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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark one)

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

For the fiscal year ended December 31, 2021

or

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

For the transition period from to

Commission file number 001-37558

Nabriva Therapeutics plc

(Exact name of registrant as specified in its charter)

Ireland	**Not applicable**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
25-28 North Wall Quay	
IFSC, Dublin 1, Ireland	**Not applicable**
(Address of principal executive offices)	(Zip Code)

+353 1 649 2000

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Ordinary Shares, nominal value $0.01 per share	NBRV	The Nasdaq Stock Market LLC

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

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒ Smaller reporting company ☒ Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule12b-2 of the Act). Yes ☐ No ☒

As of June 30, 2021 (the last business day of the registrant's most recently completed second fiscal quarter), the aggregate market value of the registrant's voting securities held by non-affiliates was approximately $67.5 million based on the last reported sale price of the registrant's ordinary shares on June 30, 2021. As of February 28, 2022, the registrant had 60,525,366 ordinary shares outstanding.

NABRIVA THERAPEUTICS plc
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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve important risks and uncertainties. All statements contained in this Annual Report, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate, “around” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this report include, among other things, statements about:

- our ability to successfully commercialize SIVEXTRO and realize value from our agreement with Merck & Co., Inc.;
- our ability to successfully commercialize XENLETA (lefamulin) for the treatment of community-acquired bacterial pneumonia, or CABP, including the availability of and ease of access to XENLETA through hospital formularies, managed care plans and major U.S. specialty distributors;
- our expectations regarding how far into the future our cash on hand and anticipated revenues from product sales will fund our ongoing operations and the continued availability and cost of capital to sustain our operations on a longer term basis;
- our sales, marketing and distribution capabilities and strategy;
- the potential extent of revenues from future sales of SIVEXTRO, XENLETA and/or CONTEPO, if approved;
- our ability to build, manage and maintain a sales force for the commercialization of SIVEXTRO, XENLETA and CONTEPO, if approved;
- our ability to resolve the matters set forth in the Complete Response Letter we received from the U.S. Food and Drug Administration, or FDA, in connection with our New Drug Application, or NDA, for CONTEPO for the treatment of complicated urinary tract infections, or cUTIs, including acute pyelonephritis;
- the timing of the resubmission of the NDA for CONTEPO for the treatment of cUTIs and potential marketing approval of CONTEPO and other product candidates, including the completion of any post marketing requirements with respect to XENLETA for CABP and any other product candidates we may develop or obtain;
- our plans to pursue development of other product candidates including XENLETA for the treatment of infections in patients with cystic fibrosis;
- our expectations regarding our strategy to expand our product pipeline through opportunistically in-licensing or acquiring the rights to complementary products, product candidates and technologies for the treatment of a range of infectious diseases or other products, including additional community products;
- our ability to comply with the restrictive covenants under our debt facility with Hercules Capital, Inc., or Hercules, including but not limited to the ability to maintain minimum cash balance requirements;
- our ability to satisfy interest and principal payments under our debt facility with Hercules;
- our ability to successfully maintain inventory levels to satisfy product demand, as well as limit the unrealizable value of inventory based on historical usage, known trends, inventory age and market conditions;

- our expectations about the impact of the COVID-19 pandemic on our business operations, ongoing clinical trials and regulatory matters, including the ability of regulatory authorities to operate;
- the uncertainties inherent in the initiation and conduct of clinical trials, availability and timing of data from clinical trials, and whether results of early clinical trials or clinical trials in different disease indications will be indicative of the results of ongoing or future trials;
- our plans and the related cost expectations to pursue development of XENLETA for additional indications other than CABP, and of CONTEPO for additional indications other than cUTI;
- the future development and commercialization of XENLETA in the greater China region and Canada;
- our expectations with respect to milestone payments pursuant to the Agreement and Plan of Merger, dated July 23, 2018, and expectations with respect to potential advantages of CONTEPO or any other product candidate that we acquired in connection with the acquisition of Zavante Therapeutics, Inc., or the Acquisition;
- our ability to establish and maintain arrangements for manufacture of our product candidates;
- the potential advantages of SIVEXTRO, XENLETA, CONTEPO, and our other product candidates;
- our estimates regarding the market opportunities for SIVEXTRO, XENLETA, CONTEPO, and our other product candidates;
- the rate and degree of market acceptance and clinical benefit of SIVEXTRO for acute bacterial skin and skin structure infections, XENLETA for CABP, CONTEPO for cUTI and our other product candidates, if approved;
- our ability to establish and maintain collaborations including additional licensing agreements for XENLETA outside the United States, Canada and the greater China region;
- the potential benefits under our license agreements with Sumitomo Pharmaceuticals (Suzhou), or the China Region License Agreement, and with Sunovion Pharmaceuticals Canada Inc., or the Sunovion License Agreement;
- our future intellectual property position;
- our ability to maintain the level of our expenses consistent with our internal budgets and forecasts;
- the demand for securities of pharmaceutical and biotechnology companies in general and our ordinary shares in particular;
- competitive factors;
- risks of relying on external parties such as contract manufacturing and sales organizations;
- compliance with current or prospective governmental regulation;
- general economic and market conditions;
- our ability to attract and retain qualified employees and key personnel;
- our business and business relationships, including with our employees and suppliers;

- our ability to satisfy milestone, royalty and transaction revenue payments pursuant to the Stock Purchase Agreement between our wholly owned subsidiary Zavante Therapeutics, Inc. and SG Pharmaceuticals, Inc.; and

- other risks and uncertainties, including those described in ‘‘Risk Factors’’ in Part I, Item 1A of this Annual Report on Form 10-K.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make.

You should refer to “Risk Factor Summary” and “Risk Factors” in Part I, Item 1A of this Annual Report for a discussion of important factors that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statements, except as required by applicable law.

Throughout this Annual Report on Form 10-K, unless the context requires otherwise, all references to “Nabriva,” “the Company,” we,” “our,” “us” or similar terms refer to Nabriva Therapeutics plc, together with its consolidated subsidiaries.

SPECIAL NOTE

On December 2, 2020, our board of directors effected a one-for-ten reverse stock split of our ordinary shares, or the Reverse Stock Split. As a result of the Reverse Stock Split, every ten ordinary shares of $0.01 each (nominal value) in the authorized and unissued and authorized and issued share capital of the company were consolidated into one ordinary Share of $0.10 each (nominal value), and the nominal value of each ordinary share was subsequently immediately reduced from $0.10 to $0.01 nominal value per share. All outstanding stock options, restricted stock units and warrants entitling their holders to purchase or acquire ordinary shares were adjusted as a result of the Reverse Stock Split. Accordingly, all ordinary share, common share, equity award, warrant and per share amounts in this Annual Report on Form 10-K have been adjusted to reflect the Reverse Stock Split.

RISK FACTOR SUMMARY

Our business is subject to a number of risks of which you should be aware before making an investment decision. Below we summarize what we believe are the principal risk factors but these risks are not the only ones we face, and you should carefully review and consider the full discussion of our risk factors in the "Risk Factors" in Part I, Item 1A, together with the other information in this Annual Report.

- We depend heavily on the success of SIVEXTRO, XENLETA and CONTEPO. The U.S. Food and Drug Administration, or FDA, has approved SIVEXTRO for oral and intravenous use by adults and adolescents for the treatment of acute bacterial skin and skin structure infections, or ABSSSI, and XENLETA for oral and intravenous use for the treatment of community-acquired bacterial pneumonia, or CABP. CONTEPO is being developed for complicated urinary tract infections, or cUTI. If we are unable to obtain marketing approval for CONTEPO, or if we fail in our commercialization efforts for SIVEXTRO and/or XENLETA, or experience significant delays in doing so, our business will be materially harmed.

- We have incurred significant losses since our inception and anticipate that we will incur losses for at least the next several years and may never generate profits from operations or maintain profitability.

- We will need substantial additional funding. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

- If we fail to meet the requirements for continued listing on The Nasdaq Global Select Market, our ordinary shares could be delisted from trading, which would decrease the liquidity of our ordinary shares and our ability to raise additional capital.

- Our level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations. We may not have cash available to us in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due or to comply with minimum cash balance requirements.

- The number of ordinary shares underlying our outstanding warrants is significant in relation to our currently outstanding ordinary shares, which could have a negative effect on the market price of our ordinary shares and make it more difficult for us to raise funds through future equity offerings.

- SIVEXTRO, XENLETA and any other product candidate that receives marketing approval may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for such products and product candidates, if approved, may be smaller than we estimate.

- We have entered into a Sales Promotion and Distribution Agreement with Merck & Co. related to the promotion, distribution and sale of SIVEXTRO. If our collaboration with Merck is not successful, we may incur significant expenses related to the distribution of SIVEXTRO without realizing adequate value from the agreement.

- We have entered into and may enter into additional collaborations with third parties for the development or commercialization of XENLETA, CONTEPO and our other product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these products and product candidates.

- If we are unable to obtain and maintain patent protection for our technology, products and product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology, products and product candidates similar or identical to ours, and our ability to successfully commercialize our technology, products and product candidates may be adversely affected.

- Business interruptions resulting from the SARS-CoV-2 infection causing COVID-19 outbreak or similar public health crises have caused and could continue to cause a disruption of the commercialization of our products and the development of our product candidates and adversely impact our business.

- If clinical trials of XENLETA, CONTEPO or any of our other product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, regulatory authorities in the European Union, or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of XENLETA, CONTEPO or any other product candidate.

- If we experience delays or difficulties in the enrollment of patients in our clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

- If serious adverse or undesirable side effects are identified in SIVEXTRO, XENLETA, or CONTEPO or any other product candidate that we develop or following their approval and commercialization, we may need to modify, abandon or limit our development or marketing of that product or product candidate.

- We are a “smaller reporting company”, and the reduced disclosure requirements applicable to smaller reporting companies may make our ordinary shares less attractive to investors.

- The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation. We are incorporated as a public limited company under Irish law.

- The intended efficiency of our corporate structure depends on the application of the tax laws and regulations in the countries where we operate, and we may have exposure to additional tax liabilities or our effective tax rate could change, which could have a material impact on our results of operations and financial position.

- U.S. persons who own 10 percent or more of our shares may be subject to U.S. federal income taxation on certain of our foreign subsidiaries’ income even if such income is not distributed to such U.S. persons.

- A transfer of our ordinary shares, other than a transfer effected by means of the transfer of book-entry interests in the Depository Trust Company, may be subject to Irish stamp duty.

- We may be classified as a passive foreign investment company for one or more of our taxable years, which may result in adverse U.S. federal income tax consequence to U.S. holders.

PART I

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company engaged in the commercialization and research and development of novel anti-infective agents to treat serious infections. We have the commercial rights to two approved products, SIVEXTRO and XENLETA, as well as one development product candidate, CONTEPO. We may potentially develop XENLETA and CONTEPO for additional indications. Both the oral and intravenous, or IV, formulations of XENLETA formulations and CONTEPO were granted Qualified Infectious Disease Product, or QIDP, and Fast Track designation by the FDA. Incentives for QIDP status include an additional five years of exclusivity, in addition to any other exclusivity periods, as well as fast track and priority review status, for which both XENLETA formulations and CONTEPO are eligible.

SIVEXTRO

SIVEXTRO is a novel oxazolidinone class antibiotic to treat susceptible Gram-positive pathogens including MRSA, one of the serious public health threats identified by the CDC. Available in both IV and oral formulations, SIVEXTRO was approved by the FDA for the treatment of adults with ABSSSI, such as cellulitis, wound infections, and Erysipelas and in 2020 the label was expanded to include adolescents 12 years of age and older.

On July 15, 2020, we announced that we entered into a Sales Promotion and Distribution Agreement, the Distribution Agreement, with MSD International GmbH, or MSD, and Merck Sharp & Dohme Corp., or the Supplier, each a subsidiary of Merck & Co. Under the Distribution Agreement, MSD appointed us as its sole and exclusive distributor of certain products containing tedizolid phosphate as the active ingredient previously marketed and sold by Supplier and MSD under the trademark SIVEXTRO® for injection, intravenous and oral use in the United States and its territories. SIVEXTRO is an oxazolidinone-class antibacterial indicated in adults and patients 12 years of age and older for the treatment of ABSSSI caused by susceptible isolates of the following Gram-positive microorganisms: *Staphylococcus aureus*, including MRSA and methicillin-susceptible, or MSSA, isolates, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group (including *Streptococcus anginosus*, *Streptococcus intermedius* and *Streptococcus constellatus*), and *Enterococcus faecalis*.

Under the Distribution Agreement and subject to the fulfillment of certain conditions, including our engaging sufficient sales representatives, restrictions relating to travel and physician office access in the United States and its territories, or SIVEXTRO Territory, due to COVID-19 having continued to decrease in a sufficient portion of the SIVEXTRO Territory so as not to hinder the successful detailing of SIVEXTRO, we have been granted the right to initially promote SIVEXTRO in the SIVEXTRO Territory and, upon satisfaction of additional conditions, including an increase in the number of our sales representatives, the right to exclusively distribute SIVEXTRO in the SIVEXTRO Territory, including the sole right and responsibility to fill orders with respect to SIVEXTRO in the SIVEXTRO Territory. In April 2021, we satisfied those conditions, including the requirement to increase the number of sales representatives, and began filling orders of SIVEXTRO with our own Nabriva National Drug Code, or NDC.

SIVEXTRO was the primary driver of our topline revenues in 2021, and we believe that will continue in the near term. We believe SIVEXTRO will serve as the foundation of our portfolio in the near-term, and serve as the primary source of our revenue as we continue to raise awareness around and establish other products in our portfolio. We plan to maximize our resource allocation in the near-term to drive SIVEXTRO sales back to historical prescription trends in order to effectively and efficiently drive our operating cash flow.

XENLETA

Discovered and developed by our team, XENLETA is a semi-synthetic pleuromutilin antibiotic that is the first in its class for intraveneous, or IV, and oral administration in humans. XENLETA is designed to inhibit the synthesis of a specific protein on the bacterial ribosome, which is required for bacteria to grow, by binding with high affinity and specificity at molecular targets that are different than other currently available antibiotic classes causing cell death.

Based on results from two global, Phase 3 clinical trials, we believe XENLETA is well-positioned for use as first-line monotherapy for the treatment of CABP due to its novel mechanism of action, short five-day course of therapy for oral XENLETA, targeted spectrum of activity, resistance profile, achievement of substantial drug concentrations in lung tissue and fluid, availability of oral and IV formulations and a generally well-tolerated profile. We believe XENLETA represents a potentially important new treatment option for the five to six million adults in the United States diagnosed with CABP each year.

We believe that pleuromutilin antibiotics can help address the major public health threat posed by bacterial resistance, which the World Health Organization, or WHO, characterized in 2017 as one of the biggest threats to human health. Increasing resistance to antibiotics currently used to treat CABP is a growing concern and has become an important issue for clinicians selecting the appropriate initial antibiotic treatment for patients prior to determining the specific microbiological cause of the infection, referred to as empiric treatment. For example, the U.S. Centers for Disease Control and Prevention, or CDC, has classified *Streptococcus pneumoniae*, currently the most common respiratory pathogen, as a serious threat to human health as a result of increasing resistance to currently available antibiotics. In a recent retrospective cohort study of *Streptococcus pneumoniae* blood and pulmonary isolates from U.S. sites, resistance to macrolide class antibiotics was observed in 47.3% of *Streptococcus pneumoniae* colonies obtained from respiratory cultures, and 29.6% from blood cultures. As resistance to macrolide class antibiotics in respiratory isolates was greater than 25% in all regions of the U.S, we believe clinicians should consider alternatives to macrolide monotherapy for community acquired pneumonia in the U.S. based on current treatment guidelines.

In addition, the CDC recently reported on the growing evidence of widespread resistance to macrolide class antibiotics, which are designed to disrupt bacterial protein synthesis, in *Mycoplasma pneumoniae*, a common cause of CABP that is associated with significant morbidity and mortality. Furthermore, *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus*, or MRSA, which has also been designated as a serious threat to human health by the CDC, has emerged as a more common cause of CABP in some regions of the world, and a possible pathogen to be covered with empiric therapy.

As a result of increasing resistance to antibiotics and the wide array of potential pathogens that cause CABP, the current standard of care for hospitalized patients with CABP whose treatment is initiated in the hospital usually involves first-line empiric treatment with a combination of antibiotics (cephalosporins and macrolides) or monotherapy with a respiratory fluoroquinolone. In patients where MRSA is suspected, fluoroquinolones are also typically administered in combination with other antibiotics. Combination therapy presents the logistical challenge of administering multiple drugs with different dosing regimens, with some drugs available only through IV administration, which may increase the risk of drug-drug interactions and the potential for serious side effects. Fluoroquinolones are associated with safety and tolerability concerns, including a relatively high risk for developing *Clostridium difficile* infection and because of their generally broad spectrum of activity, increasing rates of resistance for uropathogens.

The FDA has communicated safety information about fluoroquinolones, advising that when used systemically, in the form of tablets, capsules or injectable preparations, fluoroquinolones are associated with disabling and potentially permanent serious side effects. In December 2018, the FDA warned prescribers of an increase in the occurrence of rare but serious events of ruptures or tears in the main artery of the body, called the aorta. These tears, called aortic dissections, or ruptures of an aortic aneurysm can lead to dangerous bleeding or death. Prior communications pertaining to the safety of fluoroquinolones occurred in July 2018 (significant decreases in blood sugar and certain mental health side effects), July 2016 (disabling side effects of the tendons, muscles, joints, nerves, and central nervous system), May 2016 (restricting use for certain uncomplicated infections), August 2013 (peripheral neuropathy), and July 2008 (tendinitis and tendon rupture). The European Medicines Agency, or EMA, has also reviewed this class of antibiotics and has modified prescribing information to restrict use, and outline some of the safety risks. We believe these concerns have contributed to the increase in restrictions imposed by hospitals on and overall decline in the use of fluoroquinolones.

Many currently available antibiotic therapies are only available for IV administration and are prescribed for seven to fourteen days, requiring prolonged hospitalization or a switch to a different orally administered antibiotic, with the attendant risk that the patient might respond differently.

Effective January 1, 2017, the Joint Commission & Center for Medicare and Medicaid Services, or CMS, began requiring all U.S. hospitals to have antibiotic management guidelines, also known as “stewardship” committees, in place to identify antibiotics most appropriate and targeted to each individual patient’s infection. Past efforts to “cast the widest net possible” with broad-spectrum antibiotics that affect many types of bacteria have caused problems, such as *Clostridium difficile* infections, by killing good bacteria or increased antibiotic resistance in other bacteria in different areas of the body. Additionally, in 2016, the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America, or IDSA/SHEA, updated their antibiotic stewardship guidelines for antibiotic use. We believe that three key goals from these guidelines are applicable to the treatment of CABP:

- Reduce use of antibiotics associated with a high risk of *Clostridium difficile* infections;
- Increase use of oral antibiotics as a strategy to improve outcomes or decrease costs; and
- Reduce antibiotic therapy to the shortest effective duration.

Consistent with the Antimicrobial Stewardship principles, we believe that XENLETA could be well suited as either a first-line or second-line empiric monotherapy for the treatment of CABP patients in the hospital setting, outpatient-transition of care setting or in the community setting, because of its novel mechanism of action, spectrum of activity for CABP pathogens, including against multidrug resistant strains, achievement of substantial drug concentrations in lung fluids and lung immune cells, the flexibility to step down from IV to oral administration and a favorable safety and tolerability profile.

On September 9, 2019, we announced that the oral and IV formulations of XENLETA were available in the United States for the treatment of CABP in adults through major specialty distributors. This followed the approval by the FDA of our NDA for XENLETA on August 19, 2019 for the treatment of adults with CABP. XENLETA is the first oral and IV treatment in the pleuromutilin class of antibiotics available for the systematic administration in humans.

We primarily market XENLETA to community-based physicians. This strategy has been implemented given XENLETA’s convenient 5-day dosing of its oral formulation and given that it is widely covered under most commercial insurance plans.

We entered into a license and commercialization agreement in March 2019 with Sunovion Pharmaceuticals Canada Inc., or Sunovian, for the commercial rights to XENLETA in Canada. On July 16, 2020, we announced that Sunovian received approval from Health Canada to market oral and IV formulations of XENLETA® (lefamulin) for the treatment of community-acquired pneumonia, or CAP, in adults, with the related Notice of Compliance from Health Canada dated July 10, 2020.

On July 28, 2020, we announced that the European Commission, or EC, issued a legally binding decision for approval of the marketing authorization application for XENLETA™ (lefamulin) for the treatment of CAP, in adults when it is considered inappropriate to use antibacterial agents that are commonly recommended for initial treatment or when these agents have failed following a review by the EMA. The EC approved XENLETA for countries of the European Economic Area, or EEA, and United Kingdom, or U.K. We intend to work with a commercial partner to make XENLETA available to patients in the EEA and U.K.

In May 2021, Sumitomo Pharmaceuticals (Suzhou) and we announced positive topline results from Sumitomo Pharmaceuticals (Suzhou)’s Phase 3 clinical trial of lefamulin in Chinese adults with CABP. Sumitomo Pharmaceuticals (Suzhou)’s multi-center, randomized, double-blind trial was designed to evaluate the safety and efficacy of IV to oral lefamulin compared to IV/oral moxifloxacin in 125 patients with CABP. The results were similar to those observed in our global Phase 3 LEAP 1 and LEAP 2 clinical trials of lefamulin conducted. Consistent with previously reported clinical trial results, lefamulin was observed to be generally well-tolerated, with an overall rate of treatment-emergent adverse events, or TEAEs, comparable to that of moxifloxacin. The vast majority of TEAEs in both treatment arms were mild-to-moderate in severity, with serious adverse events occurring in 4% of lefamulin-treated patients and 10% of moxifloxacin-treated patients. TEAEs leading to discontinuation were uncommon and observed in just 5% of subjects in both treatment arms.

In September 2021, Sumitomo Pharmaceuticals (Suzhou) and we announced Sumitomo Pharmaceuticals (Suzhou) received approval to market oral and IV formulations of XENLETA for the treatment of community-acquired pneumonia in adults in Taiwan.

In November 2021, we announced that Sumitomo Pharmaceuticals´ (Suzhou) NDA to market oral and IV formulations of lefamulin for the treatment of community-acquired pneumonia, or CAP, in adults in mainland China was accepted for review by the Chinese Center for Drug Evaluation, or CDE, China's regulatory authority, on November 23, 2021. The expected time for the application review is up to 24 months.

COVID-19 has demonstrated the devastating impact that infectious diseases can have on public health and the economy. Similar to other acute respiratory virus infections, including influenza virus, patients infected with COVID-19 are at increased risk of developing concomitant bacterial pneumonia. In published reports, bacterial pneumonia has been shown to affect nearly 50% of hospitalized patients with COVID-19, with an associated mortality of almost 50%. Some physisians routinely administer broad-spectrum antibiotics as an empiric therapy for bacterial pneumonia to all patients with COVID-19 and moderate or severe hypoxemia. Other physisians administer antibiotics only for certain situations, such as the presence of a lobar infiltrate on a chest X-ray, leukocytosis, an elevated serum lactate level, microbiologic data, or shock. If antimicrobials are initiated, the NIH Panel recommends that their use should be reassessed daily to minimize the adverse consequences of unnecessary antimicrobial therapy. In addition to XENLETA's potential role in treating COVID-19 patients with superimposed bacterial pneumonia, we are assessing the anti-inflammatory activity of XENLETA and what role, if any, these characteristics may play in the management of patients with COVID-19.

CONTEPO

On July 24, 2018, we completed the acquisition of Zavante Therapeutics, Inc., or Zavante, together with its lead product candidate CONTEPO™ (fosfomycin for injection, previously referred to as ZTI-01 and ZOLYD), or the Acquisition. With the Acquisition, Zavante became our wholly owned subsidiary.

The prevalence of antibiotic-resistant bacteria is increasing and is considered a significant threat to global health. Complicated urinary tract infections, or cUTIs, including acute pyelonephritis, or AP, are among the most common infections due to multi-drug resistant, or MDR bacteria, including carbapenem-resistant Enterobacteriaceae, or CRE, and are often healthcare-associated. Global mortality attributable to CRE infections has been estimated in some studies to be over 20% and reflects the need for safe, alternative, carbapenem-sparing options.

CONTEPO is a novel, potentially first-in-class investigational IV antibiotic in the United States with a broad spectrum of Gram-negative and Gram-positive activity, including activity against most MDR strains such as extended-spectrum β-lactamase-, or ESBL-producing Enterobacteriaceae. Intravenous fosfomycin has been approved for a number of indications and utilized for over 45 years in Europe to treat a variety of serious bacterial infections, including cUTIs. CONTEPO utilizes a new dosing regimen that optimizes its pharmacokinetics and pharmacodynamics. We believe these attributes, the extensive worldwide clinical experience and the positive efficacy and safety results from the Phase 2/3 clinical trial support CONTEPO as a first-line treatment for cUTIs, including AP, suspected to be caused by MDR pathogens. At least 20% of cUTIs are caused by MDR bacteria and limited treatment options are available in the U.S. In addition, non-clinical data have shown that CONTEPO acts in combination with certain other antibiotics to improve bacterial killing.

We submitted an NDA for marketing approval of CONTEPO for the treatment of cUTI including AP in adults in the United States, to the FDA in October 2018. The NDA submission is utilizing the 505(b)(2) regulatory pathway and is supported by a robust data package, including a pivotal Phase 2/3 clinical trial (known as ZEUS™), which met its primary endpoint of statistical non-inferiority to high dose piperacillin/tazobactam in patients with cUTI, including AP. In April 2019, the FDA issued a CRL in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP, stating that it was unable to approve the application in its current form. The CRL requested that issues related to facility inspections and manufacturing deficiencies at our active pharmaceutical ingredient contract manufacturer be addressed prior to the FDA approving the NDA. We requested a "Type A" meeting with the FDA to discuss its findings and this meeting occurred in July 2019. As the FDA did not request any new clinical data and did not raise any other concerns with regard to the safety or efficacy of CONTEPO in the CRL, the purpose of the meeting was to discuss and

gain clarity on the issues related to facility inspections and manufacturing deficiencies at one of our contract manufacturers that were described in the CRL and other matters pertaining to the steps required for the resubmission of the NDA for CONTEPO. We resubmitted our NDA in December 2019 and the FDA acknowledged the resubmission in January 2020. On June 19, 2020 we received a second CRL from the FDA. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cites observations at our manufacturing partners that could not be resolved due to FDA's inability to conduct onsite inspections because of travel restrictions. On October 30, 2020, we participated in a "Type A" meeting with the FDA to obtain any new information related to the FDA´s pending conduct of inspections of foreign manufacturers during the COVID-19 pandemic that has negatively impacted a number of FDA product reviews, including our NDA for CONTEPO. On April 14, 2021, the FDA issued industry guidance on remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities during the COVID-19 pandemic specifying that when it cannot perform a Pre-Approval Inspection, or PAI, or a Pre-License Inspection, or PLI, or when the FDA determines that it would be useful to supplement a planned inspection, the agency will consider using tools other than a physical inspection and select the most appropriate method to address the specific risks that justify the need for the PAI or PLI. The FDA informed us that onsite inspections of our manufacturing partners in Europe are required in order for the FDA to complete the review of a potential CONTEPO NDA resubmission. Due to travel restriction related to the COVID-19 pandemic, the FDA suspended onsite inspections of ex-US manufacturers for all non-COVID products. As a result, we requested an extension of the timeline for a potential CONTEPO NDA resubmission until June 2023, which the FDA granted on March 21, 2022. We are awaiting further clarity from the FDA regarding their ability to complete onsite inspections at our manufacturing partners in Italy and Spain before determining specific timing of the potential NDA resubmission, which we plan to submit promptly once we have clarity from the FDA. We currently do not have a forecasted date for the resubmission of our NDA for CONTEPO, for the treatment of cUTI, including AP. The FDA released the Resiliency Roadmap for FDA Inspectional Oversight that describes the systematic approach that FDA will utilize to manage postponed inspections and other oversight activities. The prioritization plan considers public health risks related to conducting an inspection, such as the impact of the product's availability on public health, as well as investigator safety and travel restrictions/advisories. In addition, the FDA informed us that, while they cannot predict when an inspection may occur and when the pandemic may prevent the FDA from completing inspections, tier 1 mission-critical inspections and tier 2 higher priority inspections, which includes PAIs, will continue to be prioritized going forward. We cannot predict the outcome of any further interactions with the FDA or when CONTEPO will receive marketing approval, if at all.

Our Strategy

We are a biopharmaceutical company engaged in the commercialization and research and development of novel anti-infective agents to treat serious infections. The key elements of our strategy are:

- ***Maximize the commercial potential of SIVEXTRO for ABSSSIs , XENLETA for CABP, and CONTEPO for cUTIs.*** We have established a scalable commercial infrastructure focused on maximizing the value of SIVEXTRO, XENLETA, and if approved, CONTEPO. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021. We may also adjust the allocation of our sales representatives across our portfolio from time to time to maximize sales. We have distribution rights to SIVEXTRO in the United States under a Sales Promotion and Distribution Agreement, or the Distribution Agreement, with MSD International GmbH, or MSD, and Merck Sharp & Dohme Corp., or the Supplier, each a subsidiary of Merck & Co. We own exclusive, worldwide rights to XENLETA and U.S. rights to CONTEPO and we have out licensed the rights to XENLETA in Canada and China. We plan to continue to explore licensing of rights to XENLETA in other territories outside the United States. Our initial target population for SIVEXTRO in the United States focused on historial SIVEXTRO prescribers for ABSSI. Our initial target patient population for XENLETA in the United States consists of adult patients with moderate to severe CABP and the initial target population for CONTEPO is expected to be hospitalized adult patients with cUTIs, including AP. If CONTEPO receives marketing approval from the FDA, we plan to commercialize it in the United States with either internal or external sales resources. We believe CONTEPO has an innovative profile which, if

approved, would support its adoption in the United States for adult cUTI patients treated in the hospital. XENLETA also has the opportunity to be adopted as outpatient transition of care from the hospital, or emergency department, or as an out-patient treatment in a community setting, each of which we believe represents a significant commercial opportunity. Outside the United States we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with multiple third parties to commercialize XENLETA in such markets. We currently have a Market Access team that is working with large payors, including managed care organizations to secure favorable formulary placement for SIVEXTRO and XENLETA. In addition we offer Patient Assistance Programs to reduce the cost of our drugs at the point of sale. Medical science liaisons are engaging with health care providers to serve as a resource for learning about XENLETA.

- ***Evaluate business development opportunities and potential collaborations.*** As part of our corporate strategy, we continue to evaluate business development opportunities and potential collaborations. We may further expand our product pipeline through opportunistically in licensing or acquiring the rights to complementary products, product candidates and technologies for the treatment of a range of infectious diseases or other products that we would efficiently leverage with our commercial infrastructure, including additional community products, which could involve an acquisition of or combination or other strategic transaction with another operating business. We plan to evaluate the merits of entering into collaboration agreements with other pharmaceutical or biotechnology companies that may contribute to our ability to efficiently advance our product candidates, build our product pipeline, concurrently advance a range of research and development programs and leverage our commercial infrastructure. We may consider out-licensing certain products for certain market segments. Potential collaborations may provide us with funding and access to the scientific, development, regulatory and commercial capabilities of the collaborators. We expect to continue to explore opportunities from domestic and international governments, foundations, and non-governmental entities to provide additional funding and support for potential future development programs.

