the annual meeting. If you are a shareholder of record and you received a Notice in the mail, your admission ticket is your Notice. Please bring your Notice and valid photo identification with you to the annual meeting. If your shares are held in the name of a bank, broker or other holder of record, your admission ticket is on your voting instruction form. If you do not bring your admission ticket, you will need proof of ownership to be admitted to the annual meeting. A recent brokerage statement or letter from a bank or broker is an example of proof of ownership. If you arrive at the annual meeting without an admission ticket, we will admit you only if we are able to verify that you are a shareholder of our company. For directions to attend the annual meeting in person, please contact our

Investor Relations department at +353.1.634.7892 (Ireland) or +1.650.496.2800 (United States) or by email at investorinfo@jazzpharma.com.

Q: How are votes counted?

A: Votes will be counted by the inspector of elections appointed for the meeting. The inspector of elections will separately count, with respect to the proposal to elect directors (*Proposal 1*), votes "FOR," "AGAINST," abstentions and broker non-votes; and, with respect to each of the other proposals, votes "FOR," "AGAINST," abstentions, and, as applicable, broker non-votes.

Q: What are "broker non-votes"?

A: As discussed above, when a beneficial owner of shares held in street name does not give voting instructions to his or her broker, bank or other securities intermediary holding his or her shares as to how to vote on matters deemed to be "non-routine" under NYSE rules, the broker, bank or other such agent cannot vote the shares. These un-voted shares are counted as "broker non-votes." We have been advised by the NYSE that Proposals 1 and 3 are considered to be "non-routine" under NYSE rules and we therefore expect broker non-votes in connection with those proposals.

As a reminder, if you are a beneficial owner of shares held in street name, in order to ensure your shares are voted in the way you would prefer, you must provide voting instructions to your broker, bank or other agent by the deadline provided in the materials you receive from your broker, bank or other agent.

Q: How many votes are needed to approve each proposal?

A: Assuming that a quorum is present at the annual meeting, the following votes will be required for approval:

Proposal	Vote Required for Approval
Proposal 1	Each director nominee must receive the affirmative vote of a majority of the votes cast on his or her election to hold office until the 2026 annual meeting of shareholders.
Proposal 2	Affirmative vote of a majority of the votes cast
Proposal 3	Affirmative vote of a majority of the votes cast
Proposal 4	Affirmative vote of 75% of the votes cast
Proposal 5	Affirmative vote of a majority of the votes cast

Q: What are the treatment and effect of abstentions and broker non-votes?

A: Abstentions and broker non-votes will be treated as shares present for purposes of determining the presence of a quorum for the transaction of business at the annual meeting. Abstentions and broker non-votes will not, however, be considered votes cast at the annual meeting. Because the approval of all of the proposals is based on the votes cast at the annual meeting, abstentions and, as applicable, broker non-votes will not have any effect on the outcome of voting on the proposals.

Q: What is the quorum requirement?

A: A quorum of shareholders is necessary to hold a valid meeting. A quorum will be present if shareholders holding a majority of the issued and outstanding ordinary shares entitled to vote as of the record date are present at the annual meeting or represented by proxy. On the record date, there were 64,139,500 ordinary shares outstanding and entitled to vote. Your shares will be counted towards the quorum only if you submit a valid proxy (or if one is submitted on your behalf by your broker, bank or other agent) or, provided that you are a shareholder of record, if you vote in person at the annual meeting. Abstentions and broker non-votes will be counted towards the quorum requirement. If there is no quorum within one hour of the time scheduled for the annual meeting, the annual meeting will stand adjourned to August 10, 2023 at 9:45 a.m. local time at the same location, or such other time or place as the board of directors may determine.

Q: How can I find out the results of the voting at the annual meeting?

A: Preliminary voting results will be announced at the annual meeting. In addition, final voting results will be published in a quarterly report on Form 10-Q or a current report on Form 8-K that we expect to file with the SEC within four business days after the annual meeting. If final voting results are not available to us in time to file a Form 10-Q or a Form 8-K within four business days after the annual meeting, we intend to file a Form 8-K to publish preliminary results and, within four business days after the final results are known to us, file an additional Form 8-K to publish the final results.

Q: What are the Irish statutory financial statements and where can I access them?

