Risk Factors Comparison 2025-02-26 to 2024-02-28 Form: 10-K

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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 **revenues** ~~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 was substantially dependent on Xyrem, and our financial results were significantly influenced by sales of Xyrem. Our **current** operating plan assumes that Xywav, ~~our~~ **with 92 % lower sodium compared to high- sodium** ~~oxybate~~ **oxybates** ~~product launched in November 2020~~ **(depending on the dose) and absence of a sodium warning** , will remain the **# 1 branded** ~~treatment of choice for patients who can benefit from~~ oxybate treatment **for narcolepsy; the position it held based on revenue in the fourth quarter of 2024** . While we expect that our business will continue to be meaningfully dependent on oxybate revenues, there is no guarantee that oxybate revenues will remain at current levels ~~, or that oxybate revenues will otherwise grow in future periods~~ . In this regard, our ability to maintain ~~or increase~~ oxybate revenues and realize the anticipated benefits from our investment in Xywav are subject to a number of risks and uncertainties as discussed in greater detail below, including **:** those related to the ~~launch~~ **commercialization** of Xywav for the treatment of ~~idiopathic hypersomnia, or~~ IH ~~,~~ in adults and adoption in that indication; competition from the introduction of ~~authorized generic, or~~ AG ~~,~~ versions of **high-** sodium oxybate and ~~new~~ **branded** products, such as Avadel' s once- nightly dose, high- sodium oxybate branded product Lumryz, for treatment of cataplexy and / or ~~excessive daytime sleepiness, or~~ EDS ~~,~~ in adults with narcolepsy in the U. S. market, as well as potential future competition from additional AG and generic versions of **high-** sodium oxybate 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. ~~For example, Xyrem product sales have decreased since the launch of Xywav due to the continued adoption of Xywav among existing Xyrem patients and new- to- oxybate narcolepsy patients driven by educational initiatives around the benefit of lowering sodium intake.~~ In addition, a wholly owned subsidiary of Hikma ~~Pharmaceuticals PLC, or Hikma,~~ launched its AG version of **high-** sodium oxybate in January 2023 and Amneal ~~Pharmaceuticals LLC, or Amneal,~~ launched its AG version of **high-** sodium oxybate in July 2023. **For a discussion of risks associated with maintaining the AG royalty revenue from these AG products, see the risk factor below titled " The introduction of new products in the U. S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products. "** We have seen a negative impact and expect to see a further negative impact on our oxybate revenues as a result of these AG products and Avadel' s Lumryz and any generic products and new branded products. A substantial ~~further~~ decline in oxybate revenues could cause us to reduce our operating expenses or seek to raise additional funds **and** ~~, 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 has adversely affected and may continue to adversely affect sales of our oxybate products~~ . 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, Xywav and Xyrem. Ten companies have sent us notices that they had filed ~~abbreviated new drug applications, or~~ ANDAs ~~,~~ seeking approval to market a generic version of Xyrem. We filed patent lawsuits against all ten companies and have settled with all ten of the 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, Hikma launched its AG version of **high-** sodium oxybate ~~,~~ in the U. S. beginning on January 1, 2023. Accordingly, beginning in January 2023, Xywav and Xyrem face competition from an AG version of **high-** sodium oxybate. We also granted Hikma a license to launch its own generic **high-** sodium oxybate 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, 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 to be paid to us. Amneal launched its AG version of **high-** sodium oxybate in July 2023. At this time, Amneal has rights to sell a low- single- digit percentage of historical Xyrem sales over each 6- month sales period. At this time, Lupin and Par have elected not to launch an AG product. AG products are 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 **high-** 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 six other ANDA filers,

we granted each a license to launch its own generic **high-** 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 **high-** 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 **and / or additional competition for our oxybate products** . Any ANDA holder launching an AG product or another generic **high-** sodium oxybate product will independently establish the price of the AG product and / or its own generic **high-** 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 and Amneal launched their AG products in 2023 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 have been, and will likely **continue to** 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 has resulted in reduced sales of, and revenue from, Xyrem. We continue to receive royalties and other revenue based on sales of AG products in accordance with the terms of our settlement agreements. Other companies may develop sodium oxybate products for **the** treatment of narcolepsy, using an alternative formulation or a different delivery technology, and seek approval in the U. S. using **an** ~~a new drug application, or~~ NDA ~~,~~ approval pathway under Section 505 (b) (2) and referencing the safety and efficacy data for Xyrem. For example, we face competition from branded products for treatment of cataplexy and / or EDS in narcolepsy, such as Avadel' s Lumryz. On May 1, 2023, Avadel announced that it had received FDA approval and **ODE** ~~orphan drug exclusivity~~ through May 1, 2030 for Lumryz, a fixed- dose, **high-** sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy. For additional information on litigation involving this matter, see" FDA Litigation" in Note ~~14~~ **13** , Commitments and Contingencies- Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on ~~Form10~~ -- **Form 10** - K. Xyrem and Xywav also face increased competition from other branded entrants to treat EDS in narcolepsy such as pitolisant and Sunosi. 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 AG **high-** sodium oxybate products or branded entrants in narcolepsy, such as Avadel' s Lumryz **,** notwithstanding FDA recognizing ~~Orphan Drug Exclusivity, or~~ ODE ~~,~~ for Xywav. For example, we received notices in June 2021 and February 2023, that Lupin and Teva, respectively, filed ANDAs for generic versions of Xywav. On October 13, 2023, Lupin announced that it has received tentative approval for its application to market a generic version of Xywav. **We have filed patent infringement suits against these ANDA filers. For additional information see " Xywav Patent Litigation " in Note 13, Commitments and Contingencies — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K.