- ***Pursue the continued development of XENLETA in additional indications.*** We are evaluating the cost and benefits of the continued development of XENLETA for indications in addition to CABP. Pediatric oral formulation development is ongoing, and a Phase 1 clinical trial of intravenous lefamulin in pediatric patients is ongoing. We initiated screening of our Phase 1 clinical trial of XENLETA for the treatment of resistant bacterial infections in patients with cystic fibrosis, or CF, in March 2022, and are on track to begin dosing in April 2022. Given the ongoing COVD-19 pandemic and the high risk it puts CF patients under, it is difficult to estimate recruitment timelines at this time. We believe XENLETA may have the potential to treat infections in patients with CF, acute bacterial skin and skin-structure infection, or ABSSSI, ventilator-associated bacterial pneumonia, or VABP, or hospital-acquired bacterial pneumonia, or HABP, and sexually transmitted infections, or STIs. In addition, we may explore longer duration of treatment with XENLETA to support development of a treatment for osteomyelitis and prosthetic joint infections. We believe that XENLETA would be differentiated from existing treatment options for these potential indications because of its novel mechanism of action, spectrum of activity, including activity against multi-drug resistant pathogens, achievement of substantial concentrations in relevant tissues, availability in both an IV and oral formulation and favorable safety and tolerability profile. We continue to evaluate these opportunities and consider their development if and when there is adequate funding which meets our business and financial objectives.

- ***Continue the development of CONTEPO for a pediatric indication.*** We are continuing the development of CONTEPO for use in pediatric patients with cUTIs. In June 2018, we initiated a Phase 1, non-comparative, open-label study of the pharmacokinetics and safety of a single dose of CONTEPO in pediatric subjects less than 12 years of age. As a result of COVID-19, research sites were temporarily closed for enrolment for a large part of 2020, and part of 2021, only a minority of sites are currently screening patients and allowing access to the institution. As a result, our development timeline for CONTEPO for use in pediatric patients with cUTIs was modified to reflect approximately a two-year delay due to COVID-19.

Background

Anti-Bacterial Market and Scientific Overview

Antibiotics that are active against both Gram-positive and Gram-negative bacteria are referred to as broad spectrum, while those that are active only against a select subset of Gram-positive or Gram-negative bacteria are referred to as narrow spectrum. Bacteria that cause infections are often referred to as bacterial pathogens. Because it often takes from 24 to 72 hours to definitively identify the particular bacterial pathogen causing an infection, and the difficulty associated with obtaining adequate bacterial cultures in some patients and infections, the causative pathogen(s) often remains unidentified. Since the introduction of antibiotics in the 1940s, numerous new antibiotic classes have been discovered and developed for therapeutic use. The development of new antibiotic classes and new antibiotics within a class is important because of the ability of bacteria to develop resistance to existing mechanisms of action of currently approved antibiotics. However, the pace of discovery and development of new antibiotic classes slowed considerably in the past few decades. The CDC estimates that the pathogens responsible for more than 70% of U.S. hospital infections are resistant to at least one of the antibiotics most commonly used to treat them. The CDC also estimated in 2019 that annually in the United States at least 2.8 million people become infected with bacteria that are resistant to antibiotics and at least 35,000 people die as a direct result of these infections.

Antibiotic resistance is primarily caused by genetic mutations in bacteria selected by exposure to antibiotics that do not kill all of the bacteria. In addition to mutated bacteria being resistant to the drug used for treatment, many bacterial strains can also become cross-resistant, meaning that they become resistant to multiple classes of antibiotics. As a result, the effectiveness of many antibiotics has declined, limiting physicians' options to treat serious infections and exacerbating a global health issue. For example, the WHO estimated in 2014 that people with infections caused by MRSA, a highly resistant form of bacteria, are 64% more likely to die than people with a non-resistant form of the bacteria. Resistance can increase the cost of healthcare because of the potential for lengthier hospital stays and more intensive care. Growing antibiotic resistance globally, together with the low level of investment in research and development, is considered one of the biggest global health threats. In 2010, the WHO stated that antibiotic resistance is one of the three greatest threats to human health. Partially in response to this threat, the U.S. Congress passed the GAIN Act in 2012, which provides incentives, including access to expedited FDA review for approval, fast track designation and five years of potential data exclusivity extension for the development of new QIDPs. Additional legislation is also being considered in the United States, including the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms Act of 2019, or DISARM, which is intended to establish a new reimbursement framework to enable product specific reimbursement to hospitals for anti-infective products. In addition, the CMS has launched an alternative New Technology Add-On Payment, or NTAP, to increase access to innovative antibiotics for hospital inpatients, by improving reimbursement rates for new generation anti-infectives, and specifically those considered QIDP. In September 2020, the Centers for Medicare & Medicaid Services, or CMS, granted a NTAP for XENLETA for injection, when administered in the hospital inpatient setting. Both the IV and oral formulations of XENLETA were granted QIDP and Fast Track designation by the FDA. NTAP was also grated for CONTEPO, making it the first QIDP antibiotic to be granted conditional NTAP approval prior to receiving FDA approval. CONTEPO was granted QIDP and Fast Track Designation by the FDA for the treatment of complicated urinary tract infections, or cUTIs, including acute pyelonephritis.

In 2018, sales of antibiotics to treat humans totaled approximately $45 billion globally. Although judicious use of antibiotics is important to reduce the rate of antibiotic resistance, this approach alone cannot fully address the threat from increasing antibiotic resistance. New antibiotics, and particularly new antibiotic classes, are needed to ensure the availability of effective antibiotic therapy in the future.

Acute Bacterial Skin and Skin-Structure Infections

Market Overview

ABSSSIs are very common and are characterized by a wide range of disease presentations. Over 10.7 million unique patients are diagnosed annually with ABSSSIs and lead to over 850,000 hospitalizations based on our market research. The vast majority of ABSSSI patients are successfully treated in the community setting with oral medications.

The frequency of ABSSSI is increasing. From 2000 to 2004, total hospital admissions attributed to ABSSSIs increased by 30%, followed by another 17% increase from 2005 to 2011. During a similar time period, from 1993 to 2005, the number of emergency department visits attributed to ABSSSIs almost tripled, from 1.2 million to 3.4 million patients. The increase in frequency of ABSSSI is attributed to the spread of resistant bacteria, in particular, community-associated methicillin-resistant *Staphylococcus aureus*, or CA-MRSA. ABSSSI includes infections of deeper soft tissues, cellulitis, wound infections, burns, and major abscesses. They often lead to substantial morbidity and mortality, can be resource intensive and incur high healthcare costs.

Causes of ABSSSIs

ABSSSIs are a frequent reason for seeking care at in both the outpatient and hospital settings. *Staphylococcus aureus* is one of the most common pathogens associated with these infections, and the emergence of community-associated MRSA, has represented a significant challenge in their treatment.

Gram-positive bacteria, in particular *Staphylococcus aureus, Staphylococcus pyogenes*, and other *ß-hemolytic streptococci* are the most common pathogens in ABSSSI. Of increasing concern is the rapidly rising frequency of ABSSSI caused by MRSA. There has been a dramatic increase in the occurrence of CA-MRSA infections since 2000. In many U.S. cities CA-MRSA is the most common pathogen cultured from patients with skin and skin structure infections in emergency departments. The emerging incidence of resistance to multiple antibiotics in pathogens makes ABSSSI increasingly difficult to treat. The most recent practice guidelines published by the IDSA for the treatment of ABSSSIs reflect the impact of MRSA, because a large focus is on antibiotic regimens covering *Staphylococcus aureus*, in particular, MRSA. The introduction of community-associated MRSA organisms has also influenced the selection of empirical antibiotic therapy to treat ABSSSIs. Additionally, knowledge of regional microbial resistance and susceptibility patterns is essential to identify appropriate empirical coverage for MRSA. Therefore, empiric coverage for MRSA has been recommended for treatment of skin and soft tissue infections, given the high community prevalence of MRSA. Empiric antibiotic therapy with activity against MRSA is particularly important in the following circumstances:

- History of MRSA infection
- Recurrent infection in the setting of underlying predisposing condition(s)
- Skin and soft tissue infection not associated with purulence, in the setting of inadequate clinical response (within 72 hours) to antibiotic therapy with no activity against MRSA

It is recommended that ABSSSI patients with mild infection (localized involvement with no systemic symptoms), due to known or suspected MRSA, may be treated with oral antibiotic therapy. However, treatment with IV formulations of antibiotic therapy may be appropriate in the following circumstances:

- Extensive soft tissue involvement
- Signs of systemic toxicity
- Rapid progression of clinical manifestations
- Persistence or progression of symptoms after 48 to 72 hours of oral therapy
- Immunocompromise
- Proximity of soft tissue infection to an indwelling device (such as a prosthetic joint or a vascular graft); soft tissue infection should be considered a manifestation of device infection if it originates on the skin directly overlying the prosthesis site.

About MRSA

According to the CDC, "Antibiotic resistance threats in the United States, 2019" report, in contrast to the 2013 report, while the burden of antibiotic-resistance threats in the U.S. was greater than initially estimated, deaths are decreasing. However, the number of Americans who must deal with antibiotic resistant infections remains high. According to the CDC, more than 2.8 million antibiotic-resistant infections occur in the U.S. yearly and lead to the deaths of 35,000 Americans.

One of the serious public health threats identified by the CDC is MRSA, which continues to be a clinical and economic burden. Based on the CDC 2019 report, there were 323,700 estimated MRSA cases in hospitalized patients in 2017, and an estimated 10,600 deaths in the U.S due to MRSA. The European Centre for Disease Prevention and Control, or ECDC, estimates that more than four million patients in the European Union, or EU, healthcare acquired infections annually, resulting in 37,000 deaths and that a large proportion of these deaths are due to the most common multidrug-resistant bacteria, including MRSA. According to the ECDC, MRSA is still the most commonly identified antimicrobial-resistant pathogen in hospitals in many parts of the world, including Europe, the Americas, North Africa, the Middle East, and Asia. Data from the Eurosurveillance journal estimates MRSA infections affect more than 150,000 patients annually in the EU.

Currently Available Treatment Options

Since it may take as long as 48 to 72 hours to identify the pathogen(s) causing an infection and most of the currently available oral therapy options that cover resistant pathogens are narrow-spectrum treatments, physicians frequently prescribe two or more antibiotics to treat a broad-spectrum of potential pathogens. In general, empiric therapy choice has typically been guided by the patients' clinical circumstances including regional antibiotic resistance patterns, allergy history, and concomitant medications. A recent 12 month analysis of oral treatment options in the outpatient setting by IQVIA indicated cephalosporins (Keflex), sulfonamide/trimethoprim combinations (Bactrim), tetracyclines and fluroquinolones (Baxdela), are some of the most frequently prescribed oral treatments for certain serious bacterial skin infections. However, these commonly prescribed therapies must be dosed more frequently, and many have adverse drug effects such as drug-drug interactions and central nervous system effects. The efficacy of tetracyclines is supported by susceptibility testing and observational and retrospective reports; however their efficacy for treatment of skin and soft tissue infections due to MRSA has not been rigorously evaluated or compared in clinical trials. Fluroquinolones are not recommended as a treatment option for ABSSSIs caused by MRSA because of decreased susceptibility of MRSA to fluoroquinolones, which also highlights the need for additional treatment options for skin infections that are caused by fluoroquinolone-resistant organisms.

Limitations of Currently Available Treatment Options

The most common treatments for serious bacterial skin infections are beta-lactams, such as cephalosporins (cephalexin (Keflex), cefazolin (Anef)) or penicillin, or its derivates such as dicloxacillin, nafcillin or oxacillin. Other agents include, sulfonamide/trimethoprim combinations (Bactrim), tetracyclines, vancomycin, linezolid and fluroquinolone (Baxdela). Although many of these agents have an effective oral equivalent of dicloxacilin, some such as vancomycin or daptomycin (Cubicin) for MRSA infections do not; the lack of an effective bioequivalent oral formulation of these and many other commonly prescribed antibiotics requires continued IV therapy, which is inconvenient for the patient and may result in longer hospital stays and greater cost. Alternatively, because of the absence of the same antibiotic in an oral, well-tolerated formulation, physicians may switch the patient to a different orally available antibiotic at the time of hospital discharge. This carries the risk of new side effects and possible treatment failure if the oral antibiotic does not cover the same bacteria that were being effectively treated by the IV antibiotic therapy. While linezolid is a twice-daily IV and oral therapy, it is a narrow-spectrum treatment that is associated with increasing bacterial resistance, side effects from interactions with other therapies and other serious safety concerns.

Adverse Effects

Concerns about antibiotic safety and tolerability are among the leading reasons why patients stop treatment and fail therapy. The most commonly used antibiotics to treat ABSSSIs, such as cephalosporins (Keflex), sulfonamide/trimethoprim combinations (Bactrim), and fluroquinolones (Baxdela) are associated with safety and tolerability concerns. For example, Bactrim is associated with severe reactions including Stevens-Johnsons syndrome a rare and serious disorder of the skin and mucus membranes. As previously noted, fluoroquinolones are associated with tendon rupture, peripheral neuropathy and, more recently, valvular abnormalities, aortic aneurysm and/or dissection. In addition, fluoroquinolones have been associated with an increased frequency of *Clostridium difficile* colitis, an overgrowth of a bacteria in the colon that produces a toxin that results in inflammation of the colon and repeated bouts of watery diarrhea. Linezolid should not be taken by patients who are also on many commonly prescribed anti-depressants, such as monoamine oxidase inhibitors and serotonin reuptake inhibitors.

Our Solution : SIVEXTRO for the treatment of ABSSSI

SIVEXTRO (tedizolid phosphate) is a novel oxazolidinone class antibiotic to treat susceptible Gram-positive pathogens including MRSA, one of the serious public health threats identified by the CDC.

SIVEXTRO, available in both IV and oral formulations, was approved by the FDA in 2014 for the treatment of adults with ABSSSI such as cellulitis, wound infections and erysipelas and in 2020 the label was expanded to include adolescents 12 years of age and older.

Administered once-daily, SIVEXTRO offers an effective, short six-day course of therapy. Convenient dosing enables greater patient compliance and is one of the key therapeutic and commercial benefits of the drug over existing treatments, many of which must be taken more frequently and for longer periods of time. SIVEXTRO has proven efficacy and demonstrated 80% early clinical response in 48-72 hours, so clinicians can have confidence that the drug will work quickly and is well tolerated with a low incidence of side effects. There is no need for monitoring and no drug-drug interactions with selective serotonin reuptake inhibitors, or SSRIs, another significant competitive advantage, and SIVEXTRO is not a substrate for hepatic CYP450. Additionally, many older ABSSSI treatments can only be administered intravenously, and therefore require hospital treatment leading to increased healthcare costs.

Community-Acquired Bacterial Pneumonia

Market Overview

Our analysis of the LexisNexis data indicates that approximately 2.4 million of adult CABP patients were treated as inpatients with IV or injectable antibiotics, and we found that the majority of CABP patients enter the hospital inpatient setting following the initiation of antibiotic therapy during an Emergency Department, or ED, visit. Additionally, our analyses show that approximately 1.4 million adult CABP patients were treated with antibiotic courses, IV or oral, in the ED or as hospital outpatients and subsequently released without hospital admission.

Based on data collected from July 1, 2015 through June 30, 2018, on the Medicare.gov Hospital Compare website, the current national rate of readmissions for Medicare pneumonia patients is 16.6%, which is the percentage of patients who have had a recent hospital stay that must return to a hospital for unplanned care within 30 days of being discharged. The national average death rate for Medicare pneumonia patients, excluding Medicare Advantage plan data, is 15.6%, which is the percentage of patients who die, for any reason, within 30 days of admission to a hospital.

Based on data from LexisNexis Risk Solutions, as well as analysis of data from US hospitals and other healthcare facilities, we believe that the number of adult CABP patients who were treated with antibiotic therapy in hospitals in the United States exceeded 3.8 million for full-year 2016. Our analysis of the LexisNexis data also indicates that approximately 2.4 million of these adult CABP patients were treated as inpatients with IV/injectable antibiotics, and we find that the majority of CABP patients enter the hospital inpatient setting following the initiation of antibiotic therapy during an ED visit. Additionally, our analyses show that approximately 1.4 million adult CABP patients were treated with antibiotic courses (IV or oral) in the ED or as hospital outpatients and subsequently released without hospital admission.

Additionally, approximately 1.4 million adult CABP patients were treated with antibiotic courses (IV or oral) in the ED or as hospital outpatients and subsequently released without hospital admission. Furthermore, as a result of our market research in 2017-18, we believe that once adult CABP patients are released from ED or are discharged from U.S. hospitals, approximately 60-70%, receive oral antibiotic outpatient prescriptions as continuation of their antibiotic treatment. As hospitals look to minimize the total cost of care and duration of hospital stay for CABP patients toward improved outcomes, efficient transition of adult CABP inpatients to an oral antibiotic treatment as outpatient therapy can significantly reduce days of hospitalization and overall treatment cost.

IQVIA estimated that in 2017 approximately 2.0 million adult CABP patients were actively treated with antibiotics from prescribers in community clinics and at other non-hospital based sites of urgent care. As a result, we believe that approximately 6 million CABP patients are treated with antibiotics in the United States on an annual basis and 6 out of every 10 adult CABP patients have treatment initiated in a hospital setting versus. the community setting.

Overall, the impact of pneumonia is serious. Based on CDC data, approximately 50,000 patients died from CABP in the United States in 2014.

Causes of CABP

Pneumonia can be caused by a variety of micro-organisms, with bacteria being the most common identifiable cause. CABP refers to bacterial pneumonia that is acquired outside of a hospital setting. Signs and symptoms of CABP include cough, fever, sputum production and chest pain. A number of different types of bacteria can cause CABP, including both Gram-positive and Gram-negative bacteria. Pneumonia that is caused by atypical bacterial pathogens often has different symptoms and responds to different antibiotics than pneumonia caused by pathogens referred to as typical bacteria. However, atypical bacteria are not uncommon. The most common bacterial pathogens noted in current treatment guidelines from the Infectious Diseases Society of America, or IDSA, for hospitalized CABP patients who are not in the intensive care unit are *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Chlamydophila pneumoniae*, and *Legionella* species. In addition, IDSA notes the emergence of resistance to commonly utilized antibiotics for CABP, specifically drug-resistant *Streptococcus pneumoniae* and community-acquired MRSA, or CA-MRSA, as a major consideration in choosing empiric therapy. However, a majority of patients do not have a pathogen identified using routine diagnostic tests available to physicians.

Currently Available Treatment Options

In 2019, based on the most likely bacteria to cause CABP, IDSA and the American Thoracic Society, or ATS, updated their recommendations for the empiric treatment of non-severe hospitalized patients with CABP without risk factors for MRSA and *Pseudomonas aeruginosa* with either:

- a combination of a cephalosporin plus a macrolide or
- monotherapy with a respiratory fluoroquinolone; or
- combination therapy with a β-lactam and doxycycline when macrolides or fluoroquinolones are contraindicated.

Given concerns over increasing drug resistance (macrolides) and safety issues (macrolides, fluoroquinolones), the guidelines noted a need for additional research of new therapeutic agents, like XENLETA, for adults with CABP. As a new therapeutic agent for the treatment of CABP, we believe the treatment of CABP with XENLETA is consistent with the guidelines.

Regarding outpatient therapy, the updated guidelines now only conditionally recommend macrolide monotherapy for CABP patients with or without comorbidities or risk factors only if local pneumococcal macrolide resistance is less than 25% and reiterated that physicians need to be aware of the local susceptibility profiles of the common bacterial pathogens associated with CABP because of increasing resistance to first-line antibiotics. For example, rates of pneumococcal resistance to macrolides now exceed 25% in most areas of the US and resistance to

tetracyclines (another first line outpatient recommended therapy) exceed 25% in some areas, while resistance in *Mycoplasma pneumoniae* associated with severe disease has been recently reported by the CDC in the United States. Antibiotic resistance is widespread to various degrees throughout the world.

Limitations of Currently Available Treatment Options

When confronted with a new patient suffering from a serious infection caused by an unknown pathogen, a physician may be required to quickly initiate first-line empiric antibiotic treatment, often with a combination of antibiotics, to stabilize the patient prior to definitively diagnosing the particular bacterial infection. However, currently available antibiotic therapies for first-line empiric treatment of CABP suffer from significant limitations.

Bacterial Resistance and Spectrum of Activity

As a result of bacterial resistance, the effectiveness of many antibiotics has declined. For example, the CDC estimates that in 30% of severe *Streptococcus pneumoniae* cases, the bacterial pathogen is fully resistant to one or more clinically relevant antibiotics, with 44% of strains resistant to a macrolide in the United States. Antibiotic resistance has a significant impact on mortality and contributes heavily to healthcare system costs worldwide. According to the CDC, cases of resistant *Pneumococcal pneumonia* result in 32,000 additional doctor visits, approximately 19,000 additional hospitalizations and 7,000 deaths each year. None of the currently available treatment options provides a monotherapeutic, empiric, narrow spectrum of antibacterial coverage that sufficiently covers all of the most common bacterial causes of CABP, including multi-drug resistant strains.

Difficult, Inconvenient and Costly Regimens

Currently available antibiotics used to treat CABP and other serious infections can be difficult, inconvenient and costly to administer. Physicians typically prefer IV administration for patients hospitalized with more serious illness to ensure adequate delivery of the drug. Many IV antibiotics are prescribed for seven to 14 days or more and patients can be hospitalized for much or all of this period or require in-home IV therapy. The diagnosis related group, or DRG, reimbursement system often used in the U.S. hospital setting pays a fixed fee for an episode of CABP that may not fully compensate hospitals for the duration of hospitalized care. Prolonged IV treatment that extends the period of hospitalization may cause hospital costs to increase in excess of the fixed reimbursement fee, resulting in significant negative financial impact on healthcare institutions. In addition, to address all likely bacterial pathogens in a patient with a more serious illness, IDSA guidelines recommend using a combination of antibiotics. Combination therapy presents the logistical challenge of administering multiple drugs with different dosing regimens and may increase the risk of drug-drug interactions. While IV treatment delivers the drug more rapidly than is typical orally, once a patient is stabilized, oral treatment with the same drug allows for more convenient and cost-effective out-patient treatment. Because many commonly used antibiotics are only available in IV form, a switch to an oral therapy often requires changing to a different antibiotic, which may be less effective for the patient due to the different mechanism of action of the drug prescribed upon discharge.

Adverse Effects

Currently available antibiotic therapies can have serious side effects. These side effects may include severe allergic reactions, decreased blood pressure, nausea and vomiting, suppression of platelets, pain and inflammation at the site of injection, muscle, renal and oto-toxicity, optic and peripheral neuropathies, aortic dissection, valvular abnormalities, tendinopathy, hypoglycemia and headaches. At times, these side effects may be significant and require discontinuation of therapy. As a result, some treatments require clinicians to closely monitor patients' blood levels and other parameters, increasing the expense and inconvenience of treatment. This risk may increase with combination therapy, which exposes patients to potential adverse effects from each of the antibiotics used in treatment. For example, fluoroquinolones are associated with tendon rupture, peripheral neuropathy and, more recently, valvular abnormalities, aortic aneurysm and/or dissection. In addition, fluoroquinolones have been associated with an increased frequency of *Clostridium difficile* colitis, an overgrowth of a bacteria in the colon that produces a toxin that results in inflammation of the colon and repeated bouts of watery diarrhea. This has resulted in limitations on the use of fluoroquinolones in several countries. In November 2015, the FDA convened an Advisory Committee meeting to review the benefits and risks of

fluoroquinolones in less severe indications, such as uncomplicated UTI, acute bacterial sinusitis and acute bacterial exacerbations of chronic bronchitis. Based on the committee's recommendation, in July 2016, the FDA approved changes to the labels of fluoroquinolones to indicate that fluoroquinolones should be reserved for use in patients who have no other treatment options for the indications mentioned above, because the risk of these serious side effects generally outweighs the benefits in these patients. These changes included a requirement that a separate patient Medication Guide be given with each prescription that describes the safety issues associated with this class of drugs. In December 2018, an FDA review found that fluoroquinolone antibiotics can increase the occurrence of rare but serious events of ruptures or tears in the aorta. These tears, called aortic dissections, or ruptures of an aortic aneurysm can lead to dangerous bleeding or even death. They can occur with fluoroquinolones for systemic use given by mouth or through an injection. As a result, fluoroquinolone use has declined substantially in recent years.

Our Solution: XENLETA for the treatment of CABP

We believe that XENLETA, which is the first new class of antibiotic approved by the FDA in nearly 20 years for CABP, can fill the current treatment gap by providing clinicians the ability to treat a patient with suspected or confirmed CABP where there may be concerns about resistance, or adverse event profiles for available antibiotic classes, or for elderly patients or patients with co-morbidities where they are at higher risk for negative outcomes from pneumonia. XENLETA has demonstrated efficacy and a favorable safety profile as an empiric, short-course monotherapy for the treatment of CABP with targeted activity against Gram-positive, Gram-negative, and atypical bacteria that are commonly associated with CABP, including drug-resistant strains. The novel mechanism of action of XENLETA provides for a low risk of resistance development and low probability of cross resistance with other antibiotics, which is important given the increase in antimicrobial resistance to relevant CABP pathogens. XENLETA, with IV and oral formulations, and no need for a loading dose, has versatility to meet the health care provider and patient's clinical needs. For example, XENLETA can be utilized in patients as an IV antibiotic in the hospital setting with discharge on oral therapy, which provides significant advantages to the patients' health while potentially reducing the total cost of care to the hospital. Additionally, we believe a short course treatment with XENLETA oral monotherapy could benefit moderate to severe CABP patients treated in the Emergency Department, or ED, by potentially avoiding hospitalization. And finally, XENLETA can be utilized effectively in the community setting by primary care practitioners who can potentially avoid an ED visit, thereby, reducing patient hospitalization exposure and related significant associated costs to managed care plans.

Complicated Urinary Tract Infections

Market Overview

Infections due to a bacterial pathogen that are resistant to one or multiple antibiotic classes have become increasingly common and present a risk to our fight against infectious diseases and the management of complications in vulnerable patients. According to the CDC, more than 2.8 million hospital infections caused by bacteria resistant to one or more antibiotics occur every year in the United States, and over 35,000 patients with an antibiotic-resistant pathogen die each year. The prevalence of β-lactamase enzymes among Gram-negative pathogens threatens the usefulness of many β-lactam antibiotics and has resulted in greater reliance on last line antibiotics, including carbapenems.

cUTIs, including AP, are among the most common infections due to MDR bacteria, including CRE, and are often healthcare-associated. Global mortality attributable to CRE infections has been estimated in some studies to be over 20% and reflects the need for safe, alternative, carbapenem-sparing.

Surveillance and epidemiological studies suggest that some traditional, first line antibiotics may no longer be acceptable choices for early therapy. In one third party, large scale surveillance study, approximately one out of three patients hospitalized in the United States with cUTI, hospital associated pneumonia, or a bloodstream infection did not receive timely effective antibiotic therapy, and this delay was associated with increased morbidity and mortality. Based on third party studies, the rate of antibiotic resistance appears to be two to four times higher in patients who were admitted to the hospital from a nursing home or were recently hospitalized. Antibiotic therapy within the past six months has also been identified in these third party studies as a risk factor for antibiotic resistance.

New classes of antibiotics that are effective against drug-resistant pathogens are needed for early, appropriate treatment of serious infections in hospitalized patients and to treat patients who have failed to respond to standard, first-line antibiotics due to acquired drug resistance.

For over 45 years, oral and IV formulations of fosfomycin have been used in the EU, Australia, Canada, Africa, Asia, and South America, and an oral formulation of fosfomycin has been used in the United States. Oral fosfomycin is available in the United States as single dose therapy for cystitis and is noted as an appropriate treatment option for cystitis in treatment guidelines by the IDSA and the CDC. However, oral administration of fosfomycin provides inadequate concentrations that are required for treatment of more serious infections due to its limited bioavailability and dose limiting gastrointestinal tolerability.

Outside of the United States, IV fosfomycin is approved for patients with a variety of infections, often severe, including cUTI, bacteremia, osteomyelitis, nosocomial lower respiratory tract infections, surgical site infections, bone and joint infections, endocarditis, skin infections and bacterial meningitis. The efficacy and safety profile of IV fosfomycin has been established by more than 45 years of clinical use outside of the United States and has been evaluated in more than 60 clinical trials. Fosfomycin has retained high *in vitro* activity with a low and stable resistance profile, and continues to be suitable for use as a monotherapy for cUTI despite long term use.

Causes of cUTIs

cUTI is defined as a clinical syndrome characterized by pyuria (the presence of puss in the urine) and a documented microbial pathogen on culture of urine or blood, accompanied by local and systemic signs and symptoms, including fever, chills, malaise, flank pain, back pain or costo-vertebral angle pain or tenderness that occur in the presence of a functional or anatomical abnormality of the urinary tract, or in the presence of catheterization. Indwelling urethral catheters account for 70% to 80% of cUTIs, or 1 million cases per year in the United States. Catheter-associated UTI is the most common cause of secondary bloodstream infections and is linked to increased morbidity and mortality. Patients with pyelonephritis, regardless of underlying abnormalities of the urinary tract, are considered a subset of patients with cUTI.

cUTI are usually caused by a greater variety of pathogens, with a greater likelihood of associated antimicrobial resistance, than uncomplicated UTIs, or uUTIs. *Escherichia coli*, or *E. coli*, is isolated in approximately 75% to 95% of uUTIs and approximately 50% of cUTIs and is the most common etiologic agent of cUTIs. Additional commonly-identified Gram-negative uropathogens include other Enterobacteriaceae (such as *Klebsiella spp.*, *Proteus spp.*, *Enterobacter cloacae*) and non-fermenting Gram-negative bacilli (such as *Pseudomonas aeruginosa* and *Acinetobacter spp.*). Gram-positive organisms, such as Enterococci and coagulase-negative *Staphylococci*, may also be contributing pathogens.

Limitations of Currently Available Treatment Options

We believe bacterial resistance against antimicrobials has created the need for more antibiotic treatment options, particularly among MDR, Gram-negative bacilli (including CRE, ESBL, producers, and MDR *Pseudomonas aeruginosa*). Gram-negative antimicrobial resistance is particularly common among urinary tract pathogens. Enterobacteriaceae, including *E. coli* and *Klebsiella pneumoniae*, may acquire plasmids that encode ESBLs and confer resistance to third-generation cephalosporins and other broad-spectrum antibiotics. Third-generation cephalosporins and β-lactamase inhibitors, or BLIs, are also commonly ineffective against Enterobacteriaceae that generate AmpC enzymes.

The recent spread into hospitals of Enterobacteriaceae expressing emergent β-lactamases, including members of the serine carbapenemases and metallo-β-lactamases, endanger antibiotic options. The lack of available and effective antibiotic classes for these organisms has created an unmet medical need. For example, infections with CRE are difficult to treat, as there are limited treatment choices available. Mortality rates as high as 40% to 50% have been associated with CRE infections, making them a serious threat to public health. The available treatment choices are associated with serious potential toxicity, in the case of colistin and aminoglycosides, or concerns of allergy or hypersensitivity, in the case of β-lactams or penicillin derivatives.