A: We are presenting for consideration our Irish statutory financial statements, and the respective reports of the directors and the auditors thereon, at the annual meeting. Since we are an Irish company, we are required to prepare Irish statutory financial statements under applicable Irish company law and to deliver those financial statements together with the respective reports of the directors and the auditors thereon to shareholders of record in connection with our annual meetings of shareholders. The Irish statutory financial statements cover the results of operations and financial position of Jazz Pharmaceuticals plc for the year ended December 31, 2022. The Irish statutory financial statements were prepared in accordance with the International Financial Reporting Standards as adopted by the European Union and as applied in accordance with the 2014 Act. There is no requirement under Irish law that the Irish statutory financial statements be approved by the shareholders, and no such approval will be sought at the annual meeting.

Our Irish statutory financial statements, and the respective reports of the directors and the auditors thereon, will be delivered to shareholders of record in accordance with our obligations under Irish law. We will mail without charge, upon written request, a copy of the Irish statutory financial statements, together with the respective reports of the directors and the auditors thereon, to beneficial “street name” owners of our shares. Requests should be sent to: Jazz Pharmaceuticals plc, Attention: Company Secretary, Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland.

Q: What proxy materials are available on the internet?

A: This proxy statement, our letter to shareholders and the 2022 Annual Report on Form 10-K are available at https://materials.proxyvote.com/G50871.

Q: Who should I call if I have any questions?

A: If you require any assistance in voting your shares or have any other questions, please contact Alliance Advisors, our proxy solicitor, at +1.855.600.8108.

OTHER MATTERS

Presentation of Irish Statutory Financial Statements

Our Irish statutory financial statements for the fiscal year ended December 31, 2022, together with the reports of the directors and auditors thereon, will be presented and considered at the annual meeting in accordance with the requirements of the 2014 Act. Our Irish statutory financial statements have been approved by the board of directors. There is no requirement under Irish law that such statements be approved by shareholders, and no such approval will be sought at the annual meeting.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, executive officers and persons who beneficially own more than 10% of the outstanding shares of our ordinary shares to file reports of their stock ownership and changes in their ownership of our ordinary shares with the SEC. Based solely on a review of the reports filed for fiscal year 2022 and related written representations, we believe that all Section 16(a) reports were filed on a timely basis, except for a late filing due to an inadvertent administrative error of one Form 4 (each) to report the grant of time-based restricted stock unit awards ("RSUs") to our executive officers at such time (namely: Bruce C. Cozadd, Daniel N. Swisher, Jr., Renée Galá, Robert Iannone, Neena M. Patil, Kim Sablich, Chris Tovey, Patricia Carr, Finbar Larkin and Samantha Pearce) in March 2022.

Registered and Principal Executive Offices

The registered and principal executive offices of Jazz Pharmaceuticals plc are located at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland. Our telephone number there is +353.1.634.7800.

Shareholder Proposals and Director Nominations for the 2024 Annual Meeting

Our shareholders may submit proposals on matters appropriate for shareholder action at shareholder meetings in accordance with Rule 14a-8 promulgated under the Exchange Act. For such proposals to be included in our proxy materials relating to our 2024 annual meeting of shareholders, all applicable requirements of Rule 14a-8 must be satisfied and, pursuant to Rule 14a-8, such proposals must be received by us no later than February 21, 2024. However, if our 2024 annual meeting of shareholders is not held between July 4, 2024 and September 2, 2024, then the deadline will be a reasonable time prior to the time that we begin to print and mail our proxy materials. Such proposals should be delivered to Jazz Pharmaceuticals plc, Attention: Company Secretary, Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland.