** 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 **and / or additional competition** . Moreover, generic or AG **high-** sodium oxybate products or branded **high-** sodium oxybate entrants in narcolepsy, such as Avadel' s Lumryz, as well as non- oxybate products intended for the treatment of EDS or cataplexy in narcolepsy or IH including new market entrants, even if not directly competitive with Xywav or Xyrem, have had and may continue to 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 of non- oxybate products 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 **. Harmony Biosciences has announced a phase 3 study for pitolisant for IH after receiving a refusal to file from FDA in February 2025** . In addition, we are also aware that prescribers often prescribe branded or generic medications for cataplexy **and IH** , before or instead of prescribing oxybate therapy ~~in~~ **including** 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 AG products or other generic versions of Xyrem or Xywav and the approval and launch of any other sodium oxybate product, such as Avadel' s Lumryz, or alternative product that treats narcolepsy will continue to have a negative impact **on,** and 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~~ **facilitating** 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~~ **continues to** evaluate the Xywav and Xyrem REMS on an ongoing basis and ~~will~~ **has required, and may in the future** require **,** modifications ~~as may be appropriate~~ **to the Xywav and Xyrem REMS** . In 2023, FDA requested certain modifications to the Xywav and Xyrem REMS ~~that~~ **, which** FDA approved in January 2024 as part of additional modifications to the REMS that we requested. We cannot predict whether FDA will request, seek to require or ultimately require additional 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 AGs, 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 **or Xywav as a treatment for IH** , and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our 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 **ESSDS** ~~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 with the Xywav and Xyrem REMS, approving Hikma' s ANDA with a generic **high-** sodium oxybate REMS separate from the Xywav and Xyrem REMS, except for the requirement that the **high-** sodium oxybate REMS program pharmacies contact the Xywav and Xyrem REMS by phone to verify and report certain information. The generic **high-** sodium oxybate REMS was approved with the condition that it be open to all future sponsors of ANDAs or NDAs for **high-** sodium oxybate products. In its approval of Avadel' s **high-** sodium oxybate product, FDA also approved a separate REMS for that product, also with a requirement that the pharmacies in the Avadel- sponsored REMS contact the Xywav and Xyrem REMS to verify and report certain information. Administration of multiple sodium oxybate REMS systems ~~, including sodium oxybate distribution systems that are less restrictive than the Xywav and Xyrem REMS (such as the generic sodium oxybate REMS or Avadel' s sodium oxybate REMS),~~ could increase the risks associated with oxybate distribution, could make it more difficult or expensive for us to distribute Xywav and Xyrem and disrupt patient access to Xywav or Xyrem. Because patients, consumers and others may not differentiate **other high-** sodium oxybate products from ~~Xyrem~~ **our sodium oxybate products** or differentiate between the different REMS programs, any negative outcomes, including risks to the public, caused by or otherwise related to a separate **high-** 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 **or Xywav for the treatment of IH** , and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our business. We may face pressure to further modify the Xywav and Xyrem REMS, including **sharing data, which may be** 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 has been approved or may be submitted or approved in the future. 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 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 **an** ~~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 REMS 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 **high-** 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" Xyrem Antitrust Litigation" (and for other litigation involving our listing of our REMS patent in FDA' s publication " Approved Drug Products with Therapeutic Equivalence Evaluations, " or Orange Book, see" Avadel Litigation") in Note ~~14~~ **13** , 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 **LGS** ~~Lennox-Gastaut syndrome~~ , **DS** ~~Dravet syndrome~~ and **TSC** ~~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~~ **13** , Commitments and Contingencies ~~-~~ — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K. **Additional companies may file ANDAs seeking to market a generic version of Epidiolex which could lead to additional patent litigation or challenges with respect to Epidiolex.** While we expect **Xywav** ~~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~~ **Ziihera** . 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; **competition from a newly approved product for** ~~and our ability to educate health care providers about Zepzelca in~~ the treatment of ~~relapsed,~~ **extensive- stage** metastatic SCLC **;** ~~in the U. S.~~ and patients' access to lung cancer screening, diagnosis and treatment **. In July and August 2024, we received notices from Zepzelca ANDA filers. On September 11, 2024, we and PharmaMar filed a patent infringement suit against the Zepzelca ANDA Filers in the United States District Court for the District of New Jersey. For additional information see " Zepzelca Patent Litigation " in Note 13, Commitments and Contingencies — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K. Additional companies may file ANDAs seeking to market a generic**

version of Zepzelca which could lead to additional patent litigation or challenges with respect to Zepzelca . 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 including creating awareness among health care professionals and ensuring that patients with **ALL** ~~acute lymphoblastic leukemia~~ or **LBL** ~~lymphoblastic lymphoma~~ will be given the appropriate course of therapy and dosing regimen based on the currently approved label. Our ability to realize the anticipated benefits from our ~~investment~~ **investments** in ~~Vyxeos~~ **Ziihera** is subject to a number of ~~risks and~~ uncertainties, including our ability to **successfully commercialize Ziihera** ~~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 **BTC** ~~the U. S., the European Union, or 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~~ - **clinical development** ~~may find challenging to incorporate; the use of new and novel compounds in AML that are either used off~~ - **of** ~~- 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; ongoing trends in the U. S. towards lower- intensity treatments and away from intensive chemotherapy regimens, such as Vyxeos; and competition from new and existing products that are used in place of intensive chemotherapy treatments like Vyxeos and~~ potential **future** ~~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~~ **indications** ~~of