Our Solution: CONTEPO for the Treatment of cUTI

- CONTEPO is an IV formulation of fosfomycin and the sole member of the epoxide antibiotic class.
- CONTEPO has a different mechanism of action than other IV antibiotics available in the United States.
- CONTEPO has a broad spectrum of *in vitro* activity against a variety of clinically important MDR Gram-negative pathogens, including ESBL-producing Enterobacteriaceae, CRE, and Gram-positive pathogens, including MRSA and vancomycin-resistant enterococci.
- CONTEPO has demonstrated *in vitro* additivity or synergy when used in combination with other classes of antibiotic agents in pre-clinical studies.
- CONTEPO has a small molecular size, which may enable high levels of tissue penetration and facilitate renal elimination, both of which are important for treatment of cUTIs.
- CONTEPO is supported by a long history of IV fosfomycin use outside the United States in a variety of indications, including cUTI.
- CONTEPO completed the ZEUS Study, a pivotal registrational Phase 2/3 clinical trial in cUTI, achieving non-inferiority to an active comparator.

CONTEPO is a potentially first-in-class epoxide IV antibiotic in the United States with a broad spectrum of bactericidal Gram-negative and Gram-positive activity, including activity against many contemporary MDR strains that threaten hospitalized patients. IV fosfomycin has an extensive commercial history in markets outside the United States, where it has been used broadly for over 45 years to treat a variety of indications, including cUTIs, bacteremia, pneumonia and skin infections with little resistance shown to date.

CONTEPO works differently than other IV antibiotics approved in the United States. CONTEPO inhibits an early step in bacterial cell wall synthesis, so the cell wall lacks integrity and the bacteria die quickly. We believe that because of its different mechanism of action, we have not observed any cross resistance to date between CONTEPO and any of the existing classes of intravenous antibiotics. In addition, CONTEPO has demonstrated in *in vitro* studies an additive or synergistic antibacterial effect with other classes of antibiotics when used in combination therapy in preclinical studies, and has been shown to restore susceptibility of resistant strains.

Our Products and Product Candidate

SIVEXTRO

Overview

SIVEXTRO (tedizolid phosphate) is a novel oxazolidinone class antibiotic to treat susceptible Gram-positive pathogens including MRSA, one of the serious public health threats identified by the CDC.

SIVEXTRO, available in both IV and oral formulations, was approved by the FDA in 2014 for the treatment of adults with ABSSSI such as cellulitis, wound infections and erysipelas and in 2020 the label was expanded to include adolescents 12 years of age and older.

Sales Promotion and Distribution Agreement with Merck & Co.

On July 15, 2020, we entered into a Sales Promotion and Distribution Agreement, or the Distribution Agreement, with MSD International GmbH, or MSD, and Merck Sharp & Dohme Corp., or Supplier, each a subsidiary of Merck & Co., Inc. Under the Distribution Agreement and subject to the satisfaction of certain conditions, MSD

appointed us as its sole and exclusive distributor of certain products containing tedizolid phosphate as the active ingredient previously marketed and sold by Supplier and MSD under the trademark SIVEXTRO® for injection, intravenous use and oral use, or the Products, in the United States and its territories, or the SIVEXTRO Territory. SIVEXTRO is an oxazolidinone-class antibacterial indicated in adults and pediatric patients 12 years of age and older for the treatment of acute bacterial skin and skin structure infections caused by certain susceptible Gram-positive microorganisms. On April 12, 2021, in accordance with the terms of the Distribution Agreement, we began exclusive distribution of SIVEXTRO under our own National Drug Code, or NDC, and we recognize 100% of net product sales of SIVEXTRO in our results of operations.

Under the Distribution Agreement and subject to the fulfillment of certain conditions, including us having engaged sufficient sales representatives, restrictions relating to travel and physician office access in the SIVEXTRO Territory due to COVID-19 having continued to decrease in a sufficient portion of the SIVEXTRO Territory so as not to hinder the successful detailing of SIVEXTRO, we have been granted the right by MSD initially to promote the Products in the SIVEXTRO Territory and, upon satisfaction of additional conditions, including an increase in sales representatives, the right to exclusively distribute the Products in the SIVEXTRO Territory, including the sole right and responsibility to fill orders with respect to the Products in the SIVEXTRO Territory. We successfully satisfied those conditions, including the increase in the number of sales representatives, and began filling orders of SIVEXTRO with our own Nabriva NDC beginning on April 12, 2021. Subject to applicable law, we are entitled to determine the final selling prices of the Products charged by us to our customers at our sole discretion, subject to an overall annual limit on price increases, and will be solely responsible for sales contracting and all market access activities, including bidding, hospital listing and reimbursement. We are responsible for all costs related to the promotion, sale and distribution of the Products by us, as well as all costs required to meet our staffing obligations under the Distribution Agreement. We are obligated to use commercially reasonable efforts to promote and distribute the Products and to maximize the sales of the Products throughout the SIVEXTRO Territory. We have agreed to employ a sales force or retain the services of a contract sales organization to fulfill our obligations under the Distribution Agreement. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

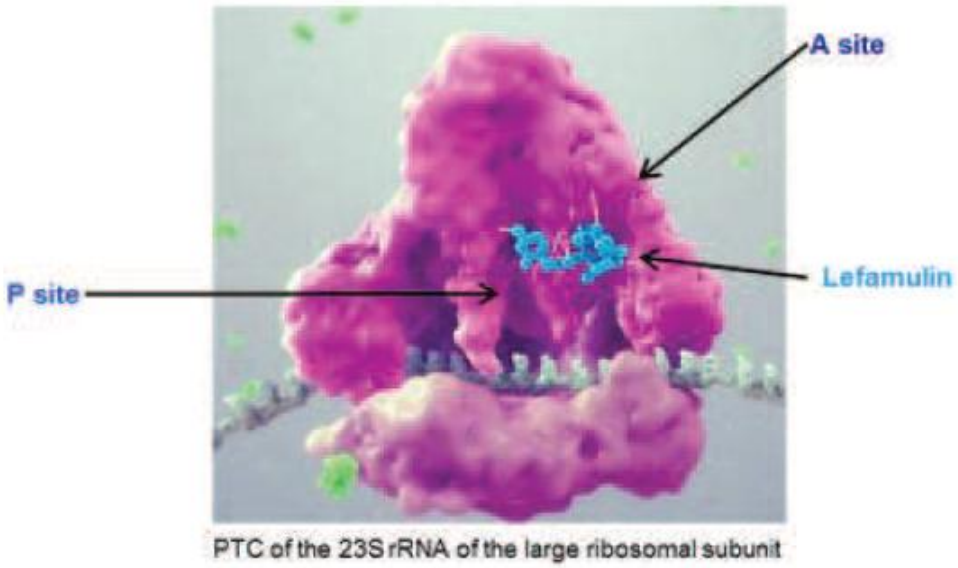
Furthermore, a subsidiary of Merck will sell to us, and we have agreed to purchase SIVEXTRO from such subsidiary at specified prices in such quantities as we may specify. Although we are entitled, subject to appliable law, to determine the final selling prices of SIVEXTRO in our sole discretion, subject to an overall annual limit on price increases, we may not be able to sell SIVEXTRO at prices high enough to recoup our investment in a sales force and other commercialization activities.

XENLETA

Overview

XENLETA is a semi-synthetic derivative of the naturally occurring antibiotic, pleuromutilin, which was originally identified from a fungus called *Pleurotus mutilius*. XENLETA is designed to inhibit the synthesis of bacterial protein, which is required for bacteria to grow. XENLETA acts by binding to the peptidyl transferase center, or PTC, on the bacterial ribosome in such a way that it interferes with the interaction of protein production at two key sites known as the “A” site and the “P” site, resulting in the inhibition of bacterial proteins and the cessation of bacterial growth. XENLETA’s binding occurs with high affinity, high specificity and at molecular sites that are different than other antibiotic classes. We believe that XENLETA’s novel mechanism of action is responsible for the lack of cross-resistance with other antibiotic classes that we have observed in our preclinical studies and clinical trials and a low propensity for

development of bacterial resistance to XENLETA. The binding of XENLETA to the PTC on the bacterial ribosome is depicted in the graphic below.



We believe that XENLETA is well suited to be used empirically as monotherapy for the treatment of respiratory tract infections, such as CABP, because of its spectrum of antibacterial activity against both the typical and atypical pathogens causing CABP. XENLETA is a pleuromutilin antibacterial indicated for the treatment of adults with CABP caused by susceptible microorganisms. In addition, in preclinical studies, XENLETA showed potent antibacterial activity against a variety of Gram-positive bacteria, Gram-negative bacteria and atypical bacteria, including multi-drug resistant strains. In preclinical studies and in Phase 1 clinical trials, XENLETA achieved substantial concentrations in the epithelial lining fluid, or ELF, of the lung, the site infected during pneumonia. XENLETA also provides the ability to switch from IV to oral therapy and maintain therapy with the same antibacterial treatment. The efficacy of XENLETA in humans has been shown in a proof-of-concept Phase 2 clinical trial with 207 patients with ABSSSI comparing two XENLETA doses (100 mg and 150 mg i.v. q12 h) with vancomycin (≥ 1,000 mg) over 5-14 days. This trial enrolled patients with severe skin and skin structure infections, excluding any patients with minor and uncomplicated infections. In total, 90.8 % of patients in the Modified Intent to Treat, or mITT population had *Staphylococcus aureus* infection; 69.1 % of patients had MRSA. The results of the clinical Phase 2 trial in ABSSSI provided the first proof of concept for the systemic use of a pleuromutilin antibiotic for the treatment of serious bacterial infections in humans. Thereafter, the clinical program for XENLETA progressed with completion of two Phase 3 clinical trials in CABP (LEAP 1, LEAP 2). These trials demonstrated that XENLETA treatment, administered as IV only, IV to oral, and oral only regimens, was non-inferior to the standard of care moxifloxacin for the treatment of adults with CABP. Each trial provided independent evidence of the treatment effect and safety in this population with unmet medical need. In May 2021, we and Sumitomo Pharmaceuticals (Suzhou) announced positive topline results from Sumitomo Pharmaceuticals (Suzhou)'s Phase 3 clinical trial of lefamulin in Chinese adults with CABP. Sumitomo Pharmaceuticals (Suzhou)'s multi-center, randomized, double-blind trial was designed to evaluate the safety and efficacy of IV to oral lefamulin compared to IV/oral moxifloxacin in 125 subjects with CABP. The results were similar to those observed in our global Phase 3 LEAP 1 and LEAP 2 clinical trials of lefamulin. Consistent with previously reported clinical trial results, lefamulin was observed to be generally well-tolerated, with an overall rate of treatment-emergent adverse events, or TEAEs, comparable to that of moxifloxacin. The vast majority of TEAEs in both treatment arms were mild-to-moderate in severity, with serious adverse events occurring in 4% of lefamulin-treated patients and 10% of moxifloxacin-treated patients. TEAEs leading to discontinuation were uncommon and observed in just 5% of subjects in both treatment arms.

The FDA has designated each of the IV and oral formulations of XENLETA as a QIDP, which provides for the extension of statutory exclusivity periods in the United States for an additional five years upon FDA approval of the product for the treatment of CABP and granted fast track designation to these formulations of XENLETA. Fast track designation is granted by the FDA to facilitate the development and expedite the review of drugs that treat serious conditions and fill an unmet medical need. The fast track designation for the IV and oral formulations of XENLETA will allow for more frequent interactions with the FDA, the opportunity for a rolling review of any NDAs, eligibility for priority review and a shortening of the FDA's goal for taking action on a marketing application from ten months to six months. Two NDAs for IV and oral formulations of XENLETA for treatment of CABP were submitted to the FDA December 19, 2018 and were approved on August 19, 2019. On July 16, 2020, we announced that Sunovion Pharmaceuticals Canada Inc., received approval from Health Canada to market oral and intravenous formulations of XENLETA for the treatment of CAP in adults, with the Notice of Compliance from Health Canada dated July 10, 2020. On July 28, 2020, we announced that the EC, issued a legally binding decision for approving of the marketing authorization application for XENLETA for the treatment of CAP, in adults when it is considered inappropriate to use antibacterial agents that are commonly recommended for initial treatment or when these agents have failed following a review by the EMA. The EMA approved XENLETA in the EEA and the U.K. In September 2021, we and Sumitomo Pharmaceuticals (Suzhou) announced the approval received by Sumitomo Pharmaceuticals (Suzhou) to market oral and IV formulations of XENLETA for the treatment CAP in adults in Taiwan.

We own exclusive, worldwide rights to XENLETA, other than our rights in People's Republic of China, Hong Kong, Macau, and Taiwan, which were licensed to Sumitomo Pharmaceuticals (Suzhou), and Canada, which was licensed to Sunovian. XENLETA is protected by issued patents in the United States, Europe and Japan covering composition of matter, which are scheduled to expire no earlier than 2028. We also have been granted patents for XENLETA relating to process and pharmaceutical crystalline salt forms in the United States, which are scheduled to expire no earlier than 2031 before any regulatory exclusivity such as QIDP or pediatric extensions are applied. In addition, we own a family of pending patent applications directed to pharmaceutical compositions of XENLETA, which if issued would be scheduled to expire no earlier than 2036.

Key Attributes of XENLETA

We believe that the combination of the following key attributes of XENLETA, observed in clinical trials and preclinical studies, differentiates XENLETA from currently available antibiotics and make XENLETA well suited for use as a first-line or second-line empiric monotherapy for the treatment of CABP.

The preclinical studies and clinical trials we have conducted to date suggest that XENLETA's novel mechanism of action is responsible for the low risk of cross resistance observed with other antibiotic classes and a low propensity for development of bacterial resistance to XENLETA. As a result of the favorable safety and tolerability profile we have observed in our clinical trials to date, we believe XENLETA has the potential to present fewer complications relative to the use of current therapies.

Based on our market research, we also believe that the availability of both IV and oral formulations of XENLETA, and an option to switch to oral treatment, could reduce the length of a patient's hospital stay and the overall cost of care.

Targeted Spectrum of Activity for CABP Pathogens and Low Propensity for the Development of Bacterial Resistance

We expect XENLETA's spectrum of antibacterial activity against typical and atypical pathogens could eliminate the need to use a combination of antibiotics for the treatment of CABP. In our completed Phase 2 clinical trial, IV XENLETA achieved a high cure rate against multi-drug resistant Gram-positive bacteria, including MRSA. In addition, in preclinical studies, XENLETA showed activity against a variety of Gram-positive bacteria, including *Streptococcus pneumoniae* and *Staphylococcus aureus*, that are resistant to other classes of antibiotics, Gram-negative bacteria, including *Haemophilus influenzae* and *Moraxella catarrhalis*, and atypical bacteria, including *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae* and *Legionella pneumophila*. Included in XENLETA's spectrum of activity are all bacterial pathogens identified by IDSA as the most common causes of CABP for hospitalized patients who are not in

the intensive care unit, as well as strains of the above listed bacteria that are resistant to other classes of antibiotics, including penicillins, cephalosporins, fluoroquinolones and macrolides.

Based on observations from our preclinical studies and clinical trials of XENLETA, as well as industry experience with pleuromutilins used in veterinary medicine over the last 40 years, we believe that XENLETA's novel mechanism of action is responsible for the low risk of cross-resistance observed with other antibiotic classes and a low propensity for development of bacterial resistance to XENLETA.

Convenient Dosing Regimen; Potential for Switching from IV to Oral Treatment

We have developed both an IV and oral formulation of XENLETA, which we utilized in our clinical trials of XENLETA for the treatment of CABP. The administration of XENLETA as a monotherapy avoids the need for the complicated dosing regimens typical of multi-drug cocktails. We believe the availability of both IV and oral administration, and an option to switch to oral treatment, would be more convenient for patients and could reduce the length of a patient's hospital stay and the overall cost of care. The potential reduction in the overall cost of care could be particularly meaningful to healthcare institutions, as the DRG reimbursement system pays a fixed fee for the treatment of CABP regardless of the length of hospital stay.

The efficacy and safety of XENLETA in adult patients with CABP was shown in two pivotal Phase 3 clinical trials (LEAP 1 and LEAP 2). The two trials were designed in accordance with US and EU regulatory guidelines and conducted in parallel from 2016 to 2018. Design elements of the Phase 3 clinical trials were broadly comparable. Both were global, multicenter, randomized, double-blind, active-controlled, non-inferiority studies to establish the efficacy and safety of XENLETA against the standard-of-care moxifloxacin in the treatment of adult subjects with CABP. In LEAP 1, subjects were treated with IV study drug and could be switched to oral study drug at the discretion of the Investigator after 3 full days (6 doses) of IV treatment if, in the opinion of the Investigator, pre-defined criteria were met. In LEAP 2, subjects were treated with XENLETA for five days (ten doses) compared to seven days of moxifloxacin (seven doses).

LEAP 1 (IV to Oral) Phase 3 Clinical Trial

In LEAP 1, a total of 551 subjects with Pneumonia Outcomes Research Team (PORT) Risk Class III to V who required IV antibiotic therapy as initial treatment for the current episode of CABP were randomized 1:1 to treatment with XENLETA 150 mg IV every 12 hours (n=276) or moxifloxacin 400 mg IV every 24 hours (n=275). Subjects could be switched from IV to oral study drug (XENLETA 600 mg orally every 12 hours or moxifloxacin 400 mg orally every 24 hours) at the discretion of the Investigator after three full days (six doses) of IV treatment if pre-defined criteria were met. If the investigator determined that MRSA was a probable pathogen at Screening, adjunctive linezolid 600 mg IV every 12 hours was to be added to the moxifloxacin group and linezolid placebo was to be added to the XENLETA group.

The protocol defined different primary endpoints for the FDA and EMA to address regional differences in regulatory requirements for the development of antibacterial drugs to treat CABP. The FDA primary endpoint (EMA secondary endpoint) was the percentage of subjects with an Early Clinical Response, or ECR, of responder at 96 ± 24-hours after the first dose of study drug in the Intent-to-treat, or ITT, Analysis Set. The EMA co-primary endpoints (FDA secondary endpoints) were the percentages of subjects with an Investigator's Assessment of Clinical Response (IACR) of success at Test of Cure (TOC) Visit (5 to 10 days after the last dose of study drug) in the mITT and Clinically Evaluable at Test of Cure, or CE-TOC Analysis Sets.

Of the 551 subjects randomized, 546 received any amount of study drug (Safety Analysis Set: 273 XENLETA, 273 moxifloxacin). The mean total duration of study drug treatment (IV and oral combined) was approximately seven days in each treatment group. The two treatment groups were generally well balanced with respect to demographics and baseline characteristics. Overall, 59.9% of subjects were male. The overall mean age was 60.3 years; 43.6% were ≥65 years and 18.1% were ≥75 years. Overall, 72.1% of subjects were classified as PORT Risk Class III, 26.5% were PORT Risk Class IV, and 1.3% were PORT Risk Class V.

LEAP 1 met its primary objective and demonstrated that XENLETA is non-inferior to moxifloxacin with or without adjunctive linezolid for the treatment of adult subjects with CABP based on the FDA and EMA primary endpoints. The ECR responder rate (FDA primary endpoint) was 87.3% in the XENLETA group and 90.2% in the moxifloxacin group (treatment difference −2.9%; 95% CI: −8.5, 2.8). The lower limit of the 95% CI for the difference in ECR responder rates was greater than the non-inferiority margin of −12.5%. Success rates for IACR at TOC (EMA co-primary endpoints) were 81.7% in the XENLETA group and 84.2% in the moxifloxacin group (treatment difference −2.6%; 95% CI: −8.9, 3.9) in the mITT group, and 86.9% in the XENLETA group and 89.4% in the moxifloxacin group (treatment difference −2.5%; 95% CI: −8.4, 3.4) in the CE-TOC group. The lower limit of the 95% CI for the difference in IACR success rates was greater than the non-inferiority margin of −10% for both groups.

Early Clinical Response rates for the most frequently identified baseline pathogens in the Microbiological Intent-to-treat, or microITT, group were: *Streptococcus pneumoniae* (88.2% XENLETA vs 93.8% moxifloxacin), *Haemophilus influenzae* (92.2% XENLETA vs 94.7% moxifloxacin), *Moraxella catarrhalis* (92.0% XENLETA vs 100.0% moxifloxacin), *Mycoplasma pneumoniae* (84.2% XENLETA vs 90.0% moxifloxacin), *Legionella pneumophila* (88.9% XENLETA vs 85.7% moxifloxacin), and *Chlamydophila pneumoniae* (90.9% XENLETA vs 94.7% moxifloxacin). ECR responder rates for *Staphylococcus aureus* were 100.0% in both treatment groups. Responder rates among resistant pathogens were high in the XENLETA group (e.g., 100.0% for penicillin-intermediate *Streptococcus pneumoniae* [PISP], penicillin-resistant *Streptococcus pneumoniae* [PRSP], multi-drug resistant *Streptococcus pneumoniae*, or MDRSP, and macrolide-resistant *Streptococcus pneumoniae*), although the number of resistant pathogens was low.

Both XENLETA and moxifloxacin were well tolerated in the IV ± oral treatment regimens administered in the study. A similar rate of treatment-emergent adverse events, or TEAEs, was observed (38.1% vs 37.7% in the XENLETA and moxifloxacin groups, respectively). Gastrointestinal events were the most frequently reported TEAEs in both treatment groups (6.6% XENLETA, 13.6% moxifloxacin), with the difference between groups driven by an imbalance in TEAEs of diarrhea (0.7% XENLETA, 7.7% moxifloxacin). No gastrointestinal TEAEs led to discontinuation of study drug in either treatment group.

Administration site reactions of any type occurred more frequently for XENLETA (7.7%) than moxifloxacin (3.7%). The most common individual TEAE was infusion site pain, affecting eight (2.9%) subjects in the XENLETA group, and no subjects in the moxifloxacin group. One subject in each treatment group had an infusion site reaction that led to discontinuation of study drug.

The incidence of TEAEs leading to discontinuation of study drug was 2.9% XENLETA and 4.4% for moxifloxacin. The only TEAE preferred terms leading to discontinuation for more than 1 subject per treatment group were electrocardiogram (ECG) QT prolonged (one XENLETA-treated subject and three moxifloxacin-treated subjects) and infectious pleural effusion (one XENLETA-treated subject and two moxifloxacin-treated subjects).

Serious TEAEs occurred in 7.0% of subjects in the XENLETA group and 4.8% of subjects in the moxifloxacin group and were most frequently reported in the Infections and Infestations System Organ Class, or SOC (2.9% XENLETA, 1.5% moxifloxacin).

Nine deaths (five in the XENLETA group and, four in the moxifloxacin group) occurred by Day 28. Two additional deaths were reported after Day 28 (i.e., after the intended Late Follow-up [LFU] Visit): one XENLETA-treated subject on Day 32 and one moxifloxacin-treated subject on Day 48. None of the deaths was assessed as related to study drug by the Investigators.

There were no clinically meaningful trends or pattern of changes identified in hematology or chemistry laboratory parameters. No subjects met Hy’s Law criteria.

LEAP 2 (Oral Only) Phase 3 Clinical Trial

In LEAP 2, a total of 738 subjects with PORT Risk Class II to IV who were appropriate candidates for oral antibiotic therapy for the current episode of CABP were randomized 1:1 to treatment with XENLETA (n=370) or

moxifloxacin (n=368). Subjects received either XENLETA 600 mg orally every 12 hours for 5 days (10 doses) or moxifloxacin 400 mg orally every 24 hours for seven days (seven doses). The primary and secondary objectives were identical to those in LEAP 1.

Of the 738 subjects randomized, 736 received any amount of study drug (Safety Analysis Set: 368 XENLETA, 368 moxifloxacin). The mean duration of exposure to active XENLETA was 5.0 days, compared with 6.7 days of active moxifloxacin, which reflects the intended duration of active treatment for each drug as per the study design. The two treatment groups were generally well balanced with respect to demographics and baseline characteristics. Overall, 52.4% of subjects were male. The overall mean age was 57.5 years; 37.5% were ≥65 years and 16.3% were ≥75 years. Overall, 50.4% of subjects were classified as PORT Risk Class II, 37.7% were PORT Risk Class III, and 11.1% were PORT Risk Class IV.

LEAP 2 met its primary objective and demonstrated that XENLETA is non-inferior to moxifloxacin for the treatment of adult subjects with CABP based on the FDA and EMA primary endpoints. The ECR responder rate (FDA primary endpoint) was 90.8% in the XENLETA group and 90.8% in the moxifloxacin group (treatment difference 0.1%; 95% CI: −4.4, 4.5). The lower limit of the 95% CI for the difference in ECR responder rates was greater than the non-inferiority margin of −10%. Success rates for IACR at TOC (EMA co-primary endpoints) were 87.5% in the XENLETA group and 89.1% in the moxifloxacin group (treatment difference −1.6%; 95% CI: −6.3, 3.1) in the mITT group, and 89.7% in the XENLETA group and 93.6% in the moxifloxacin group (treatment difference −3.9%; 95% CI: −8.2, 0.5) in the CE-TOC group. The lower limit of the 95% CI for the difference in IACR success rates was greater than the non-inferiority margin of −10% for both groups.

Early Clinical Response rates for the most frequently identified baseline pathogens in the microITT group were: *Streptococcus pneumoniae* (89.4% XENLETA vs 91.3% moxifloxacin), *Haemophilus influenzae* (89.3% XENLETA vs 91.7% moxifloxacin), *Mycoplasma pneumoniae* (100.0% in both groups), *Moraxella catarrhalis* (85.7% XENLETA vs 100.0% moxifloxacin), *Legionella pneumophila* (81.3% XENLETA vs 94.1% moxifloxacin), and *Chlamydophila pneumoniae* (93.8% XENLETA vs 100.0% moxifloxacin). ECR responder rates for *Staphylococcus aureus* were 100.0% in both treatment groups. Responder rates among resistant pathogens were high in the XENLETA group (e.g., 100.0% for PISP, PRSP, MDRSP, and MRSA), although the number of resistant pathogens was low.

Both XENLETA and moxifloxacin were well tolerated in the oral treatment regimens administered in the study. The overall incidence of TEAEs was higher in the XENLETA group (32.6%) than in the moxifloxacin group (25.0%), which was driven by a difference in the incidence of mild/moderate Gastrointestinal Disorders. For XENLETA and moxifloxacin, respectively, the most frequently reported individual TEAEs in this category (and for the study overall) were diarrhea (12.2% vs 1.1%), nausea (5.2% vs 1.9%), and vomiting (3.3% vs 0.8%). Among the XENLETA-treated subjects reporting each of these TEAEs, approximately 75% had mild events and the remainder had moderate events. The only severe gastrointestinal adverse event, which was also serious, was a case of inguinal hernia strangulated in a moxifloxacin-treated subject. There were no severe or serious gastrointestinal adverse events among XENLETA-treated subjects. Furthermore, gastrointestinal events led to study drug discontinuation for 3 XENLETA-treated subjects (due to vomiting or abdominal pain) and one moxifloxacin-treated subject (due to vomiting). One patient who had a positive clinical response to XENLETA was later diagnosed with a *Clostridium difficile* infection during an extended hospital stay.

The incidence of TEAEs leading to discontinuation of study drug was 3.3% for the XENLETA group and 2.4% for the moxifloxacin group.

Serious TEAEs occurred in 4.6% of XENLETA-treated subjects and 4.9% of moxifloxacin-treated subjects, most frequently in the Infections and Infestations category (2.4% and 1.4%, respectively).

In each treatment group, three (0.8%) subjects died by Day 28. Deaths of two additional XENLETA-treated subjects were reported after Day 28 (i.e., after the intended LFU Visit): one subject on Day 57 and one subject on Day 271. None of the deaths was assessed as related to study drug by the Investigators.

No clinically meaningful trends or pattern of changes were identified in hematology or chemistry laboratory parameters. Two unique XENLETA-treated subjects had either an ALT or an aspartate aminotransferase (AST) value >10 × the upper limit of normal, or ULN; in both cases the transaminase increases were transient with no associated increase in serum bilirubin. No subjects met Hy's Law criteria.

Electrocardiogram analyses demonstrated increases from baseline in the QTcF interval in both treatment groups, but the magnitude of the change in the XENLETA treatment group was smaller than that caused by moxifloxacin. In this study the mean change from baseline in QTcF interval at the steady state assessment was 9.5 msec for XENLETA and 11.6 msec for moxifloxacin. Post-baseline QTcF increases of >60 msec occurred in 1.1% of XENLETA-treated subjects and 1.9% of moxifloxacin-treated subjects. No associated cardiac arrhythmias of concern were observed. No adverse trends in vital signs in either treatment group were observed.

Phase 1 Pediatric Clinical Trial

Not unlike treatment of infectious diseases in adults, the management of pediatric infections has become more difficult due to the continuing rise in resistance in bacteria. Further complicating antimicrobial selection in the pediatric population is the need for agents to be very well tolerated and available in a final dosage form that can be easily administered to children. Based upon the *in vitro* antimicrobial spectrum of activity, along with the safety profile observed to date, we believe XENLETA is appropriate for evaluation for the treatment of a variety of pediatric infections, including those affecting the respiratory tract and skin and skin structure. We have an agreed Pediatric Investigation Plan, or PiP, and Pediatric Study Plan, or PSP, with the EMA and FDA, respectively. Pediatric oral formulation development is ongoing with initiation of a relative bioavailability and pharmacokinetic study with said oral formulation in 2019, and we initiated a Phase 1 clinical trial evaluating safety, tolerability and PK of intravenous XENLETA in pediatric patients in mid-2018. As a result of COVID-19, research sites were temporarily closed for enrollment in 2020 and 2021 as hospitals suspended access and non-essential clinical research to focus on health care delivery to COVID-19 patients. As of July 2020, trials started to re-open, where allowed by the institution, and initiated screening of potential subjects at sites.

Additional Potential Indications for XENLETA

Cystic Fibrosis

Cystic fibrosis, or CF, is a genetically inherited multi-system rare disorder caused by defects in the CFTR gene (CF transmembrane conductance regulatory), located on chromosome 7, with a gene carrier rate of 1 in 25. In many cases, CF is apparent soon after birth and most patients are diagnosed by age 3. Approximately 10% of those affected were diagnosed after 18 years of age, but this figure has decreased due to newborn screening.

The disruption in chloride transport at the cellular level leads to dehydrated secretions within the lungs. Hence, pulmonary disease is the leading cause of morbidity and mortality in patients with CF because impaired muco-ciliary clearance in the lungs leads to recurrent pulmonary infections, inflammation, bronchiectasis and progressive lung function decline. One of the major factors influencing the impact on the lungs is infection. Infections are a leading cause of loss of lung function and take a significant physical and emotional toll, making them a top concern for people with CF. The treatment landscape for infections is becoming more challenging as antimicrobial resistance (AMR) increases. It is estimated that approximately half of the CF population will continue to require improved anti-infective treatments over the next 20 years.

Staphylococcus aureus is a ubiquitous commensal bacterial pathogen isolated in the respiratory tract and is commonly colonized in the respiratory tracts of CF patients. It is one of the main causes of recurrent acute pulmonary infections. According to the 2020 CF Foundation Patient Registry, 63.3% of patients with CF have either methicillin-susceptible *Staphylococcus aureus*, or MSSA, MRSA, or a combination of the two. Looking at the specific resistance phenotypes, 48.9% of patients have MSSA. What is concerning many CF clinicians is the prevalence of MRSA, which was identified in 19.6% of patients because MRSA is associated with greater lung damage, pulmonary function deterioration and increased risk of death.