Our articles provide that shareholder nominations of persons to be elected to the board of directors at an annual meeting must be made following written notice to our Company Secretary which is executed by a shareholder and accompanied by certain background and other information specified in our articles. Such written notice and information must be received by our Company Secretary not later than the close of business on March 22, 2024 nor earlier than January 22, 2024; provided, however, that in the event our 2024 annual meeting of shareholders is not held between July 4, 2024 and September 2, 2024, notice must be delivered no earlier than 150 days prior to nor later than the later of 90 days prior to the date of the 2024 annual meeting or the 10th day following the day on which public announcement of the date of such meeting is first made. In addition to satisfying the informational requirements in our articles, shareholders intending to solicit proxies in support of director nominees other than our nominees must provide in their notice any additional information required by Rule 14a-19(b) promulgated under the Exchange Act. Our articles provide that other proposals may only be proposed at an annual meeting if either (i) it is proposed by or at the direction of our board of directors; (ii) it is proposed at the direction of the Irish High Court; or (iii) the chairperson of the meeting decides, in his or her absolute discretion, that the proposal may properly be regarded as within the scope of the relevant meeting. In addition, the proxy solicited by our board of directors for the 2024 annual meeting of shareholders will confer discretionary voting authority with respect to (i) any proposal presented by a shareholder at that meeting for which we have not been provided with notice by May 6, 2024 and (ii), if we have received notice of such proposal by May 6, 2024, any matter, provided that (i) the 2024 proxy statement briefly describes such matter and how management's proxy holders intend to vote on it and

Other Matters (continued)

(ii) the shareholder does not comply with the requirements of Rule 14a-4(c)(2) promulgated under the Exchange Act. On any other business which may properly come before the 2024 annual meeting of shareholders, or any adjournment thereof, and whether procedural or substantive in nature (including without limitation any motion to amend a resolution or adjourn the meeting) not specified in this proxy statement, the proxy holder will act at his or her discretion.

Householding of Proxy Materials

The SEC has adopted rules that permit companies and intermediaries (such as brokers) to satisfy the delivery requirements for Notices and proxy materials with respect to two or more shareholders sharing the same address by delivering a single Notice or a single set of proxy materials, as applicable, addressed to those shareholders. This process, which is commonly referred to as "householding" potentially means extra convenience for shareholders and cost savings for companies.

A number of brokers with account holders who are Jazz Pharmaceuticals shareholders will be "householding" Notices and our proxy materials. A single Notice or a single set of proxy materials, as applicable, may be delivered to multiple shareholders sharing an address unless contrary instructions have been received from the affected shareholders. Once you have received notice from your broker that it will be "householding" communications to your address, "householding" will continue until you are notified otherwise or until you revoke your consent. If, at any time, you no longer wish to participate in "householding" and would prefer to receive a separate Notice or set of proxy materials, as applicable, in the future you may: (1) notify your broker, (2) direct your written request to Jazz Pharmaceuticals plc, Attention: Investor Relations, Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland or (3) contact our Investor Relations department at +353.1.634.7892 (Ireland) or +1.650.496.2800 (United States) or by email at investorinfo@jazzpharma.com. Shareholders who currently receive multiple copies of Notices or proxy materials at their address and would like to request "householding" of their communications should contact their broker. In addition, we will promptly deliver, upon written or oral request to the address or telephone number above, a separate copy of a Notice or set of proxy materials to a shareholder at a shared address to which a single Notice or set of proxy materials, as applicable, was delivered.

Annual Report on Form 10-K

We will mail without charge, upon written request, a copy of our 2022 Annual Report on Form 10-K, including the consolidated financial statements, schedules and list of exhibits, and any particular exhibit specifically requested. Requests should be sent to: Jazz Pharmaceuticals plc, Attention: Aislinn Doody, Company Secretary, Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland.

Special Note Regarding Forward-Looking Statements

This proxy statement contains forward-looking statements, including, but not limited to, statements related to our growth prospects and future financial and operating performance, including Vision 2025 and expectations related thereto; our strategy to create sustainable and enhanced growth and value, including statements related to the potential ways in which we intend to advance our business, grow and diversify our portfolio and revenues, and increase shareholder value; the goals of our ESG strategies, efforts and initiatives; our anticipated needs with respect to the issuance of our share capital and our ability to execute on our growth strategy; any potential future strategic opportunities, including potential acquisitions or other business development transactions; the anticipated benefits to us of our corporate development transactions and research and development efforts; the goals of I-CARE, our compliance and ethics program; the goals of our executive compensation programs; and other statements that are not historical facts. These forward-looking statements are based on our current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: maintaining or increasing sales of and revenue from our oxybate products, Zepzelca, Epidiolex/Epidyolex and other key marketed products; effectively launching and commercializing our other products and product candidates; the successful completion of development and regulatory activities with respect to our product candidates; obtaining and maintaining adequate coverage and reimbursement for our products; the time-consuming and uncertain regulatory