treatment while waiting for those symptoms to improve, or may terminate treatment before the end of the recommended dosing schedule; changes~~ in **HER2 solid tumors** ~~chemotherapy regimens and the increasing use of cell therapies to potentially lower the incidence of severe VOD; and the limited size of the population of VOD patients who are indicated for treatment with 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 other branded products, AG and other generic products, product candidates currently under development by us and others and / or future product candidates, including new **molecular and** 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 has adversely affected and may continue to adversely affect sales of our oxybate products " in this Part I, Item 1A **. Recent executive and judicial changes and flux in the regulatory landscape creates uncertainty for us and our industry. The current administration is pursuing policies to reduce regulations and expenditures across government including at HHS, FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare & Medicaid Innovation to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration' s executive order that directed HHS to establish an AI task force and develop a strategic plan. Additionally, in its June 2024 decision in Loper Bright, the U. S. Supreme Court overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper Bright decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by FDA. Finally, Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA. We cannot predict which additional measures may be adopted or the impact of current and additional measures on the marketing, pricing and demand for our products, which could have a material adverse effect on our business, financial condition and results of operations** . 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. **The market for PBM services has become highly concentrated and vertically integrated, giving these entities further leverage in negotiating rebates, discounts or other concessions.** 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. **In addition, PBMs and other third- party payors could implement alternative funding programs that could have an impact on product revenue.** 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 **. In** ~~, although beginning in~~ January 2025, the EU HTA regulation ~~will apply;~~ **entered into application.** ~~this~~ **This** regulation aims to harmonize the clinical benefit assessment of HTA across the EU **. Under this regulation, EU member states must use common HTA tools, methodologies, and procedures across the EU. However, individual member states remain responsible for determining the overall value of a new health technology within their healthcare systems, as well as making pricing and reimbursement decisions** . 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 **Enrylaze** ~~Vyxeos in August 2018 and for Epidyolex~~ in September ~~2019~~ **2023** , and, as part of our rolling ~~launches~~ -- **launch** of **Enrylaze** ~~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 **Enrylaze** ~~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. **This includes efforts by individual states in the U. S. to pass legislation and implement regulations designed to control pharmaceutical and biological product pricing, including by establishing Prescription Drug Affordability Boards (or similar entities) to review high- cost drugs and, in some cases, set upper payment limits and implementing marketing cost disclosure and transparency measures.** Further, the ~~Inflation Reduction Act of 2022, or~~ IRA, 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. The ~~Centers for Medicare & Medicaid Services, or~~ CMS ~~,~~ **has** issued final guidance implementing the Drug Price Negotiation Program ~~for the first year of the program~~ in which it finalized certain policies governing the selection of drugs for negotiation ~~for such year~~ . Among other things, CMS finalized definitions of " qualifying single source drug " and " marketed " that, especially if they persist ~~beyond the first year of the program~~ , could further disincentivize innovation. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are no longer subject to a cap on the rebate amount effective January 1, 2024, which ~~could~~ **may** 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 **and state** policy makers have taken and **may** ~~are expected to~~ continue to try to take steps **regarding** ~~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 ~~2024~~ **2025** , 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 USPTO, 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 **of this Annual Report on Form 10- K** . 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. On April 26, 2023, the EC adopted ~~a proposal~~ **proposals** for a new Directive and a new Regulation, which revise and replace the existing EU general pharmaceutical legislation. This proposal includes increased transparency on research and development costs or public contributions to these costs with a view to strengthen the negotiating position of national competent authorities of the EU member states responsible for pricing and reimbursement, as well as reinforced cooperation with these authorities on pricing and reimbursement matters **. On April 10, 2024, the European Parliament adopted its position on the proposals, whose legislative processes are expected to continue in 2025** . 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 ◦ ~~cannabidiol, 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 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 Simtra ~~Biopharma Solutions~~, which is a sole source supplier from a single site location. 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. **We currently rely on WuXi, a company based in the PRC, as the sole supplier of Ziihera. Accordingly, there is a risk that supplies of Ziihera may be significantly delayed by, or may become unavailable as a result of, manufacturing, equipment, process, regulatory or business- related issues affecting that company. We may also face additional manufacturing and supply- chain risks due to the regulatory and political structure of the PRC, or as a result of the international relationship between the PRC and the U. S., including but not limited to potential trade restrictions, sanctions, other regulatory requirements, or proposed legislation imposed by the U. S. government, which could restrict or even prohibit our ability to work with WuXi. For example, the House of Representatives of the prior Congress (the 118th Congress) passed the BIOSECURE Act, which proposed targeting U. S. government contracts, grants and loans for entities that use biotechnology equipment or services from certain named Chinese biotechnology companies, including WuXi, and potentially other biotechnology companies designated in the future. The language of the proposed BIOSECURE Act would, among other things, prohibit U. S. federal agencies from entering into or renewing any contract with any entity that uses biotechnology equipment or services produced or provided by a " biotechnology**