Sexually Transmitted Infections

Urethritis and cervicitis caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Mycoplasma genitalium* are frequently occurring sexually transmitted infections in the United States and Europe. Left untreated, these infections can cause serious health problems, particularly in women, including chronic pelvic pain, life-threatening ectopic pregnancy and infertility. Resistance in these organisms to the most commonly prescribed antibacterial treatments poses a serious public health threat. For example, the CDC estimates that half of all infections of the clinical isolates of *Neisseria gonorrhoeae* are resistant to at least one currently available antibiotic.

In preclinical studies, XENLETA has shown high potency against *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Mycoplasma genitalium*, including strains resistant to currently available antibacterial agents.

Osteomyelitis

The incidence of osteomyelitis, which is an infection of the bone, is increasing. The most common causative organism is *Staphylococcus aureus*. In the United States, the prevalence of MRSA in these cases ranges from 33% to 55%. Up to 90% of cases of hematogenous osteomyelitis, most frequently in children, are caused by *Staphylococcus aureus*. We believe that XENLETA has the potential to be an effective treatment option for osteomyelitis. XENLETA has shown substantial tissue penetration and activity against the most common causative organism in all forms of osteomyelitis. We believe that based on the safety profile observed to date, XENLETA will be well tolerated for the long term use necessary for the treatment of both adult and pediatric patients with osteomyelitis. The current standard of care for these infections is treatment with vancomycin. We believe the ability to administer XENLETA by either the IV or oral route would provide a significant advantage over existing therapies, such as vancomycin, that can only be administered by IV.

Prosthetic Joint Infections

Infection occurs in approximately 1% of joint replacement surgeries. Although the incidence of infection has been decreasing, the total number of replacement operations has been rising, such that, overall, there is increasing morbidity. The majority of these infections are caused by three organisms: coagulase negative staphylococci, *Staphylococcus aureus* (including MRSA) and *streptococci*, all organisms that are susceptible to XENLETA. The preferred treatment for joint infections with MRSA is vancomycin, with daptomycin and linezolid as alternatives. Vancomycin and daptomycin are administered only by IV for this indication, and linezolid has side effects that affect long term use. We believe that XENLETA could provide an alternative for both IV and oral therapy for these infections cases.

A 2018 Cochrane Review on interventions for the eradication of MRSA in people with cystic fibrosis reviewed the available literature to evaluate the effectiveness of current treatment regimens. Despite showing MRSA eradication in CF patients is possible, it is not clear what the long- term implications are as only two studies were identified and the quality of the evidence was found to be very low or low for the different outcomes. For acute pulmonary exacerbations due to MRSA, treatment with trimethoprim-sulfamethoxasole or doxycycline, and for moderate or severe exacerbations or if the prior regimens fail, treatment with oral linezolid, intravenous vancomycin or intravenous ceftaroline is recommended. There are limited treatment options in patients and each of the aforementioned drugs have potential safety concerns such as hypersensitivity reactions, bone marrow suppression or renal toxicity. More information on dosage and administration is needed to evaluate the effectiveness of antibiotic therapy to ensure optimal patient outcomes. Hence, there is an unmet need for new treatment options to treat *Staphylococcal* pulmonary infections, specifically acute pulmonary exacerbations due to MRSA.

We believe XENLETA has an opportunity to provide CF patients with MRSA infection an alternative treatment option. XENLETA is a potent anti-staphylococcal antibiotic from the pleuromutilin class. It has been demonstrated to be highly effective in in vitro and in vivo studies of *Staphylococcus aureus* infection, *both MSSA and MRSA*. Further it has been shown to achieve high concentrations in the lung fluid and lung macrophages. XENLETA has been developed and approved for the treatment of community-acquired bacterial pneumonia (including those caused by *Staphylococcus aureus*) in the U.S., EU, and Canada as an oral tablet and a sterile intravenous product. XENLETA is not metabolized

renally and is not nephrotoxic. We believe the confluence of non-clinical and clinical data, as well as the availability of a well-tolerated and effective oral formulation uniquely positions lefamulin to potentially address the major unmet need of exacerbations of cystic fibrosis caused by *Staphylococcus aureus, both MSSA and MRSA*. We initiated screening of our Phase 1 clinical trial to evaluate the pharmacokinetics, safety and tolerability of XENLETA in patients with CF in March 2022. Results from this trial will inform further development of XENLETA as a treatment for staphylococcal lung infections in this patient population.

Sexually Transmitted Infections

The CDC reports gonorrhea (caused by *Neisseria gonorrhoeae*) as one of the most common STIs in the US, with more than 800,000 cases estimated to occur each year. Left untreated, these infections can cause serious health problems, particularly for women, including chronic pelvic pain, life-threatening ectopic pregnancy, and infertility. Gonorrhea infection also increases a person's risk of contracting and transmitting human immunodeficiency virus. Chlamydial infections and gonorrhea are the most frequently reported sexually transmitted and reportable infections in both Europe and the United States with high occurrence rates among young persons, particularly women.

The WHO has estimated that there are over 1.0 million new STI cases per day globally, the majority of which are asymptomatic. In 2020, the WHO estimated that there are 374.0 million new STI infections globally each year, of which 129.0 million are infected with *Chlamydia trachomatis*, 82.0 million are infected with *Neisseria gonorrhoeae*, 7.1 million are infected with *Treponema pallidu* and 156.0 million are infected with *Trichomonas vaginalis*.

The CDC estimates that approximately 20% of the population of the United States was infected with an STI organism on any given day in 2018, costing the healthcare system nearly $16.0 billion in healthcare costs alone. The total number of new cases of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* reported to the CDC in 2018 was 4.0 million and 1.6 million, respectively.

STI organisms are progressively developing resistance to antibiotics prescribed for treatment: sulfonilamides, penicillin, cephalosporins, azithromycin, tetracycline, and ciprofloxacin, and gonococcal resistance to all of these antibiotics have been reported globally. Declining susceptibility to cefixime (an oral cephalosporin antibiotic) resulted in a change to the CDC treatment guidelines in 2015, so that dual therapy with ceftriaxone (an injectable cephalosporin) and azithromycin is now the only CDC recommended treatment regimen for gonorrhea. The emerging threat of cephalosporin resistance highlights the need for continued surveillance of *Neisseria gonorrhoeae* antimicrobial susceptibility. In 2014, 38.2% of all *Neisseria gonorrhoeae* collected in the national surveillance program exhibited resistance to penicillin, tetracycline, or ciprofloxacin or reduced susceptibility to cefixime, ceftriaxone, or azithromycin. Resistance or reduced susceptibility to one antibiotic was identified in 20.8% of isolates, to two in 9.6%, to three in 7.2%, to four in 0.5%, and to five in 0.1%. In 2019, the prevalence of ciprofloxacin resistance continued to increase to 35.4%, the highest recorded in the Gonococcal Isolate Surveillance Project (GISP).

Mycoplasma genitalium has become a well-established cause for STIs and several studies have demonstrated the association between *Mycoplasma genitalium* and urethritis in men and urethritis, cervicitis, endometritis, and pelvic inflammatory disease in women. Decreases in the treatment efficacy of azithromycin, and treatment failure after second line moxifloxacin leaves no validated treatment options for the treatment of *Mycoplasma genitalium* infections.

XENLETA is a highly potent novel antimicrobial of the pleuromutilin class. Initial in vitro studies demonstrated high susceptibility of STI pathogens to lefamulin. Notably, susceptibility of *Chlamydia trachomatis* (MIC50/90, 0.02/0.04 mg/liter) and susceptible and resistant *Neisseria gonorrhoeae* (MIC50/90, 0.12/0.5 mg/liter) were good, and susceptibility of *Mycoplasma genitalium* was excellent (MIC range, 0.002 to 0.063 mg/liter for multi-drug resistant strains). Given this high degree of *in vitro* susceptibility and its favorable safety profile, we believe lefamulin holds great promise for a first-line antibiotic for the syndromic treatment of STIs, particularly in populations with high rates of resistance to standard-of-care antibiotics.

Acute Bacterial Skin and Skin Structure Infections

The effect of lefamulin in treating ABSSSI was demonstrated in a Phase 2 clinical trial with 207 subjects with ABSSSI comparing two lefamulin doses (100 mg and 150 mg IV q12h) with vancomycin over 5-14 days. This clinical trial enrolled patients with significant skin and skin structure infections with a median lesion size of 175.0 cm2 (greater than the minimum surface area of 75 cm2 specified in the FDA draft guidance), excluding any patients with minor and uncomplicated infections. In total, 90.8% of patients in the MITT population had *Staphylococcus aureus* infection; 69.1% of subjects had MRSA. Lefamulin 100 mg and 150 mg had consistently high efficacy rates across a wide range of clinical and microbiological outcomes at several time points including the TOC, 7 to 14 days after the completion of therapy. These response rates were comparable to vancomycin. The clinical success rate at TOC with lefamulin 100 mg and 150 mg q12h treatment was high for all subgroups of subjects defined by primary infection type, bacteremia status, diabetic status, baseline fever status, age group, antibiotic therapy category, prior treatment failure status, baseline area of erythema, baseline body mass index, and gender. No important differences between or among the compared subgroups in the response to lefamulin treatment were observed. The Day 3 clinical responder rate for lefamulin was also high and comparable to vancomycin.

We may advance these programs into clinical development based on available funding.

CONTEPO Clinical Development Program

Overview

CONTEPO is under development in the United States for the treatment of cUTI, including AP. The clinical development plan for CONTEPO utilized a modernized dosing regimen to optimize coverage of the predominant pathogens in hospital infections, including strains recognized by the CDC as an urgent or serious antibiotic resistant threat to public health in the United States. The FDA has designated CONTEPO as a QIDP. We submitted an NDA for marketing approval of CONTEPO for the treatment of cUTI in adults in the United States, to the FDA in October 2018. The NDA submission utilized the 505(b)(2) regulatory pathway and is supported by a robust data package, including a pivotal Phase 2/3 clinical trial (known as ZEUS™), which met its primary endpoint of statistical non inferiority to piperacillin/tazobactam in patients with cUTI, including AP. In April 2019, the FDA issued a CRL in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP, stating that it was unable to approve our application in its current form. The CRL requested that issues related to facility inspections and manufacturing deficiencies at our active pharmaceutical ingredient contract manufacturer be addressed prior to the FDA approving the NDA. We requested a “Type A” meeting with the FDA to discuss its findings and this meeting occurred in July 2019. As the FDA did not request any new clinical data and did not raise any other concerns with regard to the safety or efficacy of CONTEPO in the CRL, the purpose of the meeting was to discuss and gain clarity on the issues related to facility inspections and manufacturing deficiencies at one of our contract manufacturers that were described in the CRL and other matters pertaining to the steps required for the resubmission of the NDA for CONTEPO. We resubmitted our NDA in December 2019 and the FDA acknowledged the resubmission in January 2020. On June 19, 2020, the FDA issued a second CRL on the NDA for CONTEPO. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cited observations at our manufacturing partners that could not be resolved due to FDA’s inability to conduct onsite inspections because of travel restrictions caused by the COVID-19 pandemic. In general, previously identified product quality and facility inspection related observations at our contract manufacturing partners are required to be satisfactorily resolved before the NDA may be approved. The FDA did not request any new clinical data and did not raise any other concerns with regard to the safety or efficacy of CONTEPO in the second CRL. Our contract manufacturers continue to interact with FDA to discuss its plans for conducting inspections at their sites. On October 30, 2020, we participated in a “Type A” meeting with the FDA to obtain any new information related to the FDA’s pending conduct of inspections of foreign manufacturers during the COVID-19 pandemic that has negatively impacted a number of FDA product reviews, including our NDA for CONTEPO. On April 14, 2021, the FDA issued industry guidance on remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities during COVID-19 specifying that when it cannot perform a PAI or PLI or when the FDA determines that it would be useful to supplement a planned inspection, the agency will consider using tools other than a physical inspection and select the most appropriate method to address the specific risks that justify the need for the PAI or PLI. The FDA informed us that

onsite inspections of our manufacturing partners in Europe are required in order for the FDA to complete the review of a potential CONTEPO NDA resubmission. Due to travel restriction related to the COVID-19 pandemic, the FDA suspended onsite inspections of ex-US manufacturers for all non-COVID products. As a result, we requested an extension of the timeline for a potential CONTEPO NDA resubmission until June 2023, which the FDA granted on March 21, 2022. We are awaiting further clarity from the FDA regarding their ability to complete onsite inspections at our manufacturing partners in Italy and Spain before determining specific timing of the potential NDA resubmission, which we plan to submit promptly once we have clarity from the FDA. We do not have a forecasted date for the resubmission of our NDA for CONTEPO for the treatment of cUTI, including AP.The FDA released the Resiliency Roadmap for FDA Inspectional Oversight that describes the systematic approach that FDA will utilize to manage postponed inspections and other oversight activities. The prioritization plan considers public health risks related to conducting an inspection, such as the impact of the product's availability on public health, as well as investigator safety and travel restrictions/advisories. In addition, the FDA informed us that, while they cannot predict when an inspection may occur and when the pandemic may prevent the FDA from completing inspections, tier 1 mission-critical inspections and tier 2 higher priority inspections, which includes PAIs, will continue to be prioritized going forward. We cannot predict the outcome of any further interactions with the FDA or when CONTEPO will receive marketing approval, if at all. CONTEPO has been granted QIDP and Fast Track designations by the FDA for the treatment of serious infections, including cUTI. However, we cannot predict when the NDA for CONTEPO for the treatment of cUTI, including AP, will be resubmitted or when CONTEPO would receive marketing approval, if at all.

Phase 2/3 Clinical Trial

The ZEUS Study was a multicenter, randomized, parallel-group, double-blind, pivotal Phase 2/3 clinical trial designed to evaluate safety, tolerability, efficacy and pharmacokinetics of CONTEPO compared to PIP-TAZ in the treatment of hospitalized adults with cUTI or AP. PIP-TAZ is a combination antibiotic consisting of a broad-spectrum antibiotic, piperacillin, plus a β-lactamase inhibitor, tazobactam, which extends the antibiotic spectrum of piperacillin to include many β-lactamase-producing bacteria that have acquired resistance to piperacillin alone. PIP-TAZ is widely used to treat serious Gram-negative infections. The primary objective of the ZEUS Study was to demonstrate that CONTEPO was non-inferior to PIP-TAZ in overall success based on clinical cure and microbiologic eradication in the microbiologic modified intent-to-treat, or m-MITT, population at the test-of-cure visit, or TOC, which occurred on the 19th to 21st day after completion of seven days of treatment with the study drug, or after up to 14 days of treatment for patients with concurrent bacteremia. The m-MITT population consisted of 362 patients, each of whom met the study's inclusion criteria, was randomized, received any amount of study drug, and had one or more baseline Gram-negative pathogens growing at greater than or equal to 10(5) CFU/mL from an appropriately collected, pre-treatment baseline urine or blood sample. The primary endpoint was a composite of the investigator's determination of clinical cure, meaning complete resolution or significant improvement of signs and symptoms that were present at baseline and no new symptoms, such that no further antimicrobial therapy is warranted, plus microbiologic eradication, meaning that the baseline bacterial pathogen was reduced to less than 10(4) CFU/mL on urine culture and, if applicable, negative on repeat blood culture, both in the m-MITT population at TOC. Any missing or presumed eradications were classified as indeterminates, and conservatively counted as failures in the overall success analysis.

All pathogens isolated from patients who had a baseline and TOC pathogen underwent blinded, post-hoc, pulsed-field gel electrophoresis, or PFGE, typing analysis. Microbiologic outcome was also defined utilizing the PFGE results, whereby microbiologic persistence required the same genus and species of baseline and post-baseline pathogens, as well as PFGE-confirmed genetic identity.

Patients eligible for the trial were required to be 18 years of age or older and have cUTI or AP that was considered by the clinical investigator to be serious enough to require hospitalization and IV antibiotic therapy. The diagnosis was based on pyuria, or the presence of pus or white blood cells in the urine, and cUTI or AP with at least two additional symptoms such as chills, rigors, or warmth associated with fever, nausea or vomiting, painful, difficult or frequent urination, lower abdominal or pelvic pain, or acute flank pain. Patients with cUTI were also required to have at least one risk factor, such as use of intermittent or indwelling bladder catheterization; functional or anatomical abnormality of the urogenital tract; complete or partial hindrance of normal urine flow; blood urea nitrogen greater than 20 mg/dL, blood urea greater than 42.8 mg/dL, or serum creatinine greater than 1.4 mg/dL, due to known prior renal disease; or, in male patients, chronic urinary retention. A baseline urine culture specimen was obtained within 48 hours

prior to randomization, and any indwelling bladder catheters were required to be removed or replaced, unless such removal was considered unsafe or contraindicated, before or within 24 hours after randomization.

Eligible patients were randomly assigned to receive either CONTEPO (6 grams IV fosfomycin) or PIP-TAZ (4 grams piperacillin/0.5 grams tazobactam) as one-hour infusions three times daily for seven days, except patients with concurrent bacteremia, who could have received treatment for up to 14 days at the clinical investigator's discretion. Oral step down therapy was prohibited. Throughout the study, all patients were monitored for signs and symptoms of cUTI or AP and the occurrence of adverse events. Laboratory data, including chemistry panels, complete blood counts, electrocardiograms, and samples for urine and blood cultures were collected from all patients at specified times throughout the study.

Of the total of 465 patients randomized across 92 sites in 16 countries, with studies conducted at 74 sites in 15 countries, 464 (99.8%) received at least one dose of the study drug. Of the 464 patients who received at least one dose of study drug, 233 patients were in the CONTEPO treatment group, and 231 patients were in the PIP-TAZ treatment group. The incidence of premature discontinuation from study drug was low and similar between treatment groups (6.0% in the CONTEPO treatment group compared to 3.9% in the PIP-TAZ treatment group), and the incidence of not completing the study through the last follow-up visit, or LFU, which occurred on the 24th through 28th day after completion of seven days of treatment with the study drug, or after up to 14 days of treatment for patients with concurrent bacteremia, was 5.2% in the CONTEPO group compared to 0.9% in the PIP-TAZ group.

In the ZEUS Study, CONTEPO was non-inferior to PIP-TAZ for the primary efficacy outcome of overall success, which was defined as clinical cure and microbiologic eradication at TOC. Overall success occurred in 64.7% of CONTEPO patients and 54.5% of PIP-TAZ patients. The treatment difference between the CONTEPO and PIP-TAZ groups was 10.2%, with a 95% confidence interval (−0.4, 20.8). Additionally, the lower bound of the 95% confidence interval met the pre-specified non-inferiority margin of −15%, demonstrating that CONTEPO was non-inferior to PIP-TAZ in the study. In a post-hoc primary efficacy analysis using results of blinded PFGE molecular typing of urinary tract pathogens, this difference was even greater (69.0% CONTEPO patients compared to 57.3% PIP-TAZ patients, with a treatment difference of 11.7%, with a 95% confidence interval (1.3, 22.1). Overall success rates were driven by microbiologic eradication rates, as clinical cure rates were greater than 90% and treatment differences were small at TOC. Using the PFGE molecular typing, the microbiologic eradication rates in the m-MITT population at the TOC were 70.7% for patients receiving CONTEPO compared to 60.1% for patients receiving PIP-TAZ. These rates were consistent with those observed in some contemporary cUTI studies, and most patients with microbiologic persistence at TOC had identifiable reasons or risk factors for persistence, such as functional or anatomical abnormalities of the urogenital tract, recent or indwelling urinary tract catheterization, elevated minimum inhibitory concentration, or MIC, to the study drug received, abbreviated study drug therapy, or other underlying co-morbidities. Of note, a majority of patients with microbiologic persistence at TOC were clinical cures at TOC, did not require rescue antimicrobial therapy, and remained sustained cures at LFU.

The identity and frequency of pathogens recovered at baseline from patients in the ZEUS Study were similar in both the CONTEPO and PIP-TAZ treatment groups. The most common pathogens identified were *Enterobacteriaceae*, identified in 96.2% of the CONTEPO patients and 94.9% of the PIP-TAZ patients, including *E. coli*, identified in 72.3% of the CONTEPO patients and 74.7% of the PIP-TAZ patients; *Klebsiella pneumoniae*, identified in 14.7% of the CONTEPO patients and 14.0% of the PIP-TAZ patients; *Enterobacter cloacae* species complex, identified in 4.9% of the CONTEPO patients and 1.7% of the PIP-TAZ patients; and *Proteus mirabilis*, identified in 4.9% of the CONTEPO patients and 2.8% of the PIP-TAZ patients. Gram-negative aerobes other than Enterobacteriaceae included *Pseudomonas aeruginosa*, which was identified in 4.3% of the CONTEPO patients and 5.1% of the PIP-TAZ patients, and *Acinetobacter baumannii-calcoaceticus* species complex, identified in 1.1% of the CONTEPO patients and no PIP-TAZ patients. These pathogens are representative of the pathogens that have been recovered in other studies of patients with cUTI or AP. For the predominant pathogens *E. coli and Klebsiella pneumoniae*, the clinical cure rates at TOC for CONTEPO were greater than 90% for both pathogens, and microbiologic eradication rates were 68.4%, or 72.9% with PFGE analysis, for *E. coli*, and 66.7% for *Klebsiella pneumoniae* on both a non-PFGE analysis and PFGE analysis-basis.

A total of 42.1% of CONTEPO patients and 32.0% of PIP-TAZ patients experienced at least one TEAE. Most TEAEs were mild or moderate in severity, and severe TEAEs were uncommon (2.1% of CONTEPO patients and 1.7%

of PIP-TAZ patients). The most common TEAEs in both treatment groups were transient, asymptomatic laboratory abnormalities and gastrointestinal events. Treatment-emergent serious adverse events, or SAEs, were uncommon in both treatment groups (2.1% of CONTEPO patients and 2.6% of PIP-TAZ patients). There were no deaths in the study and one SAE in each treatment group was deemed related to the study drug (hypokalemia in a CONTEPO patient and renal impairment in a PIP-TAZ patient), leading to study drug discontinuation in the PIP-TAZ patient. Study drug discontinuations due to TEAEs were infrequent and similar between treatment groups (3.0% of CONTEPO patients and 2.6% of PIP-TAZ patients).

The most common laboratory abnormality TEAEs were increases in the levels of alanine aminotransferase (8.6% of CONTEPO patients and 2.6% of PIP-TAZ patients) and aspartate transaminase (7.3% of CONTEPO patients and 2.6% of PIP-TAZ patients). None of the aminotransferase elevations were symptomatic or treatment-limiting, and none of the patients met the criteria for Hy's Law. Outside of the United States, elevated liver aminotransferases are listed among undesirable effects in labeling for IV fosfomycin.

Hypokalemia occurred in 71 of 232 (30.6%) CONTEPO patients and 29 of 230 (12.6%) PIP-TAZ patients. Most decreases in potassium levels were mild to moderate in severity. Shifts in potassium levels from normal at baseline to hypokalemia, as determined by worst post-baseline hypokalemia values, were more frequent in the CONTEPO group than the PIP-TAZ group for mild (17.7% compared to 11.3%), moderate (11.2% compared to 0.9%), and severe (1.7% compared to 0.4%) categories of hypokalemia. Hypokalemia was deemed a TEAE in 6.4% of patients receiving CONTEPO and 1.3% of patients receiving PIP-TAZ, and all cases were transient and asymptomatic. While no significant cardiac adverse events were observed in the ZEUS Study, post-baseline QT intervals calculated using Fridericia's formula, or QTcF, of greater than 450 to less than or equal to 480 msec (baseline QTcF of less than or equal to 450 msec) occurred at a higher frequency in CONTEPO patients (7.3%) compared to PIP-TAZ patients (2.5%). In the CONTEPO arm, these results appear to be associated with the hypokalemia associated with the salt load of the IV formulation.

Phase 1 Pediatric Clinical Trial

In June 2018, we initiated a Phase 1, non-comparative, open-label study of the pharmacokinetics and safety of a single dose of CONTEPO in pediatric subjects less than 12 years of age receiving standard-of-care antibiotic therapy for proven or suspected infection or peri-operative prophylaxis. A total of 24 patients are expected to be enrolled at up to ten clinical sites in the United States. As a result of COVID-19, research sites were temporarily closed in 2020 and 2021 and only a minority of sites are currently screening patients and allowing access to the institution. As a result, our development timeline for CONTEPO for use in pediatric patients with cUTIs has been modified to reflect a two-year delay due to COVID-19.

Potential Additional Indications for CONTEPO

Fosfomycin has a long history of use outside the United States in a variety of indications beyond cUTI. The FDA has granted both Fast Track and QIDP designations for the investigation of CONTEPO for the following indications in addition to cUTI:

- Complicated intra-abdominal infections
- Hospital-acquired bacterial pneumonia
- Ventilator-associated bacterial pneumonia
- Acute bacterial skin and skin structure infections

Although we have no current plans to develop CONTEPO for indications other than cUTI, including AP, these designations make CONTEPO eligible for Fast Track and GAIN incentives. We may advance these programs in the clinic based on available funding.

In August 2017, Zavante entered into an agreement with the United States National Institute of Allergy and Infectious Diseases, or NIAID, under which NIAID will conduct a clinical trial to assess CONTEPO's intrapulmonary penetration and pharmacokinetics in support of the product candidate's potential future development as a treatment for HABP and VABP. This bronchoalveolar lavage study, or the BAL study, will measure CONTEPO's pulmonary penetration by assessing drug concentrations in the lining of study subjects' bronchial pathways. Diffusion and saturation of antibiotics in patients' airways are considered important factors in assessing a drug's ability to effectively treat lower-respiratory tract infections. Prior preclinical and clinical investigations of IV fosfomycin have demonstrated that the product candidate penetrates rapidly into tissues and achieves clinically relevant concentrations in urine, soft tissues, lungs and other organs, supporting CONTEPO's potential versatility as an antibiotic treatment option. The Phase 1 BAL clinical trial is currently enrolling study subjects.

China Region License Agreement

In March 2018, we entered into the China Region License Agreement, with Sinovant Sciences, Ltd., or Sinovant, an affiliate of Roivant Sciences, Ltd., to develop and commercialize lefamulin in the greater China region. As part of the China Region License Agreement, Nabriva Therapeutics Ireland DAC and Nabriva Therapeutics GmbH, our wholly owned subsidiaries, granted Sinovant an exclusive license to develop and commercialize, and a non-exclusive license to manufacture, certain products containing lefamulin, or the China Region Licensed Products, in the People's Republic of China, Hong Kong, Macau, and Taiwan, together the Extended China Territory. In May 2021, we entered into an assignment, assumption and novation agreement, or the Assignment Agreement, pursuant to which we consented to the assignment by Sinovant, an affiliate of Roivant Sciences, Ltd., of the China Region License Agreement to develop and commercialize lefamulin in the greater China region to Sumitomo Pharmaceuticals (Suzhou), a wholly-owned subsidiary of Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo. Pursuant to the Assignment Agreement, we agreed to release Sinovant and its affiliates from their obligations under the China Region License Agreement and consented to Sumitomo Pharmaceuticals (Suzhou)'s assumption of such obligations. In addition, Sumitomo has agreed to guarantee all of the obligations of Sumitomo Pharmaceuticals (Suzhou) under the China Region License Agreement.

Under the China Region License Agreement, Sumitomo Pharmaceuticals (Suzhou) and our subsidiaries have established a joint development committee, or the JDC, to review and oversee development and commercialization plans in the Extended China Territory. The China Region License Agreement includes milestone events consisting of a non-refundable $5.0 million upfront payment, an additional $91.5 million in milestone payments upon the achievement of certain regulatory and commercial milestone events related to lefamulin for CABP, plus an additional $4.0 million in milestone payments if any China Region Licensed Product receives a second or any subsequent regulatory approval in the People's Republic of China. We received the $5.0 million upfront payment, a $1.5 million payment for the submission of a clinical trial application, or CTA, by Sinovant to the Chinese FDA, which was received in the first quarter of 2019 and a $5.0 million milestone payment in the third quarter of 2019 in connection with the Chinese FDA approval for lefamulin. We will also be eligible to receive low double-digit royalties on sales, if any, of China Region Licensed Products in the Extended China Territory. In December 2020, we announced the restructuring of our China Region License Agreement. The restructured agreement provided for additional manufacturing collaboration and regulatory support to be provided by us that is expected to help expedite the delivery of XENLETA to patients in the Extended China Territory. The restructured agreement also accelerated $3.0 million of the $5.0 million milestone payment to us that was previously payable upon regulatory approval of XENLETA in China, including a non-refundable upfront payment of $1.0 million which was received in the fourth quarter of 2020 and a $1.0 million milestone achieved during the first quarter of 2021.

Except for the manufacturing collaboration and regulatory support discussed above, Sumitomo Pharmaceuticals (Suzhou) will be solely responsible for all costs related to developing, obtaining regulatory approval of and commercializing China Region Licensed Products in the Extended China Territory and is obligated to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize China Region Licensed Products in the Extended China Territory. We are obligated to use commercially reasonable efforts to supply, pursuant to supply agreements to be negotiated by the parties, to Sumitomo Pharmaceuticals (Suzhou) a sufficient supply of lefamulin for Sumitomo Pharmaceuticals (Suzhou) to manufacture finished drug products for development and commercialization of the China Region Licensed Products in the Extended China Territory.

Unless earlier terminated, the China Region License Agreement will expire upon the expiration of the last royalty term for the last China Region Licensed Product in the Extended China Territory, which we expect will occur in 2033. Following the expiration of the last royalty term, the license granted to Sumitomo Pharmaceuticals (Suzhou) will become non-exclusive, fully-paid, royalty-free and irrevocable. The China Region License Agreement may be terminated in its entirety by Sumitomo Pharmaceuticals (Suzhou) upon 180 days' prior written notice at any time. Either party may, subject to specified cure periods, terminate the China Region License Agreement in the event of the other party's uncured material breach. Either party may also terminate the China Region License Agreement under specified circumstances relating to the other party's insolvency. We have the right to terminate the China Region License Agreement immediately if Sumitomo Pharmaceuticals (Suzhou) does not reach certain development milestones by certain specified dates (subject to specified cure periods). The China Region License Agreement contemplates that we will enter into ancillary agreements with Sumitomo Pharmaceuticals (Suzhou), including clinical and commercial supply agreements and a pharmacovigilance agreement.

Sunovion License Agreement

In March 2019, we entered into the Sunovion License Agreement with Sunovion Pharmaceuticals Canada Inc., or Sunovion. As part of the Sunovion License Agreement, Nabriva Therapeutics Ireland DAC, our wholly owned subsidiary, granted Sunovion an exclusive license under certain patent rights, trademark rights and know-how to commercialize certain products containing XENLETA in the forms clinically developed by us or any of our affiliates, or the Sunovion Licensed Products in Canada in all uses in humans in CABP and in any other indication for which the Sunovion Licensed Products have received regulatory approval in Canada. Under the Sunovion License Agreement, Sunovion and Nabriva Therapeutics Ireland DAC established a joint development committee, or the Sunovion JDC, to review and oversee regulatory approval and commercialization plans in Canada. Sunovion will be solely responsible for all costs related to obtaining regulatory approval of and commercializing Sunovion Licensed Products in the Canada and is obligated to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize Licensed Product in the Canada.