approval process, including the risk that our current and/or planned regulatory submissions may not be submitted, accepted or approved by applicable regulatory authorities in a timely manner or at all; the costly and time-consuming pharmaceutical product development and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients; global economic, financial, and healthcare system disruptions and the current and potential future negative impacts to the company's business operations and financial results; geopolitical events, including the conflict between Russia and Ukraine and related sanctions; macroeconomic conditions, including global financial markets, rising interest rates and inflation and recent and potential banking disruptions; regulatory initiatives and changes in tax laws; market volatility; protecting and enhancing our intellectual property rights and our commercial success being dependent upon obtaining, maintaining and defending intellectual property protection for our products and product candidates; delays or problems in the supply or manufacture of our products and product candidates; complying with applicable U.S. and non-U.S. regulatory requirements, including those governing the research, development, manufacturing and distribution of controlled substances; government investigations, legal proceedings and other actions; identifying and consummating corporate development transactions, financing these transactions and successfully integrating acquired product candidates, products and businesses; our ability to realize the anticipated benefits of our business development transactions and collaborations and license agreements with third parties; the effects of competitive products; the sufficiency of our cash flows and capital resources; challenges inherent in efficiently managing employees in diverse geographies and creating and maintaining a positive workplace culture; the aspirational nature of our ESG strategies, efforts and initiatives, which are not guarantees or promises that such goals, initiatives and objectives will be met; our ability to meet our projected long-term goals and objectives, including as part of Vision 2025, in the time periods that we anticipate, or at all, and the inherent uncertainty and significant judgments and assumptions underlying our long-term goals and objectives; our ability to identify, compete with others for, and successfully complete any potential future business development transactions; and other risks and uncertainties affecting us, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals' Securities and Exchange Commission filings and reports, including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2022, as supplemented by our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, and subsequent filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which we are not currently aware may also affect our forward-looking statements and may cause actual results and timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date of this proxy statement or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by us on our website or otherwise. We undertake no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in our expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

General

Your proxy is solicited on behalf of our board of directors. Unless otherwise directed, at the annual meeting (or any adjournment thereof), proxies will be voted "FOR" all of the nominees listed in Proposal 1 and "FOR" Proposals 2 through 5. If any matter other than those described in this proxy statement properly comes before the annual meeting (or any adjournment thereof), it is the intention of the persons named in the accompanying proxy to vote on such matters in accordance with their best judgment.

By order of the board of directors,

/s/ Aislinn Doody
Aislinn Doody, Company Secretary
Dublin, Ireland

June 16, 2023

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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.

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JAZZ PHARMACEUTICALS PLC
2022 ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

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.

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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.
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older.*	September 2019	EU, Great Britain, Israel, Australia and New Zealand
	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

Product	Indication(s)	Initial Approval Date	Market(s)
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.	July 2017	Canada
Defitelio® (defibrotide)	Treatment of hepatic sinusoidal obstruction syndrome (hepatic VOD).	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.