company of concern. ” The version of the bill passed by the prior House of Representatives included a “ grandfathering ” provision, which provided that the BIOSECURE Act’ s prohibitions would not apply to pre- existing contracts and agreements entered into prior to the legislation’ s effective date until 2032. The BIOSECURE Act did not become law in the 118th Congress. It is unclear whether the current Congress (the 119th Congress) will introduce the BIOSECURE Act or similar legislation in this congressional session and, if so, how the scope, prohibitions, or designated biotechnology companies of concern may differ from the version of the BIOSECURE Act passed by the House in the prior 118th Congress. Although to date there has been no impact on our ability to obtain supply of Ziihera, there can be no assurance that operations would not be impacted in the future with a negative impact on Ziihera supply. 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. **Global trade issues and changes in and uncertainties with respect to trade policies and export regulations, including import and export license requirements, trade sanctions, tariffs and international trade disputes, could adversely impact our business and operations, and reduce the competitiveness of our products and services relative to local and global competitors. There is inherent risk, based on the complex relationships among the U. S. and the countries in which we conduct our business, that political, diplomatic, and national security factors can lead to global trade restrictions and changes in trade policies and export regulations that may adversely affect our business and operations. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U. S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments and persons targeted by U. S. sanctions. The U. S. and other countries have imposed and may continue to impose new trade restrictions and export regulations, have levied tariffs and taxes on certain goods, and could significantly increase tariffs on a broad array of goods. For example, on February 1, 2025, President Donald Trump signed executive orders imposing a 25 % tariff on certain imports from Mexico and Canada, and a 10 % tariff on certain imports from China, which were to take effect on February 4, 2025. A 30- day pause was granted to Mexico and Canada. However, these newly proposed and imposed tariffs have resulted in retaliatory tariffs, and threats thereof, against U. S. goods. The ultimate impact of these potential and actual tariffs on our business and financial condition is unknown. In addition, ongoing changes in U. S. and foreign government trade policies, including potential modifications to existing trade agreements, could introduce additional uncertainty. Trade restrictions and export regulations, or increases in tariffs (including tariffs on imports from Europe) and additional taxes, including any retaliatory measures, can negatively impact end- user demand, increase our supply chain complexity and our manufacturing costs, decrease margins, reduce the competitiveness of our products, or restrict our ability to sell products, provide services or purchase necessary equipment and supplies, any or all of which could have a material and adverse effect on our business, results of operations, or financial condition and, given the nature of our products, relocating the manufacturing supply can be a complex, costly and time- consuming process making it difficult to react quickly to a changing environment.** 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, the EC 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 **and Ziihera** . These post- marketing requirements and commitments include satisfactorily conducting multiple post- marketing 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. **If a product is approved under accelerated approval, continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial.** 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. While we and our licensor PharmaMar have reached agreement with FDA regarding a confirmatory clinical development program, our inability to confirm its clinical benefit **in the second- line treatment setting for SCLC** 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 addition, FDA granted accelerated approval to Ziihera for previously treated, unresectable or metastatic HER2- positive BTC based on data from a Phase 2 trial. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. While a Phase 3 confirmatory trial is ongoing to evaluate zanidatamab in combination with standard-of- care therapy versus standard- of- care therapy alone in the first- line setting for patients with HER2- positive BTC, our inability to confirm its clinical benefit in the first- line setting for patients with HER2- positive BTC could result in the withdrawal of approval of Ziihera** , 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. Any 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 beyond its currently approved uses 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, **in each case including as a result of any executive or judicial actions as described under " — Recent executive and judicial changes and flux in the regulatory landscape creates uncertainty for us and our industry, "** 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 or from financial difficulties of our collaborators. 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 ~~Pharmaceuticals plc, or 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 FTC; • the potential need to secure shareholder approval of the transaction; • 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 or any equivalent non- U. S. regulatory agency 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 have been and 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, or similar bodies in other jurisdictions, such 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~~ **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 use thereof could be delisted from FDA' s 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 costs 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~~ **designed around** by an ANDA or Section 505 (b) (2) ~~application~~ **NDA** 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. In February 2023, we received notice from Teva that it had filed an ANDA seeking approval to market a generic version of Xywav, which notice included a paragraph IV certification with respect to certain of our patents listed in FDA' s Orange Book for Xywav. ~~In April 2023, we received notice from Alkem that it had filed an ANDA seeking approval to market a generic version of Xyrem, which notice included a paragraph IV certification with respect to certain of our patents listed in FDA' s Orange Book for Xyrem.~~ For additional information on litigation involving these matters, see Note ~~14~~ **13** , 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 each of the ten 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 AG 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 methods 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. **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.