On November 7, 2019, we, through Sunovion, submitted a New Drug Submission, or NDS to market oral and intravenous formulations of XENLETA for the treatment of CAP in adults. Health Canada determined there was a screening deficiency in December 2019 and a response from us/Sunovion was provided on December 18, 2019 and acknowledged by Health Canada on January 13, 2020. Sunovion received approval from Health Canada to market oral and intravenous formulations of XENLETA for the treatment of community-acquired pneumonia in adults, with the Notice of Compliance from Health Canada dated July 10, 2020.

Named Patient Program Agreement with WE Pharma Ltd.

On June 30, 2020 we announced that WE Pharma Ltd., or WEP Clinical, a specialist pharmaceutical services company, had signed an exclusive agreement with us to supply XENLETA on a named patient or expanded access basis in certain countries outside of the US, China and Canada. The Named Patient Program, or NPP, is designed to ensure that physicians, contingent on meeting the necessary eligibility criteria and receiving approval, can request IV or oral XENLETA on behalf of patients who live in certain countries where it is not yet available and have an unmet medical need.

Commercialization Strategy

We have distribution rights to SIVEXTRO in the United States pursuant to a Sales Promotion and Distribution Agreement, or the Distribution Agreement, with MSD International GmbH, or MSD, and Merck Sharp & Dohme Corp., or the Supplier, each a subsidiary of Merck & Co. Our initial target population for SIVEXTRO consisted of healthcare professionals who had historically prescribed SIVEXTRO for patients with ABSSSI. Other than in greater China and Canada where we have licensed development and commercialization rights to XENLETA, we own exclusive, worldwide rights to XENLETA and U.S. rights to CONTEPO. Our initial target population for XENLETA consisted of patients with moderate to severe CABP whose antibiotic treatment is hospital initiated. We received approval for XENLETA from the FDA in August 2019 and launched the product in September 2019. We previously utilized our own targeted hospital sales force and marketing organization and in early 2020 began to target high value primary care physicians in

the community near our target hospitals. Based on our market research, we believe XENLETA has an innovative profile supporting adoption in the United States for adult hospital initiated CABP patients, treated both as in patients as well as outpatient transition of care from the hospital to the community, which we believe represents a significant commercial opportunity. Due to market factors in 2020, including the COVID-19 pandemic, we transitioned to a community-based sales effort. In the third quarter of 2020 we secured a contract sales organization and began promoting SIVEXTRO and XENLETA to community-based healthcare providers. We anticipate that we will effectively be able to communicate SIVEXTRO's and XENLETA's differentiating characteristics and key attributes to clinicians and payors with the goal of establishing favorable reimbursement for patients. Outside of the United States, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize XENLETA.

Along with additional market research, we believe that medical education will be a key component of our commercialization efforts and, plan to invest in these activities to optimize the commercial potential of XENLETA. We believe that XENLETA's novel mechanism of action, status as the only member of a new class of systemically administered pleuromutilins and anticipated clinical profile will support its potential favorable reimbursement, its potential inclusion on formularies and in local and national treatment guidelines.

We plan to evaluate the merits of entering into collaboration agreements with other pharmaceutical or biotechnology companies that may contribute to our ability to efficiently advance our product candidates, build our product pipeline and concurrently advance a range of research and development programs for a variety of indications outside the United States.

We own exclusive U.S. rights to CONTEPO. Our strategic intention, supported by CONTEPO's differentiated profile, is to establish CONTEPO, if approved, as the standard of care in the United States for hospitalized patients with serious infections caused by suspected or confirmed MDR bacteria. We plan to seek a hospital based sales force to promote CONTEPO, and potentially XENLETA, to hospital-based healthcare professionals in key locations within the United States where MDR infections, including CRE, are concentrated. These include roughly 900 hospitals in high resistance locations such as New York City, Los Angeles and Chicago, and other major population centers.

Manufacturing

We do not own or operate, and currently have no plans to establish, manufacturing facilities for the production of clinical or commercial quantities of XENLETA, CONTEPO, or any of the other compounds that we are evaluating in our discovery program. We currently rely, and expect to continue to rely, on third parties for the manufacture of XENLETA, CONTEPO and any further products that we may develop. We have significant in-house knowledge and experience in the relevant chemistry associated with XENLETA and CONTEPO; and the relevant manufacturing and supply chain processes associated with the commercial supply of XENLETA and CONTEPO. In addition to these internal resources, we engage third-party consultants, to assist in the management of our third-party manufacturers. We procure our supply of SIVEXTRO from Merck & Co., Inc.

We have engaged a limited number of third-party manufacturers to provide all of our starting materials, drug substance and finished product for use in clinical trials. The active pharmaceutical ingredients, or API, and drug products have been produced under master service contracts and specific work orders from these manufacturers pursuant to agreements that include specific supply timelines and volume and quality expectations. We choose the third-party manufacturers of the drug substance based on the volume required and the regulatory requirements at the relevant stage of development. All lots of drug substance and drug products used in clinical trials are manufactured under current good manufacturing practices. Separate third-party manufacturers have been responsible for fill and finish services, and for labeling and shipment of the final drug product to the clinical trial sites.

SIVEXTRO

In July 2020, we entered into a Sales Promotion and Distribution Agreement, with subsidiaries of Merck pursuant to which a subsidiary of Merck will sell, and we have agreed to purchase, SIVEXTRO at specified prices. We

will rely on a subsidiary of Merck to supply SIVEXTRO to us, who in turn, relies on third party manufacturers for the production, packaging, and serialization of SIVEXTRO for our distribution.

XENLETA

We have entered into a long-term commercial supply agreement with SEL Biochem Xinjiang Co., Ltd, or SEL, and Fountain International Development Holding Limited for the supply of pleuromutilin, which is the key intermediate for XENLETA API production. Under this agreement, SEL is required to manufacture and supply and we are required to purchase from SEL a specified percentage of our commercial requirements of pleuromutilin. The initial term of the agreement expires on August 28, 2022, subject to automatic renewal for successive three-year periods. It will remain in force until it is terminated by either party with two-year prior written notice, expiring on or at any time after the expiry of a then-current three-year period renewal term. Either party may terminate the agreement for the other party's uncured material breach or upon the occurrence of specified bankruptcy events. The agreement includes customary supply terms, including product specifications, price, payment terms, requirements forecasting, delivery mechanics and quality assurance. Under the agreement, we have also negotiated a quality technical agreement pursuant to which SEL will conduct all quality control and release testing for the pleuromutilin produced under the agreement.

In November 2018 we entered into a long-term commercial supply agreement with Arran Chemical Company Limited, or Arran, for the supply of the chiral acid starting material required in the synthesis of XENLETA API. Under this agreement Arran is required to manufacture and supply, and we are required to purchase from Arran the amount forecast for the first six months of a twelve-month rolling forecast provided monthly by us. The agreement term expires on November 12, 2023 and continues thereafter unless terminated by either party with not less than twelve months written notice. Either party may terminate the agreement for the other party's uncured material breach or upon the occurrence of insolvency or bankruptcy events. The agreement includes customary supply terms including material specifications, price, payment terms, demand forecasting, delivery mechanics, and quality assurance.

We have entered into a long-term commercial supply agreement with Hovione Limited, or Hovione, for the supply of XENLETA API. Under this agreement, Hovione is required to manufacture and supply and we are required to purchase from Hovione a specified percentage of our commercial requirements of XENLETA API. The agreement includes customary supply terms, including product specifications, price, payment terms, requirements forecasting, delivery mechanics and quality assurance. Under the agreement, we have also negotiated a quality technical agreement pursuant to which Hovione will conduct all quality control and release testing for the pleuromutilin produced under the agreement. On August 4, 2021, we entered into an amendment to the agreement, under which Hovione agreed to cancel our May 2021 purchase order for XENLETA API, which represented our minimum purchase requirement under the Hovione Supply Agreement. In addition, pursuant to the First Amendment, Hovione agreed to reduce our annual minimum purchase requirements for XENLETA API to no minimum purchase requirement in 2021, by 50% from 2022 to 2024 and by 25% in 2025, in consideration for cash payments from us totaling €3.2 million and the right to a low single-digit royalty on total net sales of XENLETA in the United States for a period commencing on August 4, 2021 and ending on November 22, 2030, or the Royalty Term, which royalty payments shall be no greater than an aggregate of €10.0 million. If the aggregate amount of royalties payments received by Hovione under the First Amendment is less than an aggregate of €4.0 million, we are obligated to pay Hovione the difference in a lump sum payment at the end of the Royalty Term. In addition, pursuant to the First Amendment, Hovione agreed to extend the duration of the Hovione Supply Agreement from November 22, 2025 to November 22, 2030 with annual minimum purchase requirements for 2026 to 2030 at the newly agreed annual minimum purchase amount for 2025. Pursuant to the First Amendment, upon the occurrence of certain events of insolvency for us, any unpaid minimum annual commitment amounts and royalty amounts under the agreement will become immediately due and payable.

We have also entered into a long-term commercial supply agreement with Patheon UK Limited, or Patheon, for the supply of IV vials of XENLETA. Under this agreement, Patheon is required to supply and we are required to purchase a specified percentage of our commercial requirements of IV vials of XENLETA. The initial term of the agreement expires on December 31, 2023, but it will remain in force until it is terminated by either party upon 24-months prior written notice, expiring on or at any time after the expiry of the initial term. Either party may also terminate the agreement for the other party's uncured material breach or upon the occurrence of specified bankruptcy events. We may also terminate the agreement if a governmental authority takes action that prevents us from importing,

exporting, purchasing or selling the IV vials of XENLETA. Finally, Patheon may terminate the agreement if we assign any of our rights under the agreement to an assignee that it does not consider to be a creditworthy substitute or is a competitor of Patheon. The agreement includes customary supply terms, including product specifications, batch size requirements, price, payment terms, requirements forecasting, delivery mechanics and quality assurance. Under the agreement, we have also negotiated a quality agreement pursuant to which Patheon will conduct all quality control testing for the IV vials of XENLETA. In November 2021, we entered into a side agreement effective January 1, 2021 to the long-term commercial supply agreement, reducing the annual binding volume requirements for IV vials of XENLETA for the years 2022 to 2025. The side agreement also provides for a discount on the amount due to Patheon for the minimum annual conversion revenue commitment for years 2020 and 2021.

In addition, we have entered into a long-term commercial supply agreement with Almac Pharma Services Limited, or Almac, for the commercial supply of XENLETA tablets. Under this agreement, Almac is required to supply and we are required to purchase services relating to the manufactured tablets equaling a specified minimum annual spend. The initial term of the agreement expires on August 7, 2022, but it will remain in force until it is terminated by either party with 24-months prior written notice, expiring on or at any time after the expiry of the initial term. Either party may also terminate the agreement for the other party's uncured material breach or upon the occurrence of specified bankruptcy events. The agreement includes customary supply terms, including payment terms, requirements forecasting, delivery mechanics and quality assurance. Under the agreement, we have also negotiated a quality technical agreement pursuant to which Almac will conduct all quality control testing for the tablets.

In August 2018, we entered into a commercial packaging and supply agreement, or the Packaging Agreement with Sharp Corporation, or Sharp, for the commercial packaging of XENLETA acetate for oral and intravenous administration. Under the Packaging Agreement, Sharp has agreed to provide certain packaging services to us, including labeling, serialization and final packaging of the packaged products. The Packaging Agreement has an initial five-year term ending December 31, 2023 and will automatically renew after the initial term for additional one-year terms unless either party gives notice of its intention to terminate the Packaging Agreement at least 90 days prior to the end of the then-current term. In addition, either party may terminate the Packaging Agreement for the other party's uncured material breach, in addition to other specified events, including with respect to bankruptcy proceedings and governmental actions, in each case subject to notice, cure periods and other conditions set forth in the Packaging Agreement. The Packaging Agreement includes customary supply terms, including product specifications, batch size requirements, price, payment terms, requirements forecasting, delivery mechanics and quality assurance. Under the agreement, we have also negotiated a quality agreement pursuant to which Sharp will conduct quality control testing for the packaged products.

XENLETA is a semi-synthetic organic compound of low molecular weight. The pleuromutilin core of the molecule is produced by fermentation and is manufactured on a significant scale by various manufacturers. The second part of the molecule is established from a readily accessible chiral starting material. The development stage production of XENLETA was carried out at a significant scale and we believe, if required, the synthetic route to XENLETA is amenable to further scale-up. The synthetic route does not require unusual, or specialized, equipment in the manufacturing process. Therefore, if any of our current or future drug substance manufacturers were to become unavailable for any reason, we believe there are a number of potential replacements, although delays may be incurred in identifying and qualifying such replacements.

CONTEPO

Effective July 28, 2016, Zavante, Laboratorios ERN, S.A., or ERN, and Ercros, S.A., or Ercros entered into an amended and restated three-way agreement (the "Three-Way Agreement"), which established the basis for related supply agreements with ERN and Ercros in anticipation of FDA approval of fosfomycin disodium and succinic acid injection for intravenous use filled, finished and packaged into containers for use by end users, or Product, in the United States. Pursuant to the Three-Way Agreement, Zavante has the direct responsibility for the manufacture and supply of the commercial Product in the United States. Under the Three-Way Agreement, (i) ERN has agreed to provide Zavante with certain technical documentation, or Technical Documentation, and data required for submission of an NDA or Abbreviated New Drug Application, or ANDA, as applicable, for the Product , and other assistance in connection with the submission of an NDA or ANDA, pursuant to the ERN Supply Agreement (as defined below); (ii) Ercros has agreed

to provide Zavante with certain Technical Documentation and the manufacture and supply of a blend of fosfomycin disodium and succinic acid, or API Mixture, for the manufacture of the Product, pursuant to the terms of the Ercros Supply Agreement (as defined below); and (iii) Zavante has agreed to obtain the commercial supply of the Product, under one or more separate agreements with third party manufacturers. The rights and obligations of each of the parties are set forth in each of the ERN Supply Agreement and the Ercros Supply Agreement. In addition, pursuant to the Three-Way Agreement, Zavante is required to (i) contract with one or more third party manufacturers to provide quantities of the Product required by Zavante for commercial sale in the United States, perform validation activities as required by the FDA, and obtain FDA approval of such third party manufacturer's facilities and quality systems; (ii) use commercially reasonable efforts to file an NDA within one year of its receipt of all Technical Documentation for the NDA from ERN and Ercros; (iii) obtain and own all trademarks to be used for the Product in the United States and (iv) bear the cost and manage all clinical trials necessary for obtaining FDA approval of the Product and keep ERN and Ercros updated regarding the progress of such clinical trials. The Three-Way-Agreement will continue in force and effect until the Ercros Supply Agreement and the ERN Supply Agreement have both been terminated or expired in accordance with the respective terms therein, or if the Three-Way Agreement is terminated upon mutual written agreement of all of the parties. The Three-Way Agreement contains, among other provisions, customary provisions relating to legal compliance and publicity.

Effective July 28, 2016, Zavante and Ercros entered into a manufacturing and supply agreement (the "Ercros Supply Agreement") pursuant to the Three-Way Agreement. Under the Ercros Supply Agreement, Ercros has agreed, pursuant to purchase orders entered into under the Ercros Supply Agreement, to manufacture (i) the exclusive supply of the API Mixture for Zavante in support of filing an NDA or an ANDA, as applicable, and (ii) the commercial supply of fosfomycin disodium and succinic acid injection for intravenous use in the United States. In addition, Ercros has agreed to provide access to certain technical documentation as may be requested by Zavante in connection with the filing of an NDA. The Ercros Supply Agreement has an initial ten-year term ending July 28, 2026 and will automatically renew after the initial term for additional two-year terms unless either party gives notice of its intention to terminate the Ercros Supply Agreement at least 18 months prior to the end of the then-current term. Either party may terminate the Ercros Supply Agreement for the other party's uncured material breach, in addition to other specified events, including with respect to bankruptcy proceedings, governmental actions and legal proceedings, in each case subject to notice, cure periods and other conditions set forth in the Ercros Supply Agreement. The Ercros Supply Agreement contains customary supply terms, including requirements forecasting, purchase orders, product specifications, price, payment terms, delivery mechanics and quality insurance. In addition, the Ercros Supply Agreement contains, among other provisions, customary representations and warranties by the parties, a grant by Ercros to Zavante of certain limited license rights to Ercros' intellectual property in connection with Zavante's performance under the Ercros Supply Agreement, certain indemnification rights in favor of both parties and customary confidentiality provisions. Under the Ercros Supply Agreement, Zavante and Ercros have also entered into a quality agreement, pursuant to which Ercros will conduct all quality control and release testing for the API Mixture produced under the Ercros Supply Agreement.

Effective July 28, 2016, Zavante and ERN entered into an amended and restated pharmaceutical manufacturing and exclusive supply agreement, as amended on December 1, 2016, March 1, 2017, May 1, 2017 and December 20, 2017, pursuant to the Three-Way Agreement (the ERN Supply Agreement). Under the ERN Supply Agreement, each party is required to use commercially reasonable efforts to complete certain development activities required for submission of an NDA or an ANDA for fosfomycin sodium and succinic acid (the bulk formulation of CONTEPO). In addition, ERN has agreed to provide to Zavante (i) certain technical documentation and data as required by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use's guidelines and the FDA for submission of an NDA or an ANDA for the bulk formulation of CONTEPO, and (ii) certain regulatory support in connection with the bulk formulation of CONTEPO sold or intended for commercial sale and human use. Upon the first commercial sale of the bulk formulation of CONTEPO, Zavante is obligated to make a one-time cash payment to ERN and subsequent quarterly payments thereafter based on the number of vials of the bulk formulation of CONTEPO sold during each calendar quarter. The ERN Supply Agreement has an initial ten-year term ending July 28, 2026 and will automatically renew after the initial term for additional two-year terms unless either party gives notice of its intention to terminate the ERN Supply Agreement at least 18 months prior to the end of the then-current term. Either party may terminate the ERN Supply Agreement by mutual written agreement and for the other party's uncured material breach, in addition to other specified events, including with respect to bankruptcy proceedings and governmental actions, in each case subject to notice, cure periods and other conditions set forth in the ERN Supply Agreement. The ERN

Supply Agreement contains, among other provisions, customary representations and warranties by the parties, a grant to each party by the other party of certain limited license rights to such other party's intellectual property in connection with the parties' performance of the services under the ERN Supply Agreement, certain indemnification rights in favor of both parties and customary confidentiality provisions.

On April 25, 2017, Zavante and Fisiopharma, S.r.l., or Fisiopharma, entered into a manufacturing and supply agreement, as amended on May 8, 2017, or the Fisiopharma Supply Agreement. Under the Fisiopharma Supply Agreement, Fisiopharma has agreed, pursuant to purchase orders entered into under the Fisiopharma Supply Agreement, to manufacture and supply fosfomycin disodium for intravenous injection in bulk drug vials, or the Bulk Drug Vials, to Zavante in support of filing an NDA or an ANDA, as applicable, and a specified percentage of Zavante's commercial requirements of Bulk Drug Vials for the United States. The Fisiopharma Supply Agreement has an initial ten-year term ending April 25, 2027 and will automatically renew after the initial term for additional one-year terms unless Zavante gives notice of its intention to terminate the Fisiopharma Supply Agreement at least six months prior to the end of the then-current term. Either party may terminate the Fisiopharma Supply Agreement for the other party's uncured material breach or upon the occurrence of specified bankruptcy events, and Zavante may terminate the Fisiopharma Supply Agreement upon the occurrence of other specified events, including with respect to governmental actions and legal proceedings instituted against Fisiopharma, in each case subject to notice, cure periods and other conditions set forth in the Fisiopharma Supply Agreement. The Fisiopharma Supply Agreement contains customary supply terms, including requirements forecasting, purchase orders, product specifications, price, payment terms, delivery mechanics and quality insurance. In addition, it contains, among other provisions, customary representations and warranties by the parties, a grant to Fisiopharma of certain limited license rights of Zavante's intellectual property in connection with Fisiopharma's performance of services under the Fisiopharma Supply Agreement, certain indemnification rights in favor of both parties, limitations of liability and customary confidentiality provisions. Under the Fisiopharma Supply Agreement, Zavante and Fisiopharma have also entered into a quality control agreement, pursuant to which Fisiopharma will conduct all quality control and release testing for the bulk drug vials produced under the Fisiopharma Supply Agreement. Any default under the quality control agreement constitutes a default under the Ercros Supply Agreement.

On December 26, 2017, Zavante entered into a commercial packaging agreement, or the PCI Packaging Agreement, with AndersonBrecon Inc., doing business as PCI of Illinois, or PCI for the commercial packaging of fosfomycin disodium for intravenous injection in bulk drug vials, or the Packaged Product. Under the PCI Packaging Agreement, PCI had agreed to provide certain packaging services to Zavante, including labeling, serialization and final packaging of the PCI Packaged Product. The PCI Packaging Agreement has been extended until December 26, 2022.

These five commercial supply agreements relating to CONTEPO are filed as exhibits to this Form 10-K. Other than these five agreements, we do not have long-term agreements with any other third parties for the manufacture of commercial supplies of CONTEPO, but we may enter into additional agreements with third-party contract manufacturers for additional commercial supplies of CONTEPO pending potential regulatory approval.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and private and public research institutions. Our products compete, and any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also

prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain marketing approvals for their products more rapidly than we obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers. SIVEXTRO and XENLETA are priced at a significant premium over competitive generic products. This may make it difficult for us to replace existing therapies with SIVEXTRO and XENLETA.

The key competitive factors affecting the success of SIVEXTRO, XENLETA and CONTEPO are likely to be their efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

There are a variety of available therapies marketed for the treatment of ABSSSI and CABP. Currently, the treatment of CABP is dominated by generic products. For hospitalized patients, combination therapy is frequently used. Many currently approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. We also are aware of various drugs under development or recently approved by the FDA for the treatment of ABSSSI and CABP, including omadacycline (Nuzyra approved by the FDA in October 2018 on behalf of Paratek Pharmaceuticals Inc. for both ABSSSI and CABP), delafloxacin (Baxdela approved by the FDA for ABSSSI in June 2017 and expanded for CABP in October 2019 on behalf of Melinta Therapeutics Inc.), and oral nafithromycin (Phase 2 clinical development by Wockhardt Ltd. for CABP).

If approved, we expect CONTEPO will face competition from commercially available antibiotics such as ceftazidime-avibactam, meropenem-vaborbactam, ceftolozane-tazobactam, imipenem-cilastatin-relebactam, cefiderocol, tigecycline, plazomicin, and from other product candidates currently in development for the treatment of cUTI, including AP, such as ceftazidime-avibactam (Avycaz), meropenem-vaborbactam (vabomere), plazomicin (Zemdri), ceftolozane-tazobactam (Zerbaxa), as well as imipenem-cilastatin-relebactam (Recarbrio approved by the FDA in July 2019 on behalf of Merck & Co., Inc.), cefiderocol (Fetroja approved by the FDA in November 2019 on behalf of Shionogi Inc.), or drugs under development such as tebipenem HBr (NDA to FDA for the Treatment of Complicated Urinary Tract Infections including Pyelonephritis in October 2021– Spero Therapeutics), cefepime-taniborbactam (under Phase 3 clinical development by Venatorx Pharmaceuticals), cefepime-enmetazobactam (under Phase 3 clinical development by Allecra Therapeutics), ETX0282-cefpodoxime proxetil (under Phase 1 clinical development by Entasis Therapeutics) tebipenem (under development by Spero), sulopenem (under development by Iterum Therapeutics), and LYS228 (under development by Novartis).

Intellectual Property

Our success depends in large part on our ability to obtain and maintain proprietary protection for our approved product, product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We strive to protect the proprietary technology that we believe is important to our business by, among other methods, seeking and maintaining patents, where available, that are intended to cover our approved product, product candidates, compositions and formulations, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary and competitive position.

As of January 31, 2022, we owned 26 different families of patents and patent applications, including 24 families directed to the various pleuromutilin derivatives as compositions of matter, processes for their manufacture, and their use in pharmaceutical compositions and methods of treating disease. The remaining two families are directed to ß lactamase inhibitors and siderophore cephalosporin conjugates. Our patent portfolio includes 20 issued U.S. patents, 23

granted European patents 10 granted Chinese patents, 11 granted patents in Taiwan, 6 granted patents in Canada, 12 granted patents in Hong Kong and 16 granted Japanese patents, as well as patents in other jurisdictions. We also have pending patent applications in the United States, Europe, China, Taiwan, Canada, Hong Kong, Japan and other countries and regions, including Asia, Australia, Eastern Europe, and South America, including notably Brazil, Israel and India among others.

All of these patents and patent applications are assigned solely to us and were either originally filed by us or originally filed by Sandoz and subsequently assigned to us.

As of January 31, 2022, XENLETA, was protected by the following six patent families:

- The first patent family includes patents and applications with claims that specifically recite XENLETA and/or its use in the treatment of microbial infections. This family includes two issued patents in each of the United States, Europe, China, Hong Kong and Japan and one issued patent in Taiwan and Canada, as well as issued patents in 16 other jurisdictions and 4 pending patent applications in other jurisdictions, including one divisional application in the United States. The standard term for patents in this family expires in 2028. A patent term adjustment of 303 days has already been obtained in the United States for one patent. A patent term extension for this patent has been filed extending the term to 2033. A patent term extension application for the second United States patent has also been filed extending the term of this patent to 2032. Supplementary Patent Certificates, or SPCs, have been filed for the first granted European patent extending the patent term to 2033. Similarly, a Certificate of Supplementary Protection was filed for the granted patent in Canada extending the patent term to 2030.

- The second patent family includes patents and applications with claims directed to the processes for the manufacture of XENLETA, crystalline intermediates useful in the processes, and the resulting crystalline salts. This family includes 23 granted patents including issued patents in the United States, Europe, China, Taiwan, Canada, Hong Kong and Japan and 8 pending patent applications in other jurisdictions. The standard term for patents in this family expires in 2031. A patent term extension application for the United States patent has been filed extending the term to 2033.

- The third patent family includes patents and applications with claims directed to processes for the synthetic manufacture of crystalline intermediates useful in the manufacture of XENLETA. This family includes granted patents in the United States, Europe, China, Taiwan, Hong Kong and Japan and 2 granted patents in other jurisdictions. The standard term for patents in this family expires in 2031.

- The fourth patent family includes patents and applications with claims directed to pharmaceuticals and treatments for *Helicobacter* infection, including pleuromutilins, such as XENLETA. This family includes issued patents in the United States, Europe and Hong Kong. The standard term for patents in this family expires in 2023. A patent term adjustment of 921 days has already been obtained for the U.S. patent.

- The fifth patent family is directed to pharmaceutical compositions of XENLETA and covers 11 granted patents including issued patent in Europe, China, Taiwan, Hong Kong and Japan and 6 pending patent applications in various other jurisdictions including the United States and Canada. The standard term for patents in this family expires 2036.

- The sixth patent family is directed to methods for purification of pleuromutilin, key intermediate in the XENLETA drug substance synthesis, and covers 5 granted patents including an issued patent in the United States, Europe and 6 pending patent applications in various jurisdictions such as China, Taiwan, Canada, Hong Kong and Japan. The standard term for patents in this family expires in 2038.

Our second most advanced product candidate, BC-7013, is covered specifically in one patent family with patents granted in the United States, Europe, and Japan. In other jurisdictions ten patents of this family are granted. The standard term for patents in this family expires in 2027.

The remaining 17 pleuromutilin patent families are directed to either molecules in the intellectual property landscape surrounding our approved product and product candidates in development including specific medical use or molecules which can be potentially further developed by us but have not yet been pursued. All patent applications in these families have been filed at least in the United States and/or Europe, and most have been filed in other countries. Many of these patent applications have already resulted in granted patents.

Finally, we own one patent family directed to ß lactamase inhibitor compounds and one patent family directed to siderophore cephalosporin conjugates. Patent applications in the ß lactamase inhibitors family have been filed and granted in the United States and Europe. The standard term for patents in this family expires in 2030. The published PCT patent application for the siderophore cephalosporin conjugates will be nationalized on or before the filing deadline.

Zavante holds two issued United States patents (U.S. 9,345,717 and U.S. 10,086,006) directed to methods for identifying dosing regimens that decrease the potential for on-therapy drug resistance. Zavante filed patent applications directed to dosing regimens of Fosfomycin in renally impaired patients. Additionally, Zavante has filed a patent application based on results from the ZEUS Study that relates to methods for treating patients with resistant bacterial infections and, specifically, Gram-negative bacterial infections. However, these patents may not ensure exclusivity through the patent terms and we may not be able to secure any additional patent protection. We plan to rely on regulatory protection afforded to CONTEPO ™ through QIDP designation, data exclusivity, and market exclusivity where available.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the filing date of a non provisional patent application. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a U.S. patent that covers a drug, biological product or medical device approved pursuant to a pre market approval, or PMA, may also be eligible for patent term extension when FDA approval is granted, provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug may be extended. Similar provisions are available in Europe, Canada, Taiwan and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug, provided that statutory and regulatory requirements are met. Thus, in the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for additional patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. The expiration dates of our patents and patent applications referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us unless otherwise indicated that a patent term extension application has been filed.

In addition to patents, we may rely, in some circumstances, on trade secrets to protect our technology and maintain our competitive position. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, corporate and scientific collaborators, consultants, scientific advisors, contractors and other third parties. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, pricing, reimbursement, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of

pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA reviews, approves and regulates drugs under the federal Food, Drug, and Cosmetic Act, or FDCA, and associated implementing regulations. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-approval may result in delays to the conduct of study, regulatory review and subject a sponsor to a variety of administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new drug product in the United States must typically undertake the following before a product candidate will be approved by the FDA:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- design of a clinicial protocol and submission to the FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, summarizing available data to support the proposed approval of the new drug product for the proposed use;
- review of the product application by an FDA advisory committee, where appropriate or if applicable and as may be requested by the FDA;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of PDUFA fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, where applicable, and the potential to conduct post-approval studies required by the FDA.

Preclinical Studies

Before a sponsor begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in*

vitro and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable.The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Additional long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Companies usually must complete some long-term preclinical testing, such as animal tests of long term exposure and reproductive adverse events, and must also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the candidate product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the candidate product does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with FDA regulatory requirements, including GCP requirements, in order to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in

compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial applicant, known as a data safety monitoring board or committee, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated check points based on unblinded safety data from the study to which only the DSMB has access. Suspension or termination of development during any phase of clinical trials may occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following four sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

- Phase 4: Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called “compassionate use”, is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, sponsors are required to make policies for evaluating and responding to requests for expanded access for patients publicly available upon the earlier of initiation of a Phase 2 or Phase 3 clinical trial, or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Special Protocol Assessment Agreements

A Special Protocol Assessment, or SPA, agreement is an agreement between a drug manufacturer and the FDA on the design and size of studies and clinical trials that can be used for approval of a drug or biological product. The FDA’s guidance on such agreements states that an agreement may not be changed by the manufacturer or the agency

unless through a written agreement of the two entities or if FDA determines a substantial scientific issue essential to determining the safety or effectiveness of the drug. The protocols that are eligible for SPA agreements are: animal carcinogenicity protocols, final product stability protocols and clinical protocols for Phase 3 trials whose data will form the primary basis for an efficacy claim.