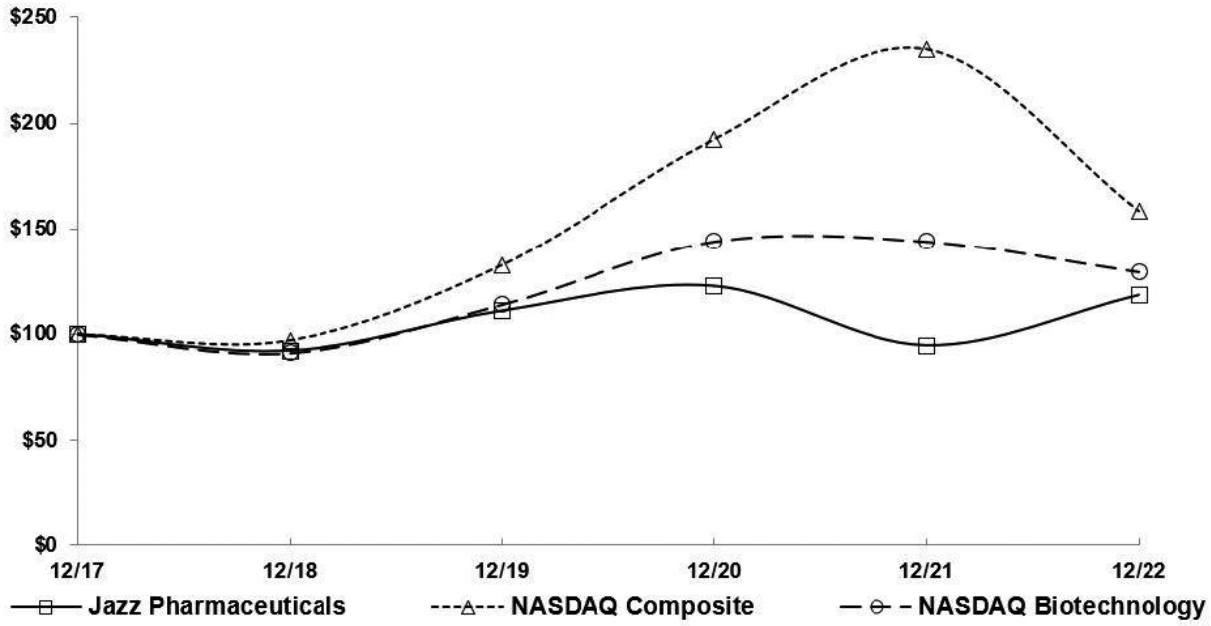
Stamp Duty. Irish stamp duty (if any) may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through Depository Trust Company, or DTC, to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp 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.

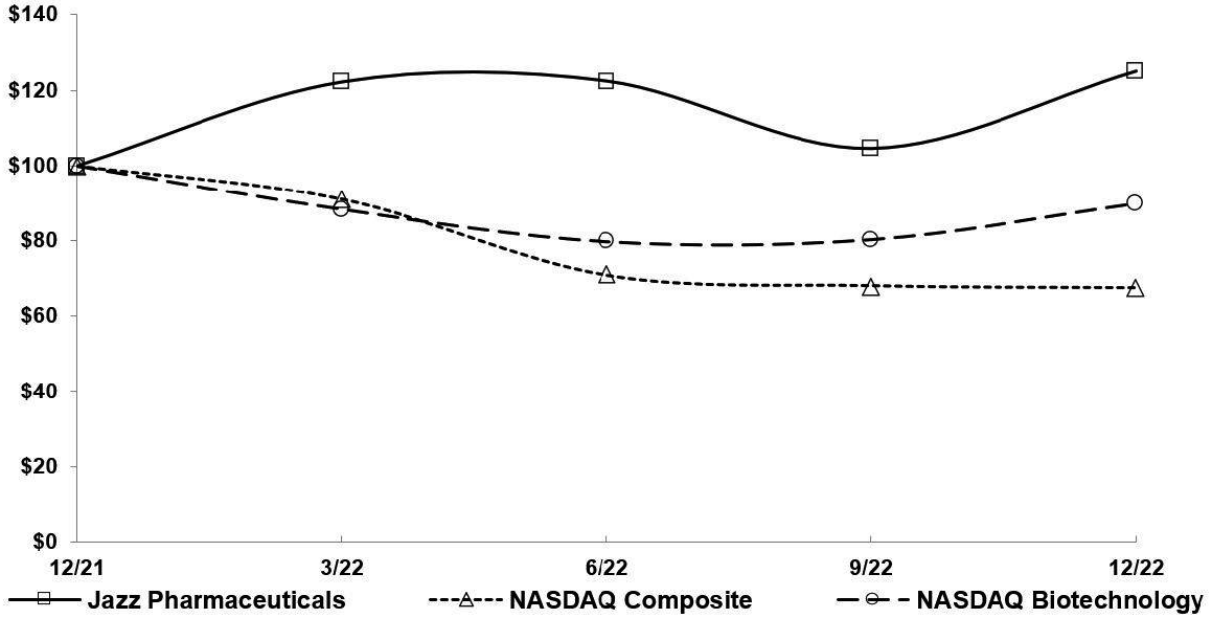
Performance Measurement Comparison (1)