** 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. On January 3, 2023, we filed a patent infringement suit against the ten Epidiolex ANDA filers in the United States District Court for the District of New Jersey. In June and July 2023, we received notice from certain of the Epidiolex ANDA Filers that they had each filed a paragraph IV certification regarding a newly- issued patent listed in the Orange Book for Epidiolex. On July 21, 2023, we filed an additional lawsuit against all of the Epidiolex ANDA Filers in the United States District Court for the District of New Jersey alleging that, by filing its ANDA, each Epidiolex ANDA Filer infringed the newly- issued patent related to a method of treatment using Epidiolex **. For additional information on litigation involving this matter, see " Epidiolex Patent Litigation " in Note 13, Commitments and Contingencies — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K** . 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. **In March 2024,** ~~The suit seeks an injunction to prevent Avadel from launching a product that would infringe these~~ -- **the jury upheld the validity of both of our asserted** patents ~~, and an~~ **and** ~~award~~ **awarded us** ~~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~~ **for** ~~not enforceable, and that its product, if approved, will not infringe~~ **infringement** ~~our patents~~ **for past sales of Lumryz in the U. S** . For additional information on litigation involving this matter, see " Avadel ~~Patent~~ Litigation " in Note ~~14~~ **13** , 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~~ **In July and August 2024, Zepzelca ANDA filers sent us notices that** ~~the~~ **they** ~~EU~~ **had filed ANDAs seeking approval to market a generic version of Zepzelca (lurbinectedin), which notices each included a paragraph IV certification with respect to our Orange Book listed patent for Zepzelca on the date of the receipt of the applicable notice. In September 2024** , we ~~are aware that generic~~ **filed patent**

infringement suits against these ANDA filers. ~~or~~ **For** ~~hybrid generic applications have been approved by various EU regulatory authorities, and~~ additional ~~generic or hybrid generic applications may be submitted~~ **information on litigation involving this matter, see " Zepzelca Patent Litigation " in Note 13, Commitments** and ~~approved~~ **Contingencies — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K** . We also currently rely in part 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 USPTO. 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 **that** ~~, 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. 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, several 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 **" Xyrem Antitrust Litigation" in** Note ~~14~~ **13** , 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 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, 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. 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. 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. On June 22, 2023, we filed a complaint in the United States District Court for the District of Columbia seeking a declaration that FDA' s approval on May 1, 2023 of the **NDA** ~~New Drug Application~~ for Avadel' s drug Lumryz was unlawful. **On September 15, 2023, we filed a motion for summary judgment. On October 20, 2023, Avadel and FDA filed cross motions for summary judgment. Oral argument on these motions was held on May 10, 2024, and on October 30, 2024, the District Court issued an order denying our motion for summary judgment and granting Avadel' s and FDA' s cross-motions for summary judgment. We have appealed the matter to the United States Court of Appeals for the District of Columbia Circuit.** We cannot predict the timing or ultimate outcome of this litigation or the impact of this litigation on our business, including any potential adverse consequences to, among other things, our reputation, relationships with governmental or regulatory authorities, including FDA. For additional information, see" FDA Litigation" in Note ~~14~~ **13** , Commitments and Contingencies ~~–~~ — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K. 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 ODE and other regulatory exclusivities to protect Xywav, Epidiolex, Zepzelca, ~~Vyxeos~~ **Ziihera** 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 **ODE** ~~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. According to FDA, 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. For example, even though FDA granted seven- year ODE to Xywav, FDA also approved Lumryz and granted Lumryz seven- year ODE based on FDA' s finding that Lumryz makes a major contribution to patient care and is therefore clinically superior to Xywav and Xyrem. 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, including from us, 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 our and future challenges could lead to changes that affect the protections potentially afforded our products in ways that are difficult to predict. In this regard, we have filed a complaint in the United States District Court for the District of Columbia seeking a declaration that FDA' s approval of Lumryz was unlawful and allege that FDA acted outside its authority under the Orphan Drug Act, when, despite the ODE protecting Xywav, FDA approved Lumryz and granted Lumryz seven- year ODE. However, legal challenges like this are inherently uncertain and there can be no guarantee that the United States District Court for the District of Columbia will agree with our interpretation of applicable laws and regulations or will otherwise agree with any or all of the allegations included in our compliant, or that we will otherwise prevail in this litigation. We also cannot predict what other adverse consequences to, among other things, our reputation, our relationship with FDA or other governmental or regulatory authorities or the protections afforded our products could result from our decision to proceed with this litigation or the ultimate outcome thereof. Moreover, 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 EU, if a marketing authorization is granted for a medicinal product ~~that is~~ designated an orphan drug, that product is **currently** entitled to ten years of marketing exclusivity. We rely in part on this orphan drug exclusivity and other regulatory exclusivities to protect Epidyolex and Vyxeos. 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~~ **On April 26, 2023,**