Specifically, under the FDCA, the FDA may meet with sponsors, provided certain conditions are met, for the purpose of reaching a SPA agreement on the design and size of clinical trials intended to form the primary basis of an efficacy claim in a marketing application. If a sponsor makes a reasonable written request to meet with the FDA for the purpose of reaching agreement on the design and size of a clinical trial, then the FDA will meet with the sponsor. If an agreement is reached, the FDA will reduce the agreement to writing and make it part of the administrative record. An agreement may not be changed by the sponsor or FDA after the trial begins, except with the written agreement of the sponsor and FDA, or if the director of the FDA reviewing division determines that "a substantial scientific issue essential to determining the safety or effectiveness of the drug" was identified after the testing began. If a sponsor and the FDA meet regarding the design and size of a clinical trial and the parties cannot agree that the trial design is adequate to meet the goals of the sponsor, the FDA will clearly state the reasons for the disagreement in a letter to the sponsor.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, a marketing application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2022 is $3,117,218 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2022 is $369,413. Exceptions or waivers for these fees exist for a small company (fewer than 500 employees, including employees and affiliates) satisfying certain requirements and products with orphan drug designation for a particular indication are not subject to a fee provided there are no other intended uses in the NDA.

Following submission of an NDA, the FDA conducts a preliminary review of an NDA within 60 calendar days of its receipt and must inform the sponsor at that time or before whether the application is sufficiently complete to permit substantive review. In the event that FDA determines that an application does not satisfy this standard, it will issue a

Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information rather than accept an NDA for filing and the application may be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Standard review, representing most such applications are meant to be reviewed within ten months from the date of filing. Priority review applications are meant to be reviewed within six months of filing. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

In connection with its review of an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the data in support of the application.

In addition, as a condition of approval, the FDA may require the sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions relating to approval of a new drug product.

Expedited Review Programs

The FDA is authorized to expedite the review of NDAs in several ways. Under the Fast Track program, the sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

Any product candidate submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- *Breakthrough therapy designation*. To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence

must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- *Priority review*. A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- *Accelerated approval*. Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

- *Regenerative advanced therapy*. With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

None of these expedited programs change the standards for approval but they may help expedite the development or approval process of product candidates.

Limited Population Antibacterial Drug Pathway

With passage of the CURES Act, Congress authorized FDA to approve an antibacterial or antifungal drug, alone or in combination with one or more other drugs, as a “limited population drug”. To qualify for this approval pathway, the drug must be intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs; the standards for approval of drugs and biologics under the FDCA and PHSA must be satisfied; and FDA must receive a written request from the sponsor to approve the drug as a limited population drug pursuant to this provision. The FDA’s determination of safety and effectiveness for such a product must reflect the benefit-risk profile of such drug in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative treatment in such a limited population.

Any drug or biologic approved under this pathway must be labeled with the statement “Limited Population” in a prominent manner and adjacent to the proprietary name of the drug or biological product. The prescribing information must also state that the drug is indicated for use in a limited and specific population of patients and copies of all promotional materials relating to the drug must be submitted to FDA at least 30 days prior to dissemination of the materials. If FDA subsequently approves the drug for a broader indication, the agency may remove any post-marketing conditions, including requirements with respect to labeling and review of promotional materials applicable to the

product. Nothing in this pathway to approval of a limited population drug prevents sponsors of such products from seeking designation or approval under other provisions of the FDCA, such as accelerated approval.

The FDA's Decision on an NDA

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. Ultimately, the FDA will determine whether the expected benefits of the drug product outweigh its potential risks to patients.

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue a complete response letter, or CRL, or an approval letter. A CRL generally outlines the deficiencies in the submission and may require additional, sometimes substantial, testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. The FDA approves a new product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with or without clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with

manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications and prohibit the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in non-promotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to

NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted".

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug".

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations", also referred to as the "Orange Book". Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation of the FDCA by the FDA was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug

as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. The FDA's regulations governing patient listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any existing patent or non-patent

regulatory exclusivity, including orphan exclusivity, for a drug product. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data does not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

GAIN Exclusivity for Antibiotics

In 2012, Congress passed legislation known as the Generating Antibiotic Incentives Now Act, or GAIN Act. This legislation is designed to encourage the development of antibacterial and antifungal drug products that treat pathogens that cause serious and life-threatening infections. To that end, the law grants an additional five years of exclusivity upon the approval of an NDA for a drug product designated by FDA as a QIDP. Thus, for a QIDP, the periods of five-year new chemical entity exclusivity, three-year new clinical investigation exclusivity, and seven-year orphan drug exclusivity, would become ten years, eight years, and twelve years, respectively.

A QIDP is defined in the GAIN Act to mean "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens" or (2) certain "qualifying pathogens". A "qualifying pathogen" is a pathogen that has the potential to pose a serious threat to public health (such as resistant Gram-positive pathogens, multi-drug resistant Gram-negative bacteria, multi-drug resistant tuberculosis, and *Clostridium difficile*) and that is included in a list established and maintained by FDA. A drug sponsor may request the FDA to designate its product as a QIDP any time before the submission of an NDA. The FDA must make a QIDP determination within 60 days of the designation request. A product designated as a QIDP will be granted priority review by the FDA and can qualify for "fast track" status.

The additional five years of exclusivity under the GAIN Act for drug products designated by the FDA as QIDPs applies only to a drug that is first approved on or after July 9, 2012. Additionally, the five year exclusivity extension does not apply to: a supplement to an application under FDCA Section 505(b) for any QIDP for which an extension is in effect or has expired; a subsequent application filed with respect to a product approved by the FDA for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or a product that does not meet the definition of a QIDP under Section 505(g) based upon its approved uses. The FDA has designated IV fosfomycin, and each of the IV and oral formulations of XENLETA as a QIDP and also granted fast track designations.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of the IND and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Offices reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products.

Although FDA approval for XENLETA has been obtained, we are required to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Regulation and Marketing Authorization in the European Union

The process governing approval of medicinal products in the European Union follows essentially the same lines as in the United States and, likewise, generally involves satisfactorily completing each of the following:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the applicable E.U. Good Laboratory Practice regulations;
- submission to the relevant national authorities of a clinical trial application, or CTA, which must be approved before human clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication;
- submission to the relevant competent authorities of a marketing authorization application, or MAA, which includes the data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product in clinical development and proposed labelling;
- satisfactory completion of an inspection by the relevant national authorities of the manufacturing facility or facilities, including those of third parties, at which the product is produced to assess compliance with strictly enforced cGMP;
- potential audits of the non-clinical and clinical trial sites that generated the data in support of the MAA; and
- review and approval by the relevant competent authority of the MAA before any commercial marketing, sale or shipment of the product.

Preclinical Studies

Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animal studies, in order to assess the potential safety and efficacy of the product. The conduct of the preclinical tests and formulation of the compounds for testing must comply with the relevant E.U. regulations and requirements. The results of the preclinical tests, together with relevant manufacturing information and analytical data, are submitted as part of the CTA.

Clinical Trial Approval

Requirements for the conduct of clinical trials in the European Union including Good Clinical Practice, or GCP, are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the E.U. member states. Under this system, approval must be obtained from the competent national authority of each E.U. member state in which a study is planned to be conducted. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other

applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country. On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 cecomes applicable.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include:

- a streamlined application procedure via a single entry point, the E.U. portal;
- a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states;
- a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned;
- strictly defined deadlines for the assessment of clinical trial applications; and
- the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

As in the United States, similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries.

Marketing Authorization

Authorization to market a product in the member states of the European Union proceeds under one of four procedures: a centralized authorization procedure, a mutual recognition procedure, a decentralized procedure or a national procedure.

Centralized Authorization Procedure

The centralized procedure enables sponsors to obtain a marketing authorization that is valid in all E.U. member states based on a single application. Certain medicinal products, including products developed by means of biotechnological processes must undergo the centralized authorization procedure for marketing authorization, which, if granted by the European Commission, is automatically valid in all 28 E.U. member states. The EMA and the European Commission administer this centralized authorization procedure pursuant to Regulation (EC) No 726/2004.

Pursuant to Regulation (EC) No 726/2004, this procedure is mandatory for:

- medicinal products developed by means of one of the following biotechnological processes:
    - recombinant DNA technology;
    - controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells; and

- hybridoma and monoclonal antibody methods;

- advanced therapy medicinal products as defined in Article 2 of Regulation (EC) No 1394/2007 on advanced therapy medicinal products;

- medicinal products for human use containing a new active substance that, on the date of effectiveness of this regulation, was not authorized in the European Union, and for which the therapeutic indication is the treatment of any of the following diseases:

  - acquired immune deficiency syndrome;

  - cancer;

  - neurodegenerative disorder;

  - diabetes;

  - auto-immune diseases and other immune dysfunctions; and

  - viral diseases; and

- medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

The centralized authorization procedure is optional for other medicinal products if they contain a new active substance or if the sponsor shows that the medicinal product concerned constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization is in the interest of patients in the European Union.

Administrative Procedure

Under the centralized authorization procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP serves as the scientific committee that renders opinions about the safety, efficacy and quality of medicinal products for human use on behalf of the EMA. The CHMP is composed of experts nominated by each member state's national authority for medicinal products, with one of them appointed to act as Rapporteur for the co-ordination of the evaluation with the possible assistance of a further member of the Committee acting as a Co-Rapporteur. After approval, the Rapporteur(s) continue to monitor the product throughout its life cycle. The CHMP has 210 days, to adopt an opinion as to whether a marketing authorization should be granted. The process usually takes longer in case additional information is requested, which triggers clock-stops in the procedural timelines. The process is complex and involves extensive consultation with the regulatory authorities of member states and a number of experts. When an application is submitted for a marketing authorization in respect of a drug that is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the sponsor may pursuant to Article 14(9) Regulation (EC) No 726/2004 request an accelerated assessment procedure. If the CHMP accepts such request, the time-limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time-limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. Once the procedure is completed, a European Public Assessment Report, or EPAR, is produced. If the opinion is negative, information is given as to the grounds on which this conclusion was reached. After the adoption of the CHMP opinion, a decision on the MAA must be adopted by the European Commission, after consulting the E.U. member states, which in total can take more than 60 days.

Conditional Approval

In specific circumstances, E.U. legislation (Regulation (EC) No 726/2004 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a conditional

marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products), if (1) the risk-benefit balance of the product candidate is positive, (2) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Marketing Authorization Under Exceptional Circumstances

Under Regulation (EC) No 726/2004, products for which the sponsor can demonstrate that comprehensive data (in line with the requirements laid down in Annex I of Directive 2001/83/EC, as amended) cannot be provided (due to specific reasons foreseen in the legislation) might be eligible for marketing authorization under exceptional circumstances. This type of authorization is reviewed annually to reassess the risk-benefit balance. The fulfillment of any specific procedures/obligations imposed as part of the marketing authorization under exceptional circumstances is aimed at the provision of information on the safe and effective use of the product and will normally not lead to the completion of a full dossier/approval.

Market Authorizations Granted by Authorities of E.U. Member States

In general, if the centralized procedure is not followed, there are three alternative procedures to obtain a marketing authorization in (one or several) E.U. member states as prescribed in Directive 2001/83/EC:

- The decentralized procedure allows sponsors to file identical applications to several E.U. member states and receive simultaneous national approvals based on the recognition by E.U. member states of an assessment by a reference member state.

- The national procedure is only available for products intended to be authorized in a single E.U. member state.

- A mutual recognition procedure similar to the decentralized procedure is available when a marketing authorization has already been obtained in at least one E.U. member state.

A marketing authorization may be granted only to a sponsor established in the European Union.

Pediatric Studies

Prior to obtaining a marketing authorization in the E.U., sponsors have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Period of Authorization and Renewals

A marketing authorization, other than a conditional marketing authorization, is initially valid for five years and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the E.U. market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Regulatory Data Protection

European Union legislation also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No 726/2004, as amended, and Article 10(1) of Directive 2001/83/EC, as amended, upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder, or MAH, obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical test, preclinical tests and clinical trials.

Transparency

There is an increasing trend in the E.U. towards greater transparency and, while the manufacturing or quality information in marketing authorization dossiers is currently generally protected as confidential information, the EMA and national regulatory authorities are now liable to disclose much of the non-clinical and clinical information, including the full clinical study reports, in response to freedom of information requests after the marketing authorization has been granted. In October 2014, the EMA adopted a policy under which clinical study reports would be posted on the agency's website following the grant, denial or withdrawal of a marketing authorization application, subject to procedures for limited redactions and protection against unfair commercial use. Additional transparency provisions are contained in the new Clinical Trials Regulation (EU) No 536/2014.

Regulatory Requirements After a Marketing Authorization has been Obtained

If we obtain authorization for a medicinal product in the European Union, we will be required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products:

Pharmacovigilance and Other Requirements

We will, for example, have to comply with the E.U.'s stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. E.U. regulators may

conduct inspections to verify our compliance with applicable requirements, and we will have to continue to expend time, money and effort to remain compliant. Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the European Union. Similarly, failure to comply with the European Union's requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual E.U. member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements.

Manufacturing

The manufacturing of authorized drugs, for which a separate manufacturer's license is mandatory, must be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. The EMA enforces its GMP requirements through mandatory registration of facilities and inspections of those facilities. The EMA may have a coordinating role for these inspections while the responsibility for carrying them out rests with the member states competent authority under whose responsibility the manufacturer falls. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and could subject the sponsor to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

Marketing and Promotion

The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended. The applicable regulations aim to ensure that information provided by holders of marketing authorizations regarding their products is truthful, balanced and accurately reflects the safety and efficacy claims authorized by the EMA or by the competent authority of the authorizing member state. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Patent Term Extension

To compensate the patentee for delays in obtaining a marketing authorization for a patented product, a supplementary certificate, or SPC, may be granted extending the exclusivity period for that specific product by up to five years. Applications for SPCs must be made to the relevant patent office in each E.U. member state and the granted certificates are valid only in the member state of grant. An application has to be made by the patent owner within six months of the first marketing authorization being granted in the European Union (assuming the patent in question has not expired, lapsed or been revoked) or within six months of the grant of the patent (if the marketing authorization is granted first). In the context of SPCs, the term "product" means the active ingredient or combination of active ingredients for a medicinal product and the term "patent" means a patent protecting such a product or a new manufacturing process or application for it. The duration of an SPC is calculated as the difference between the patent's filing date and the date of the first marketing authorization, minus five years, subject to a maximum term of five years.

A six-month pediatric extension of an SPC may be obtained where the patentee has carried out an agreed pediatric investigation plan, the authorized product information includes information on the results of the studies and the product is authorized in all member states of the European Union.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's withdrawal from the European Union took place on January 31, 2020. The European Union and the United Kingdom reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods,

including healthcare products such as medicinal products. Thereafter, the European Union and the United Kingdom will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the United Kingdom is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the E.U. General Data Protection Regulation, or GDPR, is now effective in the United Kingdom, it is still unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an E.U. Member State in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the European Union and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the European Union and EEA remain unaffected. We may, however, incur liabilities, expenses, costs, and other operational losses under GDPR and applicable E.U. Member States and the United Kingdom privacy laws in connection with any measures we take to comply with them.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the E.U., including personal health data, is subject to the E.U. General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the E.U., including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and

imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

To secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, *i.e.*, arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations

that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act and civil monetary penalty laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the Affordable Care Act, or the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price", or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's

automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2031. The Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization, or PA, and step therapy, or ST, for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" in the regulations. It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our

products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs the Department of Health and Human Services, or HHS, to create a plan within 45 days to combat “excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging.” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (1) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (2) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (3) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, the U.S. Department of Health and Human Services, or HHS, has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

At the state level, California has enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Additionally, effective starting on January 1, 2023, the California Privacy Rights Act, or CPRA, will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities. In addition, other states, including Virginia and Colorado, already have passed state privacy laws and other states will likely be considering similar laws in the near future.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Employees and Human Capital

As of January 31, 2022, we had 73 employees, 3 employees are located in Dublin, Ireland, 27 of our employees are located in Vienna, Austria and 43 of our employees are located in the U.S., with 38 located in Fort Washington, Pennsylvania, one located in San Diego, California and the remaining four employees in the field.

Our employees in Austria are subject to the collective bargaining agreement of the chemical industry. This is an annual agreement between the employer representatives and the trade union of an industry. It defines conditions of employment, such as minimum wages, working hours and conditions, overtime payments, vacations and other matters.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards. We utilize third party consultants to review and update our compensation practices annually. We understand that attracting, retaining, engaging and supporting our talented team and maintaining a diverse and inclusive organization is critical to our success and to increase the value we can provide for patients, shareholders and all stakeholders. We consider our relations with our employees to be good.

In response to the COVID-19 pandemic and related mitigation efforts, we assembled a COVID-19 task force, which consists of senior leaders from various departments within our organization and is responsible for the safety of our employees, consultants and contractors throughout the world, collectively our workers, and to maintain business continuity. Our COVID-19 task force continues to monitor safety protocols and procedures to protect our workers as well as business essential operations. These protocols include: (i) limiting access to our facilities and requiring a majority of our workers to work from home (except when access to facilities is necessary) while providing additional equipment to operate successfully remotely, (ii) increasing physical distancing in workspaces for workers working onsite, (iii) adjusting schedules for workers working onsite to minimize the number of individuals in a facility at one time, (iv) requiring masks to be worn in all of our locations, (v) enhancing our cleaning protocols across all facilities, (vi) establishing emergency worker testing procedures to immediately respond to potential onsite exposure risks with subsequent testing, tracing, quarantining and re-testing to ensure a safe work environment. Our COVID-19 task force periodically provides updates to our executive team and our board of directors and provides timely communications to employees.

Our Corporate Information

On March 1, 2017, Nabriva Therapeutics plc, or Nabriva Ireland was incorporated in Ireland under the name Hyacintho 2 plc, and was renamed to Nabriva Therapeutics plc on April 10, 2017, in order to effectuate the change of the jurisdiction of incorporation of the ultimate parent company of the Nabriva Group from Austria to Ireland. Nabriva Ireland replaced Nabriva Therapeutics AG, or Nabriva Austria as the ultimate parent company on June 23, 2017, following the conclusion of a tender offer in which holders of the outstanding share capital of Nabriva Austria exchanged their holdings for ordinary shares, $0.01 nominal value per share, of Nabriva Ireland. The ordinary shares of Nabriva Ireland were issued on a one-for-ten basis to the holders of the Nabriva Austria common shares and on a one-for-one basis to the holders of the Nabriva Austria American Depositary Shares, or Nabriva Austria ADSs. On June 26, 2017, the ordinary shares of Nabriva Ireland began trading on the Nasdaq Global Select Market under the symbol “NBRV”, the same symbol under which the Nabriva Austria ADSs were previously traded. This transaction was accounted for as a merger between entities under common control; accordingly, the historical financial statements of Nabriva Austria for periods prior to this transaction are considered to be the historical financial statements of Nabriva Ireland. Our executive offices are located at 25-28 North Wall Quay IFSC, Dublin 1, Ireland, and our telephone number is +353 1 649 2000.

The predecessor of Nabriva Ireland, Nabriva Austria, was incorporated in Austria as a spin-off from Sandoz GmbH in October 2005 under the name Nabriva Therapeutics Forschungs GmbH, a limited liability company organized under Austrian law and commenced operations in February 2006. In 2007, Nabriva Austria transformed into a stock corporation (*Aktiengesellschaft*) under the name Nabriva Therapeutics AG. On October 19, 2017, Nabriva Austria was converted into a private limited liability company under Austrian law and renamed Nabriva Therapeutics GmbH.

Our U.S. operations are conducted by our wholly-owned subsidiary Nabriva Therapeutics US, Inc., a Delaware corporation established in August 2014 and located at 414 Commerce Drive, Fort Washington, Pennsylvania 19034.

Our website address is www.nabriva.com. The information contained on, or that can be accessed from, our website does not form part of this Annual Report.

Available Information

We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make these reports available through our website (www.nabriva.com) as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. Previously, as a foreign private issuer, we filed our Annual Report on Form 20-F and furnished information on Form 6-K. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% shareholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

ITEM 1A. RISK FACTORS.

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. The risks described below are not the only risks facing us. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, results of operations and/or prospects.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never generate profits from operations or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $49.5 million for the year ended December 31, 2021, $69.5 million for the year ended December 31, 2020 and $82.8 million for the year ended December 31, 2019. As of December 31, 2021, we had an accumulated deficit of $595.7 million. To date, we have financed our operations primarily through the sale of our equity securities, convertible and term debt financings and research and development support from governmental grants and loans and proceeds from our licensing agreements. We have devoted most of our efforts to research and development, including clinical trials and the commercial sale of our products. XENLETA is approved in the United States for the treatment of community-acquired bacterial pneumonia, or CABP, in adults. In July 2020, we entered into a Sales Promotion and Distribution Agreement, with subsidiaries of Merck Sharp & Dohme Corp. pursuant to which we licensed the right, subject to specified conditions, to promote, distribute and sell SIVEXTRO for acute bacterial skin and skin structure infections, or ABSSSIs, caused by certain susceptible Gram-positive microorganisms in the United States and its territories, or the SIVEXTRO Territory. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years, including in connection with our regulatory approval efforts, supply chain investments and commercialization of XENLETA, the promotion and distribution efforts for SIVEXTRO, and, if it receives marketing approval, the commercialization of CONTEPO. The net losses we incur may fluctuate significantly from quarter-to-quarter and year-to-year.

We expect to continue to invest in critical commercial promotion and distribution, medical affairs and other commercialization activities, as well as investing in our supply chain for the commercialization of SIVEXTRO, XENLETA and the potential launch of CONTEPO. We expect to seek additional funding in future periods to support these activities. In December 2019, we resubmitted an NDA for CONTEPO for the treatment of cUTIs, including AP. On June 19, 2020 we received a second Complete Response Letter from the FDA in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cited observations at our manufacturing partners that could not be resolved due to FDA's inability to conduct onsite inspections because of travel restrictions. Our contract manufacturers continue to interact with FDA to discuss its plans for conducting inspections at their sites. On October 30, 2020, we participated in a "Type A" meeting with the FDA to obtain any new information related to the FDA's pending conduct of inspections of foreign manufacturers during the COVID-19 pandemic that has negatively impacted a number of FDA product reviews, including our NDA for CONTEPO for the treatment of cUTIs, including AP. The FDA informed us that it has not yet determined how it will conduct international inspections during the COVID-19 pandemic. On April 14, 2021, the FDA issued industry guidance on remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities during COVID-19 specifying that when it cannot perform a Pre-Approval Inspection, or PAI, or a Pre-License Inspection, or PLI, or when the FDA determines that it would be useful to supplement a planned inspection, the agency will consider using tools other than a physical inspection and select the most appropriate method to address the specific risks that justify the need for the PAI or PLI. The FDA informed us that onsite inspections of our manufacturing partners in Europe are required in order for the FDA to complete the review of a potential CONTEPO NDA resubmission. Due to travel restriction related to the COVID-19 pandemic, the FDA suspended onsite inspections of ex-US manufacturers for all non-COVID products. As a result, we requested an extension of the timeline for a potential CONTEPO NDA resubmission until June 2023, which the FDA granted on March 21, 2022. We are awaiting further clarity from the FDA regarding their ability to complete onsite inspections at our manufacturing partners in Italy and Spain before determining specific timing of the potential NDA resubmission, which we plan to submit promptly once we have clarity from the FDA. The FDA released the Resiliency Roadmap for FDA Inspectional Oversight that describes the systematic approach that FDA will utilize to manage postponed inspections and other oversight activities. The prioritization plan considers public health risks related to conducting an inspection, such as the impact of the product's availability on public health, as well as investigator safety and travel restrictions/advisories. In addition, the FDA informed us that, while they cannot predict when an inspection may occur and when the pandemic may prevent the FDA from completing inspections, tier 1 mission-critical inspections and tier 2 higher priority inspections, which includes PAIs, will continue to be prioritized going forward. We cannot predict the outcome of any further interactions with the FDA or when CONTEPO will receive marketing approval, if at all. Our contract manufacturers continue to interact with FDA to discuss its plans for conducting inspections at their sites. If we obtain marketing approval of CONTEPO for cUTI, including AP, or another indication, we also expect to incur significant additional sales, marketing, distribution and manufacturing expense.

In addition, our expenses will increase if and as we:

- initiate or continue the research and development of XENLETA and CONTEPO for additional indications and of our other product candidates;
- seek to develop additional product candidates;
- seek marketing approval for any product candidates that successfully complete clinical development;
- are required by the FDA, EMA or other regulators to conduct additional clinical trials prior to or after approval;
- continue to build or re-build a medical affairs, sales, marketing and distribution infrastructure and scale up manufacturing capabilities to commercialize SIVEXTRO, XENLETA and any other product candidates for which we receive marketing approval;
- in-license or acquire other products, product candidates or technologies, including additional community products;

- maintain, expand and protect our intellectual property portfolio;
- expand our physical presence in the United States and Ireland;
- incur additional debt;
- establish and expand manufacturing arrangements with third parties; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and our operations as a public company in addition to our commercialization efforts.

Our ability to generate profits from operations, and to become and remain profitable, depends on our ability to successfully develop and commercialize drugs that generate significant revenue. Based on our current plans, we do not expect to generate significant revenue unless and until we obtain marketing approval for CONTEPO, and successfully commercialize XENLETA and, if approved, CONTEPO and actively promote SIVEXTRO. In April 2020, we announced a plan to restructure our hospital-based commercial sales force and transition to a community-based sales effort. This restructuring intended to reduce costs and to align the capabilities of our sales effort with our strategic re-focus on making sales of XENLETA to community health care professionals. This restructuring resulted in the termination of 66 employees, consisting of our entire hospital-based sales personnel and certain members of our sales force leadership team. Additional reductions in headcount occurred in the third quarter of 2020 including the restructuring of the commercial organization, which led to the elimination of the role of our Chief Commercial Officer. Our commercial operations now report directly to our Chief Executive Officer. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021. Our ability to generate significant revenue will require us to be successful in a range of challenging activities, including:

- maintaining and expanding a community-based sales effort;
- obtaining marketing approval for CONTEPO;
- establishing and maintaining medical affairs, sales, marketing and distribution capabilities to effectively market and sell SIVEXTRO, XENLETA and CONTEPO, if approved, in the United States;
- establishing and maintaining collaboration, distribution or other marketing arrangements with third parties to commercialize XENLETA in markets outside the United States;
- protecting our rights to our intellectual property portfolio related to XENLETA and CONTEPO;
- minimizing cyber-security and similar risks, which could result in the disclosure of confidential information, disruption of our technology support systems, legal exposure and financial losses;
- assessing any material effects of climate change transition risks, such as policy and regulatory changes, which could impose operational and compliance burdens in certain jurisdictions or impact market trends;
- establishing and maintaining arrangements for the manufacture of and obtaining commercial quantities of SIVEXTRO, XENLETA and CONTEPO, if approved; and
- negotiating and securing adequate reimbursement from third-party payors for SIVEXTRO, XENLETA and CONTEPO, if approved.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to generate profits from operations. Even if we do generate profits from operations, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate profits from operations, and to become and remain profitable, would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings, conduct commercial activities, maintain our commercial efforts or continue our operations. A decline in the value of our company could also cause our shareholders to lose all or part of their investment.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We may be forced to delay or reduce the scope of our development programs and/or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2021, we had cash and cash equivalents, restricted cash and short-term investments of $47.9 million. Based on our available cash resources, we believe we do not have sufficient cash on hand to support current operations for more than twelve months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about our ability to continue as a going concern within one year after the date the consolidated financial statements included elsewhere in this Annual Report on Form 10-K are issued. Management's plans in this regard are described in Note 1 of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K. However, we cannot guarantee that we will be able to obtain sufficient additional funding when needed or that such funding, if available, will be obtainable.

We will need substantial additional funding. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to continue to incur substantial costs in connection with our ongoing activities. These activities include the commercialization of SIVEXTRO and XENLETA, the process of obtaining marketing approval for CONTEPO and, possibly, other product candidates or additional indications for our products, and our ongoing research activities. Our expenses will increase if we suffer any regulatory delays or are required to conduct additional clinical trials to satisfy regulatory requirements.

Furthermore, we expect to continue to incur additional costs to service our current debt and any potential future draws on the Loan Agreement (as defined below) and costs associated with operating as a public company and as a company with a commercial rather than a research and development focus. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to further delay, reduce or eliminate our research and development programs or reduce our commercialization efforts.

On March 11, 2020, we entered into an amendment, or the Third Amendment, to our Loan and Security Agreement, or the Loan Agreement, with Hercules Capital, Inc., or Hercules, as administrative agent, collateral agent and lender. Pursuant to the Third Amendment, we repaid Hercules in March 2020, $30.0 million of the $35.0 million in aggregate principal amount of debt outstanding under the Loan Agreement, which we refer to as the Prepayment. We determined to enter into the Third Amendment following the effectiveness of a performance covenant in February 2020 under which we became obligated to either (1) achieve 80% of our net product revenue sales target over a trailing six-month period, or (2) maintain an amount of cash and cash equivalents in accounts pledged to Hercules plus a specified amount of eligible accounts receivables equal to the greater of the amount outstanding under the Loan Agreement or $40.0 million, which we refer to as the liquidity requirement. Under the Third Amendment, we and Hercules agreed to defer the end of term loan charge payment in the amount of approximately $2.1 million that would have otherwise become payable on the date of the Prepayment and to reduce the prepayment charge with respect to the Prepayment from $600,000 to $300,000 and to defer its payment, in each case, until June 1, 2023 or such earlier date on which all loans under the Loan Agreement are repaid or become due and payable. The Third Amendment also reset the revenue performance covenant to 70% of targeted revenue based on a revised net product revenue forecast and lowered our minimum liquidity requirement to $3.0 million in cash and cash equivalents, in each case, following the Prepayment.

The new minimum liquidity requirement will not apply if CONTEPO receives regulatory approval from the U.S. Food and Drug Administration and we achieve at least 70% of our revised net product revenue targets under the Loan Agreement. On June 2, 2021, we entered into a further amendment, or the Fourth Amendment, to our Loan Agreement with Hercules. Pursuant to the Fourth Amendment, the date on which we must commence repaying principal under the Loan Agreement was extended to April 1, 2022, which date may be extended until July 1, 2022, subject to our receipt of a specified amount of additional net financing proceeds and the achievement of a specified product revenue milestone. Additionally, the time during which the Tranche Advance (as defined in Note 7 to our consolidated financial statements) may be requested by us under the Loan Agreement, was extended until the Amortization Date. In addition, pursuant to the Fourth Amendment, the minimum liquidity requirement of $3.0 million in cash and cash equivalents will be waived at any time we have recognized $15.0 million of net product revenue during the applicable trailing three months. In light of the COVID-19 pandemic, the associated disruption to the healthcare delivery and the uncertainty of resuming full direct physician promotion, future sales are uncertain. Based on our current operating plans, we expect that our existing cash resources as of the date of this Annual Report on Form 10-K will be sufficient to enable us to fund our operations, debt service obligations and capital expenditure requirements well into the fourth quarter of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not obtain any additional funding through grants and clinical trial support, collaboration agreements, or equity or debt financings. This estimate also assumes that we remain in compliance with the covenants and no event of default occurs under the Loan Agreement.

We expect to continue to invest in critical commercial and medical affairs activities, as well as investing in our supply chain for the commercialization of SIVEXTRO and XENLETA and the potential commercial launch of CONTEPO. We expect to seek additional funding in future periods to support these activities.