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 markets (through licensing agreement)
Epidiolex® (cannabidiol)	Treatment of seizures associated with Lennox-Gastaut syndrome, or LGS, Dravet syndrome, or DS, or tuberous sclerosis complex, or TSC, in patients 1 year of age and older.	June 2018	U.S.
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older.*	September 2019	EU, Great Britain, Israel, Australia and New Zealand
	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, 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.	July 2017	Canada
Defitelio® (defibrotide)	Treatment of haptic sinusoidal obstruction syndrome (hepatic VOD)	June 2019	Japan

* 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 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 (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 studies) (ongoing trial) Newly diagnosed adults with standard- and high-risk AML (AML Study Group cooperative group study) (ongoing trial) Newly diagnosed pediatric patients with AML (Children's Oncology Group cooperative group study) (ongoing trial)
Pivotal Phase 2	
Zanidatamab	Previously treated, advanced HER2-expressing biliary tract cancer, or BTC (ongoing trial) (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 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 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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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).

Exhibit Number	Description of Document
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

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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	December 31, 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

Form 10-K

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.

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.

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.

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.

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		$—

	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	December 31, 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

9. Property, Plant and Equipment

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

	December 31, 2022	December 31, 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	December 31, 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

12. Debt

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

	December 31, 2022	December 31, 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

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):

Leases	Classification	December 31, 2022	December 31, 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

Lease Term and Discount Rate	December 31, 2022	December 31, 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.

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

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.

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.

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.

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)

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.

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EXECUTIVE COMMITTEE

Bruce C. Cozadd
Chairperson and Chief Executive Officer

George Eliades, Ph.D.
Senior Vice President, Corporate Development and Chief Transformation Officer

Renée Galá
Executive Vice President and Chief Financial Officer

Robert Iannone, M.D., M.S.C.E.
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Finbar Larkin, Ph.D.
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Samantha Pearce
Senior Vice President, Europe and International

Kim Sablich
Executive Vice President and General Manager, US

Daniel N. Swisher, Jr.
President, Chief Operating Officer

COMPANY SECRETARY

Aislinn Doody

ORDINARY SHARES

Jazz Pharmaceuticals plc ordinary shares are traded on the Nasdaq Global Select Market under the symbol "JAZZ"

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ANNUAL GENERAL MEETING

The annual general meeting of shareholders will be held at 9:45 a.m. local time on August 3, 2023 at the company's corporate headquarters located at Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

KPMG, Dublin, Ireland

BOARD OF DIRECTORS

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Director, BridgeBio Pharma, Inc. and Denali Therapeutics Inc.

Bruce C. Cozadd
Chairperson and Chief Executive Officer, Jazz Pharmaceuticals plc