the EC published proposals for a new package of pharmaceutical legislation that would replace the current Medicines Directive and the existing medicinal product regulation (including the pediatric and orphan ~~exclusivity for any product candidate~~ **regulations). If enacted** , the ~~exclusivity period can be reduced~~ **proposal could impact our ability** to **secure** ~~six years if at the end of the fifth year it is established that the~~ orphan designation ~~criteria are no longer met or~~ **for** ~~if it is demonstrated that~~ **future products, and would impact** the **scope and duration of market and** orphan ~~drug is sufficiently profitable that market exclusivity~~ **exclusivities in the EU** ~~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. and key markets across Europe, Canada, Australia and Japan and **manage** clinical trial sites in multiple locations around the world. 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; • 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, including clinical trials, 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; **• escalating trade tensions;** 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 and the third parties upon which we rely collect, store, process and transmit, or collectively, process large amounts of sensitive, proprietary, and / or confidential information, including intellectual property, business information, personal data, and clinical trial data, or collectively, sensitive data. We outsource 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 sensitive data **.** We and the third parties upon which we rely face a variety of evolving threats that could ~~threaten~~ **impact** the availability of our sensitive data and information technology systems and cause security incidents from inadvertent or intentional actions by our employees, third party vendors and / or business partners, or from cyber- attacks and malicious third parties. Threats of this nature are prevalent, are increasing in frequency, persistence, sophistication and intensity, are being conducted by sophisticated and organized groups and individuals, are increasingly difficult to detect, and come from a variety of sources and with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, " hacktivists, " traditional computer " hackers, " threat actors, personnel (such as through theft or misuse), nation states, nation- state- supported actors, and others. In addition to the extraction of important information, such threats could include the deployment of harmful malware, ransomware, denial- of- service attacks, social engineering, malicious code, credential harvesting, personnel misconduct or error, supply- chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, and other threats that affect service reliability and threaten the confidentiality, integrity and availability of our information technology systems and sensitive data. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, or otherwise experience significant disruptions of our, our third party vendors' and / or business partners' information technology systems or security breaches, including in our remote work environment, such occurrence 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, sensitive data, and could result in adverse consequences to us such as government enforcement actions, additional reporting requirements and / or oversight, restrictions on processing sensitive data, litigation, indemnification obligations, negative publicity, reputational harm, monetary fund diversions, diversion of management attention, interruptions in our operations, financial loss, and other similar harms. 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, notify relevant stakeholders, 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. ~~We cannot be sure that our insurance coverage will be adequate or sufficient, that such~~

~~coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.~~ 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 and sensitive data, there can be no assurance that such measures will be effective or prevent service interruptions or security breaches that could adversely affect our business. We may expend significant resources to implement and maintain security measures to try to protect against security incidents. In addition, failure to maintain effective internal accounting controls related to security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and subject us to regulatory scrutiny. In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive data about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. 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. 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 ~~our~~ **this** Annual Report on Form 10 - K ~~for the year ended December 31, 2023~~ . 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~~ **of remuneration related to** speaker **programs sponsored** ~~fees, honorariums and expenses paid~~ by ~~pharmaceutical~~ **drug** and medical device companies ~~to healthcare professionals participating~~ **, which may not** in ~~company- sponsored events~~ **all circumstances qualify 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** . 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 **. For example, we are subject to a qui tam whistleblower lawsuit originally filed under seal on May 27, 2021. For additional information see " Qui tam matter " in Note 13, Commitments and Contingencies — Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10 - K** . 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. **Any** ~~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 USPTO, 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~~ **our products** and / or reduce coverage of ~~Xyrem~~ **our products** , 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, 2023~~ , 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~~ **As of August 2024** , we **have fulfilled** ~~finalized our civil settlement agreement with~~ the ~~DOJ~~ **terms** and OIG **closed out our** ~~and entered into a~~ corporate integrity agreement ~~requiring~~ **that required** 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 **are continuing to implement our corporate compliance program and** 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, including, but not limited to, Section 5 of the Federal Trade Commission Act, the Health ~~Insurance Portability and Accountability~~ **Breach Notification Rule, HIPAA, the California Consumer Privacy** Act ~~of 1996~~ , **as amended by** ~~or HIPAA, the~~ California Privacy Rights Act **, as well as other similar state privacy laws,** and the EU' s ~~General Data Protection Regulation, or~~ **and U. K.' s** GDPR. The GDPR, for example, imposes restrictions on the processing (e. g., collection, use and disclosure) of personal data in the EU **and the U. K.** and also imposes strict restrictions on the transfer of personal data out of the EU to the U. S. The GDPR imposes penalties of **up to 20 million Euros or** up to 4 % of annual global revenue. HIPAA imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses, as well as their " business associates " – certain persons or covered entities that create, receive, maintain, or transmit protected health information in connection with providing a specified service or performing a function **for or** on behalf of a covered entity. Although we are not directly subject to HIPAA, we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive individually identifiable health information maintained by a HIPAA- covered entity in a manner that is not authorized or permitted by HIPAA. **The FTC also sets expectations** ~~In July 2023, the EC adopted its adequacy decision~~ for **failing to take appropriate steps to keep consumers'** ~~the EU- US Data Privacy Framework, meaning that~~ personal ~~data~~ **information secure or failing to provide a level of security commensurate to promises made to** ~~can~~ **an** ~~now flow freely from~~ **individual about the security of** ~~the~~ **their personal information (such as** ~~EU to U. S. companies that participate~~ in **a** ~~the Data Privacy~~ **privacy notice); such failures** ~~Framework. These laws and regulations continue to develop and are subject to interpretation, and~~ may **constitute unfair** ~~impose limitations on our~~ **or deceptive acts** ~~activities or otherwise adversely affect our~~ **or** ~~business~~ **practices in violation of Section 5 (a) of the Federal Trade Commission Act** . Compliance with these laws requires a flexible privacy framework and substantial resources, and compliance efforts will likely be an increasing and substantial cost in the future. 