Our future capital requirements will depend on many factors, including:

- the costs and timing of process development and manufacturing scale-up activities associated with XENLETA and, if approved, CONTEPO;
- the costs, timing and outcome of regulatory review of CONTEPO;
- the costs of commercialization activities for SIVEXTRO, XENLETA and CONTEPO if we receive marketing approval for CONTEPO, including the costs and timing of establishing product sales, marketing distribution and outsourced manufacturing capabilities, including the costs of building finished product inventory and its components in preparation of initial marketing of CONTEPO;
- revenue received from commercial sales of SIVEXTRO, XENLETA and, subject to the resubmission of the CONTEPO NDA and potential receipt of marketing approval, CONTEPO;
- the costs of developing XENLETA and CONTEPO for the treatment of additional indications;
- the impact of the COVID-19 pandemic;
- our ability to establish collaborations on favorable terms, if at all;
- the scope, progress, results and costs of product development of any other product candidates that we may develop;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies, including additional community products;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property-related claims;

- the continued availability of Austrian governmental grants;
- the costs of our physical presence in the United States, Ireland and Austria;
- interest expense on our debt and the eventual repayment of our debt obligations which is scheduled to begin in April 2022;
- the requirement to keep minimum cash balances per the terms of our debt obligations as well as our ability to remain in compliance with our debt covenants;
- the costs of operating as a company with a commercial rather than a research and development focus; and
- the costs of operating as a public company in the United States.

Our commercial revenues will be derived from sales of SIVEXTRO, XENLETA and from CONTEPO, if approved, or any other products that we successfully develop, in-license or acquire. SIVEXTRO, XENLETA or, if approved, CONTEPO or any other product candidate that we develop, in-license or acquire may not achieve commercial success. Additionally, the reliance on a commercial sales organization may adversely impact our sales of SIVEXTRO and XENLETA. If we fail to generate sufficient revenues from the sale of SIVEXTRO, XENLETA, or the commercialization of CONTEPO, if approved, or any other product candidate that we successfully develop, in-license or acquire, we will need to obtain substantial additional financing to achieve our business objectives.

Adequate additional financing may not be available to us on acceptable terms, or at all. Under General Instruction I.B.6 to Form S-3, or the Baby Shelf Rule, the amount of funds we can raise through primary public offerings of securities in any 12-month period using our registration statement on Form S-3 is limited to one-third of the aggregate market value of the ordinary shares held by our non-affiliates. As of March 28, 2022, the aggregate market value of our ordinary shares held by our non-affiliates was approximately $32.1 million, based on 61,197,667 ordinary shares held by non-affiliates and a price of $0.525 per share, which was the last reported sale price of our ordinary shares on the Nasdaq Global Select Market on February 9, 2022. We therefore are limited by the Baby Shelf Rule as of the filing of this Annual Report on Form 10-K, until such time as our public float exceeds $75.0 million. We will need substantial additional funding. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

In addition, as part of our corporate strategy, we continue to evaluate business development opportunities and potential collaborations. We may further expand our product pipeline through opportunistically in-licensing or acquiring the rights to complementary products, product candidates and technologies for the treatment of a range of infectious diseases or other products that we would market with our commercial infrastructure, including additional community products, which could involve an acquisition of or combination or other strategic transaction with another operating business. To the extent any additional business development opportunity is consummated, our capital expenditures may increase significantly.

Raising additional capital may cause dilution to our security holders, restrict our operations or require us to relinquish certain rights to our technologies, products or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, and funding from local and international government entities and non-government organizations in the disease areas addressed by our products or product candidates and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our security holders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our security holders. Additional debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In

addition, debt service obligations under any debt financings may limit the availability of our cash for other purposes, and we may be unable to make interest payments or repay the principal of such debt financings when due.

In June 2019, we entered into an Open Market Sale Agreement[SM], or the Jefferies ATM Agreement, with Jefferies, pursuant to which, from time to time, we may offer and sell ordinary shares, for aggregate gross sale proceeds of up to $50.0 million through Jefferies by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended.

In May 2021, we entered into an Open Market Sale Agreement[SM], or the New Sale Agreement, with Jefferies, as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share for aggregate gross sale proceeds of up to $50.0 million, from time to time through Jefferies, by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. Upon entry into the New Sale Agreement, our existing Jefferies ATM Agreement was terminated. We did not incur any termination penalties as a result of the replacement of the Jefferies ATM Agreement. As of the effective date of the termination of the Jefferies ATM Agreement, we had sold an aggregate of 5,925,699 of our ordinary shares pursuant to the Jefferies ATM Agreement for aggregate gross proceeds of $33.7 million and net proceeds to us of $31.9 million, after deducting commissions and offering expenses payable by us. The approximately $16.3 million of ordinary shares that had been available for sale pursuant to the Jefferies ATM Agreement remained unsold at the time of its replacement. The replacement of the Jefferies ATM Agreement terminated any future sales of ordinary shares through the Jefferies ATM Agreement.

As of December 31, 2021, we have issued and sold an aggregate of 18,232,689 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $30.5 million and net proceeds of $29.3 million, after deducting commissions to Jefferies and other offering expenses. From January 1, 2022 and through the date of this filing, we have issued and sold an aggregate of 1,338,282 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $595,000 and net proceeds of $580,000, after deducting commissions to Jefferies and other offering expenses.

On December 20, 2019, we sold to certain institutional investors in a registered direct offering an aggregate of 1,379,310 ordinary shares, and accompanying warrants to purchase up to an aggregate of 1,379,310 ordinary shares. Each share was issued and sold together with an accompanying warrant at a combined price of $14.50 per security. The proceeds to us from the offering were $20.0 million gross and $18.3 million net, after deducting the placement agent's fees and other offering expenses. As of December 31, 2021, there were 1,379,310 warrants outstanding from the offering, where each warrant has an exercise price of $19.00 per share and will expire on the date that is three years and six months after the initial issuance date.

On May 29, 2020, we entered into a securities purchase agreement with certain institutional investors, including Fidelity Management & Research Company, LLC pursuant to which we issued and sold in a registered direct offering an aggregate of 4,144,537 ordinary shares and accompanying warrants to purchase up to an aggregate of 4,144,537 ordinary shares. Each share we issued and sold together with an accompanying warrant at a combined price of $9.1686. The proceeds to us from the offering were $38.0 million gross and $35.2 million net, after deducting the placement agent's fees and other offering expenses. Each warrant was immediately exercisable and will expire on the two-year anniversary of the issuance date. As of December 31, 2021, there were 4,059,532 warrants outstanding from the offering at an exercise price of $7.92 per share.

On March 1, 2021, we entered into a securities purchase agreement with certain institutional investors pursuant to which we issued and sold in a registered direct offering (1) an aggregate of 9,761,010 ordinary shares, $0.01 nominal value per share, and accompanying warrants to purchase up to an aggregate of 4,880,505 ordinary shares and (2) pre-funded warrants to purchase up to an aggregate of 600,000 ordinary shares and accompanying ordinary share warrants to purchase up to an aggregate of 300,000 ordinary shares. Each share was issued and sold together with an accompanying ordinary share warrant at a combined price of $2.4525, and each pre-funded warrant was issued and sold together with an accompanying ordinary share warrant at a combined price of $2.4425. The proceeds to us from the offering were $25.4 million gross and $23.4 million net after deducting the placement agent's fees and estimated offering expenses. Each pre-funded warrant had an exercise price per ordinary share equal to $0.01 and each pre-funded warrant was

exercised in full on the issuance date. Each warrant has an exercise price per ordinary share equal to $2.39, is exercisable on the date of issuance and will expire on the five-year anniversary of the date of issuance. As of December 31, 2021, there were 5,180,505 warrants outstanding from the offering at an exercise price of $2.39 per share.

On September 24, 2021, we entered into a purchase agreement, or Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which, subject to the terms and conditions, provides that we have the right to sell to Lincoln Park and Lincoln Park is obligated to purchase up to $23.0 million of our ordinary shares. In addition, under the Purchase Agreement, we agreed to issue a commitment fee of 632,474 ordinary shares, or the Commitment Shares, as consideration for Lincoln Park entering into the Purchase Agreement and for the payment of $0.01 per Commitment Share. Under the Purchase Agreement, we may from time to time, at our discretion, direct Lincoln Park to purchase on any single business day, or a Regular Purchase, up to (i) 400,000 ordinary shares if the closing sale price of our ordinary shares is not below $0.25 per share on Nasdaq, (ii) 600,000 ordinary shares if the closing sale price of our ordinary shares is not below $2.00 per share on Nasdaq or (iii) 800,000 ordinary shares if the closing sale price of our ordinary shares is not below $3.00 per share on Nasdaq. In addition to Regular Purchases, we may also direct Lincoln Park to purchase other amounts as accelerated purchases or as additional accelerated purchases on the terms and subject to the conditions set forth in the Purchase Agreement. In any case, Lincoln Park's commitment in any single Regular Purchase may not exceed $2.5 million absent a mutual agreement to increase such amount. As of December 31, 2021, we have issued and sold an aggregate of 2,400,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $2.4 million. From January 1, 2022 and through the date of this filing, we have issued and sold an aggregate of 3,600,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $1.6 million. As of the date of this filing, we may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the Purchase Agreement, subject to the Nasdaq rules which may limit our ability to make sales of our ordinary shares to Lincoln Park in excess of a specified amount without prior shareholder approval.

In addition, in connection with the closing of the acquisition of Zavante Therapeutics, Inc., or Zavante, together with its lead product candidate CONTEPO, or the Acquisition, we issued 733,690 of our ordinary shares to former Zavante stockholders as initial upfront consideration and following the one year anniversary of the closing of the Acquisition on July 25, 2019, we issued an additional 81,518 ordinary shares to the former Zavante stockholders that had been subject to reduction in respect of certain indemnification and other obligations pursuant to the Merger Agreement. Such shares are able to be freely sold in the public market, subject to any requirements and restrictions, including any applicable volume limitations, imposed by Rule 144 under the Securities Act. In addition, the Merger Agreement provides that we may issue up to an additional $97.5 million in our ordinary shares to former Zavante stockholders upon the achievement of specified regulatory and commercial milestones in the future, and obligates us to provide registration rights with respect to the registration for resale of such additional ordinary shares that may become issuable upon the achievement of such milestones. The issuance of our ordinary shares to satisfy the milestone payments will cause dilution to our security holders, and the sale or resale of these shares in the public market, or the market's expectation of such sales, may result in an immediate and substantial decline in our share price. Such a decline would adversely affect our investors and also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, developing and securing our technology, raising capital, undertaking preclinical studies and clinical trials of our product candidates, preparing and filing NDAs for our product candidates, the commercial launch of XENLETA and the direct selling of SIVEXTRO. We have not yet demonstrated our ability to conduct sales and marketing activities necessary for successful product

commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. Also, we may encounter delays or difficulties in our efforts to, or fail to, successfully integrate CONTEPO into our business strategy. Moreover, we are in the process of transitioning from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Our level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations.

On March 11, 2020, we entered into the Amendment to the Loan Agreement pursuant to which we agreed to repay to Hercules $30.0 million of the $35.0 million in aggregate principal amount of debt outstanding under the Loan Agreement. Following the Prepayment, there remains outstanding $5.0 million in principal amount under the Loan Agreement, the end of term loan charge payment of $2.4 million and the Prepayment fee of $300,000, and we are eligible to request to borrow an additional $5.0 million subject to the lender's sole discretion. We plan to begin to repay the outstanding principal amount under the Loan Agreement in April 2022.

Our obligations under the Loan Agreement are secured by substantially all of our personal property, intellectual property and other assets owned or later acquired by us and our subsidiaries. This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including:

- the need to repay our indebtedness by making payment of interest only initially and then interest and principal, which will reduce the amount of funds available to finance our operations, our research and development efforts and our general corporate activities;

- our failure to comply with the restrictive covenants in the Loan Agreement or the occurrence of an event that has a material adverse effect on our business, operations, properties, assets, condition, our ability to pay any amounts due, the collateral securing our obligations under the Loan Agreement or the ability of Hercules to enforce any of its rights under the Loan Agreement could result in an event of default that, if not cured or waived, would accelerate our obligation to repay this indebtedness and permit the lender to enforce its security interest in the assets securing such indebtedness, including the cash accounts pledged to it; and

- the need to maintain minimum cash balances under specified circumstances, which restricts our ability to invest in the business and fund our operations.

To the extent additional debt is added to our current debt levels, the risks described above could increase.

We may not have cash available to us in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due or to comply with minimum cash balance requirements.

Failure to satisfy our current and future debt obligations under the Loan Agreement, or the occurrence of a material adverse effect as defined in the Loan Agreement, could result in an event of default and, as a result, the lender under the Loan Agreement could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Loan Agreement as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness. In addition, the lender could seek to enforce their security interests in the assets securing such indebtedness.

We are subject to certain restrictive covenants which, if breached, could have a material adverse effect on our business and prospects.

The Loan Agreement imposes operating and other restrictions on us. Such restrictions will affect, and in many respects limit or prohibit, our ability and the ability of any future subsidiary to, among other things:

- declare dividends or redeem or repurchase equity interests;
- incur additional indebtedness and liens;
- make loans and investments;
- engage in mergers, acquisitions and asset sales;
- undertake certain transactions with affiliates
- undergo a change in control;
- add or change business locations; and
- settle in cash potential milestone payment obligations that may become payable by us in the future to former security holders of Zavante.

We are also required to satisfy certain financial covenants, including an obligation to maintain specified minimum amounts of cash and cash equivalents in accounts pledged to Hercules. Under the Third Amendment, we and Hercules agreed to defer the end of term loan charge payment in the amount of approximately $2.1 million that would have otherwise become payable on the date of the Prepayment and to reduce the prepayment charge with respect to the Prepayment from $600,000 to $300,000 and to defer its payment, in each case, until June 1, 2023 or such earlier date on which all loans under the Loan Agreement are repaid or become due and payable. The Third Amendment also reset the revenue performance covenant to 70% of targeted revenue based on a revised net product revenue forecast and lowered our minimum liquidity requirement to $3.0 million in cash and cash equivalents. The new minimum liquidity requirement will not apply if CONTEPO receives regulatory approval from the U.S. Food and Drug Administration and we achieve at least 70% of our revised net product revenue targets under the Loan Agreement. Pursuant to the Fourth Amendment, the date on which we must commence repaying principal under the Loan Agreement was extended to April 1, 2022, which date may be extended until July 1, 2022, subject to our receipt of a specified amount of additional net financing proceeds and the achievement of a specified product revenue milestone. Additionally, the time during which the Tranche Advance (as defined in Note 7 to our consolidated financial statements) may be requested by us under the Loan Agreement was extended until the Amortization Date. In addition, pursuant to the Fourth Amendment, the minimum liquidity requirement of $3.0 million in cash and cash equivalents will be waived at any time we have recognized $15.0 million of net product revenue during the applicable trailing three months.

These restrictive covenants may prevent us from undertaking an action that we feel is in the best interests of our business. In addition, if we were to breach any of these restrictive covenants, or if a material adverse effect as defined under the Loan Agreement occurs, Hercules could accelerate our indebtedness under the Loan Agreement or enforce its security interest against our assets, either of which would materially adversely affect our ability to continue to operate our business.

We have relied on, and expect to continue to rely on, certain government grants and funding from the Austrian government. Should these funds cease to be available, or our eligibility be reduced, or if we are required to repay any of these funds, this could impact our ongoing need for funding and the timeframes within which we currently expect additional funding will be required.

As a company that carried out extensive research and development activities, we have benefited from the Austrian research and development support regime, under which we were eligible to receive a research premium from the Austrian government equal to 14% (12% for the fiscal years 2016 and 2017 and 10%, in the case of fiscal years prior to 2016) of a specified research and development cost base. Qualifying expenditures largely comprised research and development activities conducted in Austria, however, the research premium was also available for certain related third-party expenses with additional limitations. We received research premiums of $1.4 million for the year ended December 31, 2020 and $1.3 million for the year ended December 31, 2019. We have not received any research premium for our qualified 2021 expenditures as of December 31, 2021. As we expand our business outside of Austria, we may not be able to continue to claim research premiums to the same extent as we have in previous years or at all, as some research and development activities may no longer be considered to occur in Austria. As research premiums that have been paid out already may be audited by the tax authorities, there is a risk that parts of the submitted cost base may not be considered as eligible and therefore repayments may have to be made.

The intended efficiency of our corporate structure depends on the application of the tax laws and regulations in the countries where we operate, and we may have exposure to additional tax liabilities or our effective tax rate could change, which could have a material impact on our results of operations and financial position.

As a company with international operations, we are subject to income taxes, as well as non-income based taxes, in both the United States and various foreign jurisdictions. We have designed our corporate structure, the manner in which we develop and use our intellectual property, and our intercompany transactions between our subsidiaries in a way that is intended to enhance our operational and financial efficiency. The application of the tax laws and regulations of various countries in which we operate and to our global operations is subject to interpretation. We also must operate our business in a manner consistent with our corporate structure to realize such efficiencies. The tax authorities of the countries in which we operate may challenge our methodologies for valuing developed technology or for transfer pricing. If, for one or more of these reasons, tax authorities determine that the manner in which we operate results in our business not achieving the intended tax consequences, our effective tax rate could increase and harm our financial position and results of operations.

A change in the tax law in the jurisdictions in which we do business, including an increase in tax rates, an adverse change in the treatment of an item of income or expense, a decrease in tax rates in a jurisdiction in which we have significant deferred tax assets, or a new or different interpretation of applicable tax law could result in a material increase in tax expense.

Risks Related to Product Development and Commercialization

Business interruptions resulting from the SARS-CoV-2 infection causing COVID-19 outbreak or similar public health crises have caused a disruption of the development of our product candidates and adversely impacted our business.

Beginning in 2019, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID-19, surfaced in Wuhan, China and spread to countries across the world, including Ireland, Austria and the United States, where our offices and laboratory space are located. COVID-19 caused federal, state and local governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions and bans, heightened border scrutiny and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facility inspections by regulatory authorities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services has fallen significantly.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. The COVID-19 pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, business closures, school closures, travel restrictions and other public health safety measures, as well as reported adverse impacts on healthcare resources, facilities and providers across the United States and in other countries including Ireland and Austria. The extent to which COVID-19 further impacts our operations or those of our third-party partners will depend on future developments, including the extent there is any resurgence of the COVID-19 virus or any variant strains of the virus, the availability and effectiveness of vaccines and the impact of the foregoing on our business, which are highly uncertain and cannot be predicted with confidence.

Additionally, timely completion of clinical trials is dependent upon the availability of, for example, clinical trial sites, researchers and investigators, site monitors, screening of study subjects, regulatory agency personnel, and materials, which may be adversely affected by global health matters, such as pandemics. Our Phase 1 clinical trial CONTEPO for use in pediatric patients with cUTIs, for example, has been significantly delayed by the COVID-19 pandemic.

In particular, shelter-in-place orders and other mandated local travel prohibitions restricted the activities of our sales force and caused us to determine to terminate our entire hospital-based sales force in April 2020.

We have implemented a hybrid-remote-working policy for all of our U.S. employees, and we may take further actions that alter our operations as may be required by federal, state, or local authorities, or which we determine are in our best interests. While most of our operations can be performed remotely, there is no guarantee that we will be as effective while working remotely because our team is dispersed, many employees may have additional personal needs to attend to (such as looking after children as a result of school closures or family who become sick), and employees may become sick themselves and be unable to work. Decreased effectiveness of our team could adversely affect our results due to our inability to meet in person with customers and physicians, or other decreases in productivity that could seriously harm our business.

The effects of COVID-19 pandemic also disrupted the FDA's review of our NDA for CONTEPO. On March 10, 2020, the FDA announced that it would restrict travel of its employees to Europe for inspections as a result of the spread of COVID-19. On June 19, 2020 we received a CRL for CONTEPO in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cited observations at our manufacturing partners that could not be resolved due to FDA's inability to conduct onsite inspections because of travel restrictions. We do not have a forecasted date for the resubmission of our NDA for CONTEPO for the treatment of cUTIs, including AP.

Additionally, certain of the activities of our former collaborator, Sinovant, were delayed in China. If these delays continue and impact Sumitomo Pharmaceuticals (Suzhou)'s, Sinovant's successor, efforts to develop and commercialize lefamulin in China, our receipt of future milestone payments or potential royalties on sales of the China Region Licensed Products may be delayed. Also, the spread of COVID-19 may affect the ability of our third-party manufacturers to supply XENLETA, CONTEPO or any future product candidates. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

The COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our ordinary share price and trading in our ordinary shares. Moreover, the significant ongoing impact of the pandemic on economies worldwide could result in more extensive adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to significantly and adversely affect our business, financial condition, results of operations and prospects.

In April 2020, we announced a plan to restructure our hospital-based commercial sales force and transition to a community-based sales effort.

In April 2020, we announced a plan to restructure our hospital-based commercial sales force and transition to a community-based sales effort. This restructuring reduced costs to align the capabilities of our sales efforts with our strategic re-focus on making sales of XENLETA to community health care professionals, This restructuring resulted in

the termination of 66 employees, consisting of our entire hospital-based sales personnel and certain members of our sales force leadership team. Additional reductions in headcount occurred in the third quarter of 2020 including the restructuring of the commercial organization, which led to the elimination of the role of the Chief Commercial Officer. Our commercial operations now report directly to our Chief Executive Officer. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

We depend heavily on the success of XENLETA, which the FDA has approved for oral and IV use for the treatment of CABP, SIVEXTRO, approved by the FDA for oral and IV use of adults and adolescents for the treatment of ABSSSI, and CONTEPO, which we are developing for the treatment of cUTI, including AP. If we are unable to obtain marketing approval for CONTEPO, or if we fail in our commercialization efforts for SIVEXTRO, XENLETA, or, if approved, CONTEPO, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of XENLETA and, more recently, in CONTEPO. There remains a significant risk that we will fail to successfully develop CONTEPO for cUTI or any other indication and that we may fail to successfully commercialize XENLETA for CABP and SIVEXTRO for ABSSSI.

On August 19, 2019, the FDA approved the oral and IV formulations of XENLETA. On July 28, 2020, the European Commission issued a legally binding decision for approval of the marketing authorization application for XENLETA for the treatment of CAP in adults following a review by the EMA. In July 2020, Sunovion Pharmaceuticals Canada Inc. additionally received approval from Health Canada to market oral and IV formulations of XENLETA for the treatment of CAP in adults, upon receipt of the Notice of Compliance from Health Canada. In mid-2018, we initiated a Phase 1, non-comparative, open-label study of the pharmacokinetics and safety of a single dose of IV XENLETA in pediatric subjects from birth to 18 years of age. As a result of COVID-19, research sites were temporarily closed for enrollment in 2020 and 2021 as hospitals suspended access and non-essential clinical research to focus on health care delivery to COVID-19 patients. As of July 2020, trials started to re-open, where allowed by the institution, and initiated screening of potential subjects at sites.

In June 2016, Zavante initiated the ZEUS Study. In April 2017, Zavante announced positive topline results of the ZEUS Study. We submitted an NDA for marketing approval of CONTEPO for the treatment of cUTI in adults in the United States, utilizing the FDA's 505(b)(2) pathway, in October 2018. In April 2019, the FDA issued a CRL in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP, stating that it was unable to approve the application in its current form. In December 2019, we resubmitted our NDA for CONTEPO for the treatment of cUTIs, including AP. On June 19, 2020 we received a second CRL from the FDA. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cited observations at our manufacturing partners that could not be resolved due to FDA's inability to conduct onsite inspections because of travel restrictions. On October 30, 2020, we participated in a "Type A" meeting with the FDA to obtain any new information related to the FDA´s pending conduct of inspections of foreign manufacturers during the COVID-19 pandemic that has negatively impacted a number of FDA product reviews, including our NDA for CONTEPO. On April 14, 2021, the FDA issued industry guidance on remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities during COVID-19 specifying that when it cannot perform a PAI or PLI or when the FDA determines that it would be useful to supplement a planned inspection, the agency will consider using tools other than a physical inspection and select the most appropriate method to address the specific risks that justify the need for the PAI or PLI. The FDA informed us that onsite inspections of our manufacturing partners in Europe are required in order for the FDA to complete the review of a potential CONTEPO NDA resubmission. Due to travel restriction related to the COVID-19 pandemic, the FDA suspended onsite inspections of ex-US manufacturers for all non-COVID products. As a result, we requested an extension of the timeline for a potential CONTEPO NDA resubmission until June 2023, which the FDA granted on March 21, 2022. We are awaiting further clarity from the FDA regarding their ability to complete onsite inspections at our manufacturing partners in Italy and Spain before determining specific timing of the potential NDA resubmission, which we plan to submit promptly once we have clarity from the FDA. The FDA released the Resiliency Roadmap for FDA Inspectional Oversight that describes the systematic approach that FDA will utilize to manage

postponed inspections and other oversight activities. The prioritization plan considers public health risks related to conducting an inspection, such as the impact of the product's availability on public health, as well as investigator safety and travel restrictions/advisories. In addition, the FDA informed us that, while they cannot predict when an inspection may occur and when the pandemic may prevent the FDA from completing inspections, tier 1 mission-critical inspections and tier 2 higher priority inspections, which includes PAIs, will continue to be prioritized going forward. We cannot predict the outcome of any further interactions with the FDA or when CONTEPO will receive marketing approval, if at all.

In June 2018, we initiated a Phase 1, non-comparative, open-label study of the pharmacokinetics and safety of a single dose of CONTEPO in pediatric subjects less than 12 years of age receiving standard-of-care antibiotic therapy for proven or suspected infection or peri-operative prophylaxis. A total of 24 patients are expected to be enrolled at up to ten clinical sites in the United States. As a result of COVID-19, research sites were temporarily closed in 2020 and 2021 and only a minority of sites are currently screening patients and allowing access to the institution. As a result, our development timeline for CONTEPO for use in pediatric patients with cUTIs has been modified to reflect a two-year delay due to COVID-19.

In July 2020, we entered into a Sales Promotion and Distribution Agreement, or the Distribution Agreement, with subsidiaries of Merck pursuant to which we licensed the right, subject to specified conditions, to promote, distribute and sell SIVEXTRO for ABSSSIs, caused by certain susceptible Gram-positive microorganisms in the SIVEXTRO Territory.

We expect to incur significant additional sales, marketing, distribution and manufacturing expenses for the commercialization of SIVEXTRO, XENLETA and CONTEPO, if approved. We expect to continue to invest in critical commercial promotion and distribution, medical affairs and other commercialization activities, as well as investing in our supply chain for the commercialization of SIVEXTRO, XENLETA and the potential launch of CONTEPO. We expect to seek additional funding in future periods to support these activities.

Our ability to generate meaningful product revenues will depend heavily on the successful commercialization of SIVEXTRO and XENLETA and our obtaining marketing approval for CONTEPO. The success of SIVEXTRO, XENLETA and, if approved, CONTEPO will depend on a number of factors, including the following:

- establishing and maintaining arrangements with third-party manufacturers for commercial supply and receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities;
- the resubmission of our NDA for CONTEPO and potential receipt of marketing approval from the FDA for CONTEPO for the treatment of cUTI, including AP;
- re-establishing an effective sales and marketing organization to successfully generate recurring sales of SIVEXTRO, XENLETA and, if and when approved, CONTEPO;
- acceptance of SIVEXTRO, XENLETA and, if and when approved, CONTEPO by patients, the medical community and third-party payors, including hospital formularies;
- achieving approval of favorable prescribing information;
- effectively competing with other therapies;
- the continued acceptable safety profile of SIVEXTRO, XENLETA and, if approved, CONTEPO;
- securing contracts to allow SIVEXTRO, XENLETA and, if approved, CONTEPO to be paid for by private and public health insurance plans;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property portfolio;
- obtaining and maintaining adequate distribution levels of SIVEXTRO, XENLETA and, if approved, CONTEPO at all appropriate trade channels; and
- resolution of the COVID-19 pandemic.

Successful development of XENLETA and CONTEPO for the treatment of additional indications, if any, or for use in other patient populations and our ability to broaden the labels for XENLETA and, if approved, CONTEPO will depend on similar factors. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize XENLETA for CABP or for any other indication or CONTEPO for cUTI, including AP or for any other indication, which would materially harm our business.

SIVEXTRO, XENLETA and any other product candidate that receives marketing approval may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for such products and product candidates, if approved, may be smaller than we estimate.

SIVEXTRO, XENLETA and any other product candidate that receives marketing approval may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current treatments for ABSSSI, CABP and cUTI, including generic options, are well established in the medical community, and doctors may continue to rely on these treatments without SIVEXTRO, XENLETA, CONTEPO or any of our other product candidates that receive marketing authorization. In addition, our efforts to effectively communicate the differentiating characteristics and key attributes of SIVEXTRO, XENLETA, CONTEPO or any of our other product candidates that receive marketing authorization to clinicians and hospital pharmacies with the goal of establishing favorable formulary status for SIVEXTRO, XENLETA, CONTEPO or any of our other product candidates that receive marketing authorization may fail or may be less successful than we expect. If SIVEXTRO, XENLETA, CONTEPO or any of our other product candidates that receive marketing authorization do not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of our products and product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the ability of SIVEXTRO, XENLETA, CONTEPO or any other anti-infective product candidate to limit the development of bacterial resistance in the pathogens it targets;
- the prevalence and severity of any side effects;
- the ability to offer our product candidates for sale at competitive prices, including in comparison to generic competition;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies, physicians to prescribe these therapies and hospitals to approve the cost and use by their physicians of these therapies;
- our investment in and the strength of sales, marketing, patient access and distribution capabilities;
- the availability of third-party coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other approvals of competitive products; and

- obtaining and maintaining adequate distribution of our products to the appropriate trade channels.

Bacteria might develop resistance to SIVEXTRO, XENLETA, CONTEPO or any future product candidates more rapidly or to a greater degree than we anticipate. If bacteria develop resistance or if SIVEXTRO, XENLETA, CONTEPO or any future product candidates is not effective against drug-resistant bacteria, the efficacy of these products or product candidates would decline, which would negatively affect our potential to generate revenues from these products and product candidates.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement may be affected by political, economic and regulatory developments in the United States, the EU and other jurisdictions. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. If the level of reimbursement is below our expectations, our revenue and gross margins would be adversely affected.

Hospital formulary approval of SIVEXTRO, XENLETA, CONTEPO or any future product candidates that receive marketing authorization is an important component of our commercialization strategy. Accordingly, sales of IV formulations of SIVEXTRO, XENLETA, CONTEPO or any future IV product candidates will depend substantially on the extent to which hospital formulary approval is obtained. Hospital formulary approval may depend upon several factors, including the determination that use of a product is:

- safe, effective and medically necessary;
- appropriate for the specific patient population;
- cost-effective; and
- neither experimental nor investigational.