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FOR MORE INFORMATION

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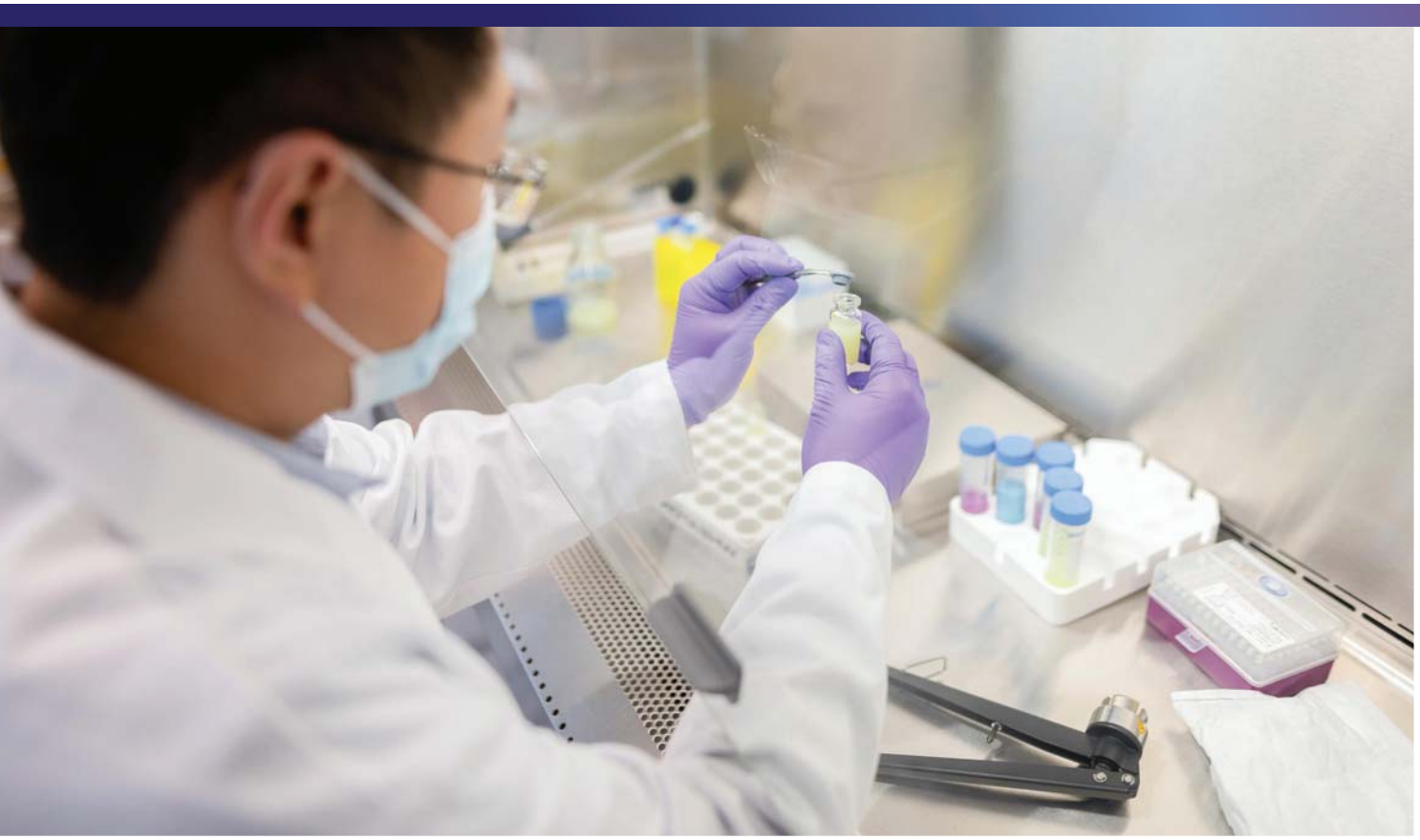
Communications concerning shares and transfer requirements, lost certificates or changes of address should be directed to the Transfer Agent.

CAUTION CONCERNING FORWARD-LOOKING STATEMENTS

This communication contains forward-looking statements, within the meaning of Section 27A of the U.S. Securities Act of 1933, as amended, and Section 21E of the U.S. Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. Forward-looking statements are based on Jazz Pharmaceuticals plc's management's beliefs and assumptions and on information currently available to management. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "propose," "intend," "continue," "potential," "possible," "foreseeable," "likely," "unforeseen" and similar expressions intended to identify forward-looking statements. These forward-looking statements are based on the company's current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: global economic, financial and healthcare system disruptions and impacts to the company's business operations and financial condition; maintaining or increasing sales of and revenue from Xywav and Xyrem; effectively commercializing the company's other products and product candidates; the time-consuming and uncertain regulatory approval process, including the risk that the company's current and planned regulatory submissions may not be submitted, accepted or approved by applicable regulatory authorities in a timely manner or at all; the costly and time-consuming pharmaceutical product development and the uncertainty of clinical success, including risks related to failure or delays in initiating or completing clinical trials; protecting and enhancing the company's intellectual property rights; delays or problems in the supply or manufacture of the company's products and product candidates; complying with applicable U.S. and non-U.S. regulatory requirements; government investigations and other actions; obtaining and maintaining adequate coverage and reimbursement for the company's products; identifying and acquiring, in-licensing or developing additional products or product candidates, financing these transactions and successfully integrating acquired businesses; the ability to achieve expected future financial performance and results and the uncertainty of future tax and other provisions and estimates; and other risks and uncertainties affecting the company, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's U.S. Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including the company's Annual Report on Form 10-K for the year ended December 31, 2022, as supplemented by the Quarterly Report on Form 10-Q for the quarter ended March 31, 2023 and future filings and reports by the company. Other risks and uncertainties of which the company is not currently aware may also affect the company's forward-looking statements and may cause actual results and timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by the company on its website or otherwise. The company undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.



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