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, or Tricare,~~ 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~~ **our** Annual Report on Form 10 - K **for the year ended December 31, 2024** . 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, 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 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, the IRA established 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~~ **be certain** that our submissions will not be found by CMS to be incomplete or incorrect. Moreover, failure to pay refunds for units of discarded drug under the discarded drug 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. CMS issued a final ~~regulation~~ **rule** 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~~ **modifications** 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 PBM " accumulator " programs were invalidated by a court **and rescinded** , such programs may continue to negatively affect us in other ways **. Our failure to comply with these price reporting and rebate payment options could negatively impact our financial results. In addition, on September 26, 2024, CMS finalized a rule modifying the regulations implementing the Medicaid Drug Rebate Program in ways that could increase the costs and complexity of compliance and that could increase manufacturer rebate liability, given that the final rule clarified certain aspects of the definition of covered outpatient drugs subject to these rebates, which could expand the number of units of drugs that qualify for this definition, among other changes** . 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 no longer subject to a cap on the rebate amount **, which negatively impacts our rebate liability** . 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. 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. If we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price, we could be subject to significant civil monetary penalties and / or such failure also could be grounds for HRSA to terminate our agreement to participate in the 340B program, in which case our covered outpatient drugs would no longer be eligible for federal payment under the Medicaid or Medicare Part B program, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including our ability to acquire, in- license or develop new products to grow our business. Moreover, HRSA established an ~~administrative dispute resolution, or~~ ADR ~~,~~ process under a final regulation 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 may be appealed to a federal court. An ADR proceeding could potentially subject us to discovery by covered entities and other onerous procedural requirements and could result in additional liability. **Additionally** ~~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 **final rule** ~~notice of proposed rulemaking~~ that ~~proposes~~ changes ~~to~~ **aspects of** the ADR process **effective June 2024** , 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 **at the state or Federal level** 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, **were** ~~are currently~~ required **through December 31, 2024** 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 **, under which manufacturers are, in general, to provide a 10 % discount on a covered Part D drug where a beneficiary is in the initial phase of Part D coverage and a 20 % discount where a beneficiary is in the catastrophic phase of Part D coverage** . Failure to pay a discount under this new program will be subject to a civil monetary penalty. In addition, the IRA established 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 comply with obligations under the Part D benefit redesign or~~ 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 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 by 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 subject to additional requirements. 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 product 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 and 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 predominantly 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 be 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, ~~2023~~ **2024**, we had total indebtedness of approximately $ ~~5~~ **6**. ~~8~~ **2** 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 a portion of borrowings under the **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement**, are at variable rates of interest; • result in dilution to our existing shareholders ~~in~~ **to** the ~~event~~ **extent that the remainder, if any, of the** ~~exchanges~~ **exchange obligation in excess** of our ~~2. 00 % exchangeable~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **Notes** ~~due 2026~~ are settled in our ordinary shares **upon exchange**; • 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~~ **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** or ~~senior secured~~ **Secured** ~~notes~~ **Notes** , the **Amended** ~~credit~~ **Credit** ~~agreement~~ **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~~ **the Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** and indenture governing our ~~senior secured~~ **Secured** ~~notes~~ **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 **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** and the indenture governing our ~~senior secured~~ **Secured** ~~notes~~ **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~~ **Secured** ~~notes~~ **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~~ **Secured** ~~notes~~ **Notes** at 100 % of the principal amount, plus accrued and unpaid interest. The **Amended** ~~credit~~ **Credit** ~~agreement~~ **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 **Amended** ~~revolving~~ **Revolving** ~~credit~~ **Credit** ~~facility~~ **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 **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** and the indenture governing our ~~senior secured~~ **Secured** ~~notes~~ **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 **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** may permit the lenders to refuse to permit additional borrowings under the **Amended** ~~revolving~~ **Revolving** ~~credit~~ **Credit** ~~facility~~ **Facility** or to terminate all commitments to extend further credit under the **Amended** ~~revolving~~ **Revolving** ~~credit~~ **Credit** ~~facility~~ **Facility** . Furthermore, if we are unable to repay the amounts due and payable under the **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** or ~~senior~~ **the** ~~secured~~ **Secured** ~~notes~~ **Notes , as the case may be** , the lenders and note holders **thereof** may be able to proceed against the collateral granted to them to secure that indebtedness. In the event our lenders or note holders **, as the case may be,** 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~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **Notes** could also lead to a default under other debt agreements or obligations, including the **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** and indenture governing the ~~senior secured~~ **Secured** ~~notes~~ **Notes** . Likewise, a default under the **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** or ~~senior~~ **the** ~~secured~~ **Secured** ~~notes~~ **Notes** could lead to a default under other debt agreements or obligations, including the indentures governing our ~~exchangeable~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **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, potential future bank failures 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 ~~August~~ **July** ~~2023~~ **2024** , 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 ~~February~~ **January** ~~2025~~ **2026** . 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. " In October 2021, the OECD released ~~a framework proposal reflecting the agreement of over 140 jurisdictions, including Ireland, to implement a two- pillar plan on global tax reform, including a global minimum tax rate of 15 % for large multinational corporations on a jurisdiction- by- jurisdiction basis, or~~ Pillar Two. In December 2022, the EU agreed to implement this global minimum tax rate for EU member states by the start of 2024. In accordance with the EU directive, Ireland adopted legislation implementing Pillar Two on December 18, 2023, with effect from the start of 2024. Other jurisdictions in which we do business have also ~~introduced or~~ adopted legislation implementing Pillar Two. **Pillar Two legislation could have an adverse impact** ~~We are currently evaluating the effect of the new law~~ on our ~~financial results~~ **effective tax rate, tax liabilities, and cash tax** . Further, the IRA **,** 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 became effective in 2023. The IRS has issued limited guidance on the corporate alternative minimum tax, the excise tax and the other **tax** provisions in the IRA, and **much of** this guidance has yet to be finalized. **Final guidance under** ~~We are currently evaluating~~ the **IRA could adversely** ~~effect~~ **affect** ~~of the law on~~ our ~~financial results~~ **tax provision, cash tax liability and effective tax rate** . The U. S. and other jurisdictions in which we operate continue to consider other changes in tax laws and regulations that apply to multinationals, including proposed **legislation and** guidance with respect to research and development expenditures and other guidance under the 2017 Tax Cuts and Jobs Act. ~~These~~ -- **The new presidential administration has included as part of its agenda a potential reform of U. S. tax laws, the details of which have not yet emerged. In addition, certain of the provisions in the 2017 Tax Cuts and Jobs Act will** ~~changes~~ - **change or expire on December 31** , ~~if implemented~~ **2025 unless Congress takes action to extend these provisions in their current form. In particular** , ~~could adversely impact~~ **a**

significant portion of our income taxable in the U. S. qualifies for preferential treatment as foreign- derived intangible income. Beginning in 2026, the effective tax rate for foreign- derived intangible income will increase from 13 % to 16 %. If U. S. tax rates increase and / or the foreign- derived intangible income deduction is reduced or eliminated, our tax provision, cash tax liability and effective tax rate **would be adversely affected** . 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. **Moreover** ~~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 **NOLs** ~~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. 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~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **Notes** who may view our ~~exchangeable~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **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~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **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~~ **the Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** and the indentures governing our ~~senior secured~~ **Secured** ~~notes~~ **Notes** and ~~exchangeable~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **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 **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** or the requirement that we offer to purchase our ~~senior secured~~ **Secured** ~~notes~~ **Notes** or ~~exchangeable~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **Notes** and / or increase the exchange rate applicable to our ~~exchangeable~~ **Exchangeable** ~~senior~~ **Senior** ~~notes~~ **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 **or exercisable or exchangeable for** our ordinary shares or rights to purchase ordinary shares or convertible **or exchangeable** 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 **Amended** ~~credit~~ **Credit** ~~agreement~~ **Agreement** and the indenture governing our ~~senior secured~~ **Secured** ~~notes~~ **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 **and key personnel** , 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~~ **In December 2024, our Chief Executive Officer notified us of his intent to retire from his role as Chief Executive Officer upon the selection and appointment of our next Chief Executive Officer, and to continue serving as Chairperson of the Board of Directors. Moreover, 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. **Anti- diversity, equity and inclusion initiatives could expose us to the risk of litigation or investigations, resulting in injunctions, penalties, or reputational harm. We have talent management efforts designed to build and maintain an inclusive environment with diverse thought, backgrounds, experiences and skillsets throughout our organization. However, there has been increasing scrutiny on corporate DEI initiatives, including from activists and policymakers challenging how such initiatives comply with civil rights protections. For example, the U. S. President recently issued an executive order opposing DEI initiatives in the private sector. Such anti- DEI initiatives and scrutiny could expose us to the risk of litigation or investigations, resulting in injunctions, penalties, or reputational harm. In addition, if we become unable to (or are perceived not to) successfully implement certain of our workforce initiatives, including in keeping with current or potential future laws or interpretations thereof, our ability to recruit, attract and retain talent may be adversely impacted.** 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.