Obtaining formulary approval from third-party payors can be an expensive and time-consuming process that will require us to provide supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to hospital formulary approval. We cannot be certain if and when we will obtain hospital formulary approval to allow us to sell SIVEXTRO, XENLETA, if approved, CONTEPO or any future product candidates that receive marketing authorization into our target markets. Even if we do obtain hospital formulary approval, third-party payors, such as government or private health care insurers, carefully review and increasingly question the coverage of, and challenge the prices charged for, drugs. Increasing efforts by hospitals in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit formulary approval. We have experienced and expect to continue to experience pricing pressures in connection with the sale of XENLETA in the hospital setting due to the trend toward reducing hospital costs, managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. These and other similar developments could significantly limit the degree of market acceptance of SIVEXTRO, XENLETA, CONTEPO or any of our other product candidates that receive marketing approval. To address this uncertainty, in early 2020 we began to utilize our hospital based sales force to call upon approximately 7,800 high prescriber community doctors in an effort to potentially increase our penetration rates in the community setting while maintaining sales efforts in the hospital setting before determining to terminate our entire sales force. This effort ceased with the termination of our entire hospital-based sales force in April 2020. Additional reductions in headcount occurred in the third quarter of 2020 including the restructuring of the commercial organization, which led to the elimination of the role of the Chief Commercial Officer. Our commercial operations now report directly to our Chief Executive Officer. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

If we are unable to establish or maintain sales, marketing and distribution capabilities or enter into or maintain sales, marketing and distribution agreements with third parties, we may not be successful in commercializing SIVEXTRO, XENLETA, CONTEPO or any other product candidate if and when they are approved.

We have a limited sales, marketing, patient access and distribution infrastructure, and as a company we have limited experience in the sale, marketing or distribution of pharmaceutical products and XENLETA is the first product that we are commercializing. To achieve commercial success for SIVEXTRO, XENLETA and any other approved product, we must re- establish and maintain an adequate sales, marketing, commercial operations, patient access and distribution organization or outsource these functions to third parties. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021. In addition, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize XENLETA in markets outside the United States. We plan to commercialize CONTEPO, if approved, in the United States with targeted sales efforts, but we do not have the right to commercialize CONTEPO in any markets outside the United States.

There are risks involved with establishing our own sales, marketing, commercial operations, patient access and distribution capabilities and entering into arrangements with third parties to perform these services. If we do not establish adequate sales, marketing, commercial operations, patient access and distribution capabilities prior to or in connection with the commercial launch of any of our products, such products may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community and may fail commercially or be less successful than we expect. If the commercial launch of a product candidate for which we establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, patient access, commercial operations and marketing personnel;
- our inability to recruit, train and retain adequate numbers of effective headquarter and field personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe SIVEXTRO, XENLETA or any future products;
- the lack of complementary products to be offered by sales personnel, which may put our sales representatives at a competitive disadvantage relative to sales representatives from companies with more extensive product lines;
- the COVID-19 pandemic;
- unforeseen costs and expenses associated with creating an independent sales, marketing, commercial operations, patient access and distribution organization; and
- a change in strategy resulting in the decrease or elimination of sales personnel.

If we enter into arrangements with third parties to perform sales, marketing, commercial operations, patient access and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market, sell and distribute ourselves any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be

unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not re-establish and maintain sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing SIVEXTRO, XENLETA, or, if approved, CONTEPO.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to SIVEXTRO, XENLETA, CONTEPO and any other products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

There are a variety of available therapies marketed for the treatment of ABSSSI, CABP and cUTI. Currently the treatment of ABSSSI, CABP and cUTI is dominated by generic products. For both hospitalized and community patients, combination therapy is frequently used for CABP and at times for cUTI. Many currently approved drugs are well-established therapies and are widely accepted by physicians, patients, medical association guidelines and third-party payors for the treatment of CABP and ABSSSI. We also are aware of various drugs under development or recently approved by the FDA for the treatment of CABP and ABSSSI, including omadacycline (Nuzyra approved by the FDA in October 2018 on behalf of Paratek Pharmaceuticals Inc. for both CABP and ABSSSI)), delafloxacin (Baxdela approved by the FDA for ABSSSI in June 2017 and expanded for CABP in October 2019 on behalf of Melinta Therapeutics Inc.), and oral nafithromycin (Phase 2 clinical development by Wockhardt Ltd. for CABP). If approved, we expect CONTEPO will face competition from commercially available branded antibiotics for the treatment of UTI such as ceftazidime-avibactam (Avycaz), meropenem-vaborbactam (vabomere), plazomicin (Zemdri), ceftolozane-tazobactam (Zerbaxa), as well as imipenem-cilastatin-relebactam (Recarbrio approved by the FDA in July 2019 on behalf of Merck & Co., Inc.), cefiderocol (Fetroja approved by the FDA in November 2019 on behalf of Shionogi Inc.), or drugs under development such as tebipenem HBr (NDA to FDA for the Treatment of Complicated Urinary Tract Infections including Pyelonephritis in October 2021– Spero Therapeutics), cefepime-taniborbactam (under Phase 3 clinical development by Venatorx Pharmaceuticals), cefepime-enmetazobactam (under Phase 3 clinical development by Allecra Therapeutics), ETX0282-cefpodoxime proxetil (under Phase 1 clinical development by Entasis Therapeutics) tebipenem (under development by Spero), sulopenem (under development by Iterum Therapeutics), and LYS228 (under development by Novartis), as well as generically available agents including piperacillin-tazobactam, fluoroquinolones, carbapenems, aminoglycosides, tigecycline, and polymyxins.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are approved for broader indications or patient populations, are more convenient or are less expensive than any products that we may develop. Our competitors may also obtain marketing approvals for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers. We expect that SIVEXTRO, XENLETA and, if approved, CONTEPO will be priced at a significant premium over competitive generic products. This pricing difference may make it difficult for us to replace existing therapies with SIVEXTRO, XENLETA and CONTEPO. The key competitive factors affecting the success of our products and product candidates are likely to be their efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approvals from regulatory authorities and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through

collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs.

Even if we are able to successfully commercialize SIVEXTRO, XENLETA, CONTEPO or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products, including XENLETA, vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize SIVEXTRO, XENLETA, CONTEPO or any other product candidate successfully also will depend in part on its availability on hospital formularies and the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A major trend in the healthcare industries in the European Union and the United States and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for SIVEXTRO, XENLETA, CONTEPO or any other product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for SIVEXTRO, XENLETA and CONTEPO may be particularly difficult because of the number of generic drugs, which are typically available at lower prices, that are available to treat ABSSSI, CABP and cUTI. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug, such as SIVEXTRO, XENLETA and CONTEPO. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize SIVEXTRO, XENLETA, CONTEPO or other product candidates for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and particularly in the hospital, coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and to limit commercialization of SIVEXTRO, XENLETA and any other products that we may develop or in-license.

We face an inherent risk of product liability exposure related to the testing of XENLETA, CONTEPO and any other product candidate that we develop in human clinical trials and an even greater risk related to the commercial sale of SIVEXTRO, XENLETA and any other products that we may develop or in-license. If we cannot successfully defend ourselves against claims that SIVEXTRO, XENLETA or our other product candidates caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for SIVEXTRO, XENLETA, or any other product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We maintain clinical trial liability insurance that covers bodily injury to patients participating in our clinical trials up to a $10.0 million annual aggregate limit and subject to a per event deductible. This amount of insurance may not be adequate to cover all liabilities that we may incur. We maintain $10.0 million in product liability insurance coverage for our marketed products. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the United States, 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 and a number of other federal and state government pricing programs in the United States in order to obtain coverage for SIVEXTRO and XENLETA by certain government healthcare programs. These programs generally require us to pay rebates or provide discounts to certain private purchasers or government payers in connection with our products when dispensed to beneficiaries of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing and rebate calculations that we report on a monthly and quarterly basis to the government agencies that administer the programs. The terms, scope and complexity of these government pricing programs change frequently. We may also have reimbursement obligations or be subject to penalties if we fail to provide timely and accurate information to the government, pay the correct rebates or offer the correct discounted pricing. Changes to the price reporting or rebate requirements of these programs would affect our obligations to pay rebates or offer discounts. Responding to current and future changes may increase our costs and the complexity of compliance, will be time-consuming, and could have a material adverse effect on our results of operations.

If clinical trials of XENLETA, CONTEPO or any of our other product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, regulatory authorities in the European Union, or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of XENLETA, CONTEPO or any other product candidate.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and early clinical trials, including Phase 1 clinical trials, in addition to extensive later-stage Phase 3 clinical trials, to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. In connection with the ZEUS Study in which CONTEPO met the primary endpoint of statistical non-inferiority versus piperacillin/tazobactam, Zavante conducted a post-hoc primary efficacy analysis of CONTEPO using results of blinded pulsed-field gel electrophoresis molecular typing of urinary tract pathogens. Regulatory authorities typically give greater weight to results from pre-specified analyses and less weight to results from post-hoc, retrospective analyses. While we believe this post-hoc analysis is illustrative information, the FDA may ultimately have a different interpretation of any of our data that may be based on such post-hoc analysis, or the FDA may conduct its own analyses and modify analysis populations which could lead to different numerical results or conclusions.

If we are required to conduct additional clinical trials or other testing or studies of XENLETA, CONTEPO or any other product candidate that we develop beyond those that we contemplate; if we are unable to successfully complete our clinical trials or other testing or studies; if the results of these trials, tests or studies are not positive or are only modestly positive; if there are safety concerns; or if they are otherwise not acceptable to the FDA, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements or restrictions;
- have the product removed from the market after obtaining marketing approval;
- be unable to obtain reimbursement for use of the product; or
- need to raise capital before we otherwise would or on terms less favorable to us.

The occurrence of any of the developments listed above could materially harm our business, financial condition, results of operations and prospects.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, the potential marketing approval or commercialization of XENLETA, CONTEPO or other product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, our clinical trials of XENLETA and CONTEPO or other product candidates that could delay or prevent our ability to receive marketing approval or commercialize XENLETA, CONTEPO or our other product candidates, including:

- clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, institutional review boards or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health or safety risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- ongoing or future restrictions resulting from the COVID-19 pandemic and its collateral consequences may result in internal and external operational delays and limitations; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the trials.

Our product development costs will increase if we experience delays in enrollment in our clinical development program or our non-clinical development program or in obtaining marketing approvals. We do not know whether any additional non-clinical tests or clinical trials will be required, or if they will begin as planned, or if they will need to be restructured or will be completed on schedule, or at all. Significant non-clinical development program delays, including chemistry, manufacturing and control activities, or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in our clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates, including with respect to XENLETA, CONTEPO or any other product candidate that we develop, if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials, including our Phase 1 clinical trial of IV XENLETA in pediatric patients. In addition, the COVID-19 pandemic has resulted in enrollment temporary and long-term suspension globally for many clinical trials. For example, research sites were temporarily closed for enrolment for a large part of 2020, and inpart of 2021 for our clinical trial to evaluate CONTEPO for use in pediatric patients with cUTIs. Some of our competitors have ongoing clinical trials for product candidates that could be competitive with XENLETA and CONTEPO, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- eligibility criteria for the clinical trial in question;
- perceived risks and benefits of the product candidate under study;
- approval of other therapies to treat the disease under investigation;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the time of year in which the trial is initiated or conducted;
- the geographic distribution of global trial sites;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients;
- delays in the receipt of required regulatory approvals, or the failure to receive required regulatory approvals, in the jurisdictions in which clinical trials are expected to be conducted;
- restrictions resulting from the COVID-19 pandemic and its collateral consequences;
- willingness of potential patients to participate in our trials; and
- delays in the receipt of approvals, or the failure to receive approvals, from the relevant institutional review board or ethics committee at clinical trial sites.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of the company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients in any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

If serious adverse or undesirable side effects are identified in SIVEXTRO, XENLETA, or CONTEPO or any other product candidate that we develop or following their approval and commercialization, we may need to modify, abandon or limit our development or marketing of that product or product candidate.

It is impossible to predict when or if the FDA, EMA or other regulators will view any of our product candidates as effective and safe in humans or if we will receive marking approval for any of our product candidates, and it is impossible to ensure that safety or efficacy issues will not arise following the marketing approval. If our products or product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to modify or abandon their marketing or development or limit marketing or development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Similarly, if we are not able to comply with post-approval regulatory requirements, including safety requirements, with respect to XENLETA or any other approved product that we may develop, we could have the marketing approvals for such products withdrawn by regulatory authorities. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects or other safety issues that prevented further development of the compound.

In the ZEUS Study, the incidence of premature discontinuation from study drug was low and similar between treatment groups (6.0% in the CONTEPO treatment group compared to 3.9% in the PIP-TAZ treatment group), and the incidence of not completing the study through the last follow-up visit, which occurred on the 24th through 28th day after completion of seven days of treatment with the study drug, or after up to 14 days of treatment for patients with concurrent bacteremia, was 5.2% in the CONTEPO group compared to 0.9% in the PIP-TAZ group. A total of 42.1% CONTEPO patients and 32.0% PIP-TAZ patients experienced at least one treatment-emergent adverse event. Most treatment-emergent adverse events were mild or moderate in severity, and severe TEAEs were uncommon (2.1% of CONTEPO patients and 1.7% of PIP-TAZ patients). The most common TEAEs in both treatment groups were transient, asymptomatic laboratory abnormalities and gastrointestinal events. TEAEs were uncommon in both treatment groups (2.1% of CONTEPO patients and 2.6% of PIP-TAZ patients). There were no deaths in the study and one TEAE in each treatment group was deemed related to study drug (hypokalemia in a CONTEPO patient and renal impairment in a PIP-TAZ patient), leading to study drug discontinuation in the PIP-TAZ patient. Study drug discontinuations due to the TEAEs were infrequent and similar between treatment groups (3.0% of CONTEPO patients and 2.6% of PIP-TAZ patients).

The most common laboratory abnormality treatment-emergent adverse events in the ZEUS Study were increases in the levels of alanine aminotransferase, or ALT, (8.6% of CONTEPO patients and 2.6% of PIP-TAZ patients) and aspartate transaminase, or AST, (7.3% of CONTEPO patients and 2.6% of PIP-TAZ patients). None of the ALT or AST elevations were symptomatic or treatment-limiting, and none of the patients met the criteria for Hy's Law. Outside the United States, elevated liver aminotransferases are listed among undesirable effects in the labeling for IV fosfomycin.

In the ZEUS Study, hypokalemia occurred in 71 of 232 (30.6%) CONTEPO patients and 29 of 230 (12.6%) PIP-TAZ patients. Most decreases in potassium levels were mild to moderate in severity. Shifts in potassium levels from normal at baseline to hypokalemia, as determined by worst post-baseline hypokalemia values, were more frequent in the CONTEPO group than the PIP-TAZ group for mild (17.7% compared to 11.3%), moderate (11.2% compared to 0.9%), and severe (1.7% compared to 0.4%) categories of hypokalemia. Hypokalemia was deemed a treatment-emergent adverse event in 6.4% of patients receiving CONTEPO and 1.3% of patients receiving PIP-TAZ, and all cases were transient and asymptomatic.

While no significant cardiac adverse events were observed in the ZEUS Study, post-baseline QT intervals calculated using Fridericia's formula, or QTcF, of greater than 450 to less than or equal to 480 msec (baseline QTcF of less than or equal to 450 msec) occurred at a higher frequency in CONTEPO patients (7.3%) compared to PIP-TAZ patients (2.5%). In the CONTEPO arm, these results appeared to be associated with the hypokalemia associated with the salt load of the IV formulation. Only one patient in the PIP-TAZ arm had a baseline QTcF of less than or equal to 500 msec and a post-baseline QTcF of greater than 500 msec.

If we elect or are forced to suspend or terminate any clinical trial of XENLETA, CONTEPO or any other product candidates that we are developing, the commercial prospects of XENLETA, CONTEPO or such other product candidates will be harmed and our ability to generate product revenues from XENLETA, CONTEPO or any of these other product candidates will be delayed or eliminated. In addition, a higher rate of adverse events in XENLETA or CONTEPO as compared to the standard of care, even if slight, could negatively impact commercial adoption of XENLETA or CONTEPO by physicians. Any of these occurrences could materially harm our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

Use of third parties to manufacture our product candidates or products may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable quality or cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of XENLETA or CONTEPO that could be used in product candidate development, including clinical trial supply, or for commercial supply, or for the supply of any other compound that we are developing or evaluating in our research program. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities and facilities to manufacture any of our product candidates or products on a clinical or commercial scale. We currently rely on third parties for supply of XENLETA and CONTEPO, and our strategy is to outsource all manufacturing, packaging, testing, serialization and distribution of our product candidates and products to third parties. We also procure supply of SIVEXTRO from Merck & Co., Inc.

We have entered into agreements, and expect to enter into additional agreements, with third-party manufacturers for the long-term commercial supply of XENLETA and CONTEPO. For example, prior to June 2015, we obtained the pleuromutilin starting material for the clinical trial supply of XENLETA from a single third-party manufacturer, Sandoz GmbH, or Sandoz, a division of Novartis AG, or Novartis. . We were required to identify and enter into a commercial supply agreement with an alternative supplier that provides pleuromutilin starting material for the commercial supply of XENLETA as a result of Novartis discontinuing its manufacture of pleuromutilin starting material.

Another third-party manufacturer synthesizes XENLETA starting from pleuromutilin and a readily accessible chiral building block and provides our supply of the active pharmaceutical ingredient, or API. We have initiated engagement with a potential secondary supplier to synthesize XENLETA, with a preliminary technology transfer and pilot scale manufacture. However, our current operating plans do not include completing technology transfer, scale-up and validation of this potential secondary supplier until they have demonstrated that they can successfully manufacture the API at pilot scale and until we obtain additional funding. We engage separate manufacturers to provide tablets, sterile vials, and sterile diluent that we are using in our clinical trials of XENLETA. We have entered into commercial supply agreements with these same manufacturers to support the commercialization of XENLETA in the United States and, if approved outside of the United States, to support future demand outside of the United States. We also entered into a long-term commercial supply agreement with Arran Chemical Company Limited, or Arran, for the supply of the chiral acid starting material required in the synthesis of XENLETA API and a commercial packaging and supply agreement with Sharp Corporation for the secondary packaging of XENLETA for distribution in the United States.

In addition, we have entered into a manufacturing and supply agreement with Ercros, S.A., pursuant to which Ercros, S.A. supplies to us, on an exclusive basis, the API mixture for CONTEPO in support of our NDA filing and, if CONTEPO is approved, will supply the commercial API mixture for CONTEPO in the United States. We have also entered into a manufacturing and exclusive supply agreement with Laboratorios ERN, S.A., pursuant to which Laboratorios ERN, S.A. has agreed to supply us with certain technical documentation and data as required for our NDA filing for CONTEPO and certain regulatory support in connection with the commercial sale and use of CONTEPO in the United States, if approved. We entered into a commercial packaging agreement with AndersonBrecon, Inc. for the commercial packaging and serialization of CONTEPO. Alternatively, we have engaged Sharp Corporation for the secondary packaging and serialization of CONTEPO completed under our existing commercial packaging and supply agreement with Sharp Corporation. We also entered into a manufacturing and supply agreement with Fisiopharma S.r.l.,

or Fisiopharma, for the supply, on a minimum commitment basis, of a percentage of our commercial requirements of CONTEPO in bulk drug vials for the United States as well as the supply of bulk drug vials of CONTEPO in connection with the submission of an NDA.

We may be unable to maintain our current arrangements for commercial supply, or conclude agreements for commercial supply with additional third-party manufacturers, or we may be unable to do so on acceptable terms. Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- reliance on the third party for the timely supply of our products or product candidates;
- an event at one of our manufacturers or suppliers causing an unforeseen disruption of the manufacture or supply of our products or product candidates;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or results in an interruption to the supply chain for our products.

Third-party manufacturers may not be able to comply with current good manufacturing practice, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and products. Such failure could also result in the delay of our obtaining regulatory approval of our product candidates. Also, the spread of COVID-19 may affect the ability of our third-party manufacturers to supply SIVEXTRO, XENLETA, CONTEPO or any future product candidates.

In April 2019, the FDA issued a CRL in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP, stating that it was unable to approve the application in its current form. Specifically, the CRL requested us to address issues related to facility inspections and manufacturing deficiencies at our API contract manufacturer prior to the FDA approving the NDA. In December 2019, we resubmitted our NDA for CONTEPO for the treatment of cUTIs, including AP. On June 19, 2020 we received a second CRL from the FDA. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cited observations at our manufacturing partners that could not be resolved due to FDA's inability to conduct onsite inspections because of travel restrictions. We do not have a forecasted date for the resubmission of our NDA for CONTEPO for the treatment of cUTIs, including AP . On October 30, 2020, we participated in a "Type A" meeting with the FDA to obtain any new information related to the FDA´s pending conduct of inspections of foreign manufacturers during the COVID-19 pandemic that has negatively impacted a number of FDA product reviews, including the our NDA for CONTEPO for the treatment of cUTIs, including AP. On April 14, 2021, the FDA issued industry guidance on remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities during COVID-19 specifying that when it cannot perform a PAI or a PLI or when the FDA determines that it would be useful to supplement a planned inspection, the agency will consider using tools other than a physical inspection and select the most appropriate method to address the specific risks that justify the need for the PAI or PLI. The FDA informed us that onsite inspections of our manufacturing partners in Europe are required in order for the FDA to complete the review of a potential CONTEPO NDA resubmission. Due to travel restriction related to the COVID-19 pandemic, the FDA suspended onsite inspections of ex-US manufacturers for all non-COVID products. As a result, we requested an extension of the timeline for a potential CONTEPO NDA resubmission until June 2023, which the FDA granted on March 21, 2022. We are awaiting further clarity from the FDA regarding their ability to complete onsite inspections at our manufacturing partners in Italy

and Spain before determining specific timing of the potential NDA resubmission, which we plan to submit promptly once we have clarity from the FDA. The FDA released the Resiliency Roadmap for FDA Inspectional Oversight that describes the systematic approach that FDA will utilize to manage postponed inspections and other oversight activities. The prioritization plan considers public health risks related to conducting an inspection, such as the impact of the product's availability on public health, as well as investigator safety and travel restrictions/advisories. In addition, the FDA informed us that, while they cannot predict when an inspection may occur and when the pandemic may prevent the FDA from completing inspections, tier 1 mission-critical inspections and tier 2 higher priority inspections, which includes PAIs, will continue to be prioritized going forward. Our contract manufacturers continue to interact with FDA to discuss its plans for conducting inspections at their sites. If these manufacturing issues are not resolved to the FDA's satisfaction, or if we or any of our third-party manufacturers, or suppliers are the subject of any other open or unresolved regulatory inspections, inspection reports, or FDA Form 483s identifying noncompliance with applicable regulations, we would be delayed in obtaining or may fail to obtain regulatory approval of our product candidates, including CONTEPO.

Our product candidates and any products that we have developed or may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

If the third parties that we engage to supply any materials or manufacture product for our non-clinical testing and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers, and we may be unable to obtain replacement supplies on terms that are favorable to us. For example, there are only a limited number of known manufacturers that produce the pleuromutilin starting material used in the synthesis of XENLETA. In early 2015, Novartis completed the sale of its animal health division, including its veterinary products, to a third party. As a result, we were required to identify an alternative supplier for pleuromutilin starting material for XENLETA. If we are not able to obtain adequate supplies of our product candidates or products, or the drug substances used to manufacture them, it will be more difficult for us to develop or commercialize our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture of our product candidates and products may adversely affect our revenues and our ability to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis. In addition, slower than forecasted commercialization of our products in approved territories, or delayed introduction of our product in approved territories, or disruptions in the supply of our approved products may adversely affect our revenue and profit margins. Moreover, disruption in the supply of our approved product may impact the availability of our approved products at retail pharmacies and may adversely impact our reputation and the willingness of physicians to prescribe our products, which could materially harm our business, financial condition, results of operations and prospects. In addition, our failure or potential failure to comply with contractual minimum order commitments or minimum revenue commitments with our third party suppliers could impact the uninterrupted supply of our products and/or subject us to additional costs. For example, in August 2021, we entered into an amendment to our supply agreement for the API for XENLETA to reduce our minimum purchase obligations under the supply agreement in exchange for cash payments to the supplier and a royalty on net sales of XENLETA in the United States.

We have entered into a Sales Promotion and Distribution Agreement with Merck & Co. related to the promotion, distribution and sale of SIVEXTRO. If our collaboration with Merck is not successful, we may incur significant expenses related to the distribution of SIVEXTRO without realizing any value from the agreement.

In July 2020, we entered into the Distribution Agreement with subsidiaries of Merck pursuant to which we licensed the right, subject to specified conditions, to promote, distribute and sell SIVEXTRO for ABSSSIs, caused by certain susceptible Gram-positive microorganisms in the SIVEXTRO Territory.

Under the Distribution Agreement and subject to the fulfillment of certain conditions, including our engaging sufficient sales representatives, restrictions relating to travel and physician office access in the SIVEXTRO Territory due to COVID-19 having continued to decrease in a sufficient portion of the SIVEXTRO Territory so as not to hinder the successful detailing of SIVEXTRO, we have been granted the right to initially promote SIVEXTRO in the SIVEXTRO Territory and, upon satisfaction of additional conditions, including an increase in the number of our sales representatives,

the right to exclusively distribute SIVEXTRO in the SIVEXTRO Territory, including the sole right and responsibility to fill orders with respect to SIVEXTRO in the SIVEXTRO Territory. In April 2021, we successfully satisfied those conditions, including the increase in the number of sales representatives, and began filling orders of SIVEXTRO with our own Nabriva NDC.

A subsidiary of Merck will sell, and we have agreed to purchase, SIVEXTRO at specified prices in such quantities as we may specify. Although we are entitled, subject to appliable law, to determine the final selling prices of SIVEXTRO in our sole discretion, subject to an overall annual limit on price increases, we may not be able to sell SIVEXTRO at prices high enough to recoup our investment in a sales force and other commercialization activities. In addition, we will rely on a subsidiary of Merck to supply SIVEXTRO to us, who in turn, relies on third party manufacturers for the production, packaging, and serialization of SIVEXTRO for our distribution. Relying on a third-party manufacturer subjects us to a number of additional risks, including the risk that we may not have sufficient supply of SIVEXTRO available for sale. See "Risk Factors—Risks Related to Our Dependence on Third Parties—Use of third parties to manufacture our product candidates or products may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable quality or cost, which could delay, prevent or impair our development or commercialization efforts."

We rely on third parties to conduct our clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials for our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. We expect to continue to rely on such third parties in conducting our clinical trials of XENLETA and CONTEPO, and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Similar GCP and transparency requirements apply in the European Union. Failure to comply with such requirements, including with respect to clinical trials conducted outside the European Union, can also lead regulatory authorities to refuse to take into account clinical trial data submitted as part of an MAA.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing approvals.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We have entered into and may enter into additional collaborations with third parties for the development or commercialization of XENLETA, CONTEPO and our other product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We are commercializing XENLETA and expect to commercialize CONTEPO, if approved, in the United States with targeted sales and marketing efforts. Outside the United States, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize XENLETA. For example, we are party to a license agreement with Sumitomo Pharmaceuticals (Suzhou), pursuant to which we granted Sumitomo Pharmaceuticals (Suzhou)certain rights to manufacture and commercialize XENLETA in the People's Republic of China, Hong Kong, Macau and Taiwan and we have also entered into a license agreement with Sunovion pursuant to which we granted Sunovion certain rights to commercialize XENLETA in Canada. We also may seek third-party collaborators for development and commercialization of other product candidates or for XENLETA for indications other than CABP.

Our likely future collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Under our license agreements with Sumitomo Pharmaceuticals (Suzhou) and Sunovion, we have, and under any such arrangements we enter into with any third parties in the future we will likely have, limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Our current collaborations pose, and any future collaborations likely will pose, numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, product and product candidate priorities, available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may need to conduct clinical trials, and these clinical trials may not be successful;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;
- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- collaborators may be unable to enforce our intellectual property rights in territories where we have licensed, or may license, them such rights, which may expose us to material adverse tax and other consequences;
- disputes may arise between the collaborators and us that result in the delay or termination of the development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaborators may elect to delay commercialization in an effort to gain more commercially favorable product pricing and reimbursement in their territory.

For example, under our license agreement with Sumitomo Pharmaceuticals (Suzhou), if any court, tribunal or governmental agency in the People's Republic of China, Hong Kong, Macau or Taiwan determines that the exclusive license granted to Sumitomo Pharmaceuticals (Suzhou) pursuant to the license agreement is not sufficiently exclusive such that Sumitomo Pharmaceuticals (Suzhou) does not have sufficient rights to enforce the licensed patent rights in such territories, we and our subsidiary, Nabriva Therapeutics GmbH, have agreed to take such commercially reasonable steps as Sumitomo Pharmaceuticals (Suzhou) reasonably requests to grant Sumitomo Pharmaceuticals (Suzhou) such rights. If a court in such jurisdictions were to determine that our license to Sumitomo Pharmaceuticals (Suzhou) was not sufficiently exclusive and that Sumitomo Pharmaceuticals (Suzhou) did not have the rights to enforce the licensed patent rights in the licensed territories, Sumitomo Pharmaceuticals (Suzhou) may require us to take such actions that it deems reasonable but that we do not and which may have a material adverse effect on our business, including requiring us to make changes to our organizational structure that may result in adverse tax and other consequences, or to conduct other activities that may cause us to incur significant expenses.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.

The commercialization of XENLETA, potential commercialization of CONTEPO, if approved, and the development and potential commercialization of other product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to further collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we intend to seek to commercialize XENLETA through a variety of types of additional collaboration arrangements outside the United States.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for additional collaborations outside greater China and Canada will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the

likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Mergers and acquisitions in the pharmaceutical and biotechnology industries may also reduce the number of potential collaborators with whom we could partner. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into additional collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We enter into various contracts in the normal course of our business in which we agree to indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically agree to indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sub licensees' exercise of rights under the agreement. With respect to our commercial agreements, we have agreed to indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party. With respect to consultants, we typically agree to indemnify them from claims arising from the good faith performance of their services.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage or not covered by insurance, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator or other third party to indemnify us and the collaborator or other third party is denied insurance coverage or otherwise does not have assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology, products and product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology, products and product candidates similar or identical to ours, and our ability to successfully commercialize our technology, products and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology, products and product candidates. We seek to protect our proprietary position by filing patent applications in the United States, Europe and in certain additional foreign jurisdictions related to our novel technologies, products and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent

applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we license technology, products or product candidates from third parties, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering this intellectual property. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted, maintained and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology, products or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies, products and product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our licensed and owned intellectual property both in the U.S. and abroad. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, China and certain other developing countries, where we currently have a number of licensed patents and licensed patent applications, currently affords less protection to a company's intellectual property than some other jurisdictions. Furthermore, certain developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third-party, which could materially diminish the value of those patents. In addition, many countries limit the enforceability of patents against government agencies or government contractors. This could also limit our potential revenue opportunities. As such, the lack of strong patent and other intellectual property protection in China and elsewhere may significantly increase our vulnerability regarding unauthorized disclosure or use of our intellectual property and undermine our competitive position. Proceedings to enforce our future patent rights, if any, in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. We also may not pursue or obtain patent protection in all major markets or may not obtain protection that enables us to prevent the entry of third parties onto the market. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our U.S. patents or pending U.S. patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. For example, we have received a Notice of Request for Invalidation of our lefamulin compound patent in China in October 2021. We filed a response defending the validity of our patent, and the petitioner withdrew his invalidation request in January 2022, so this matter is concluded. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology, products or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products and product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents

and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technology, products or product candidates.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or any licensed patents by developing similar or alternative technologies, products or product candidates in a non-infringing manner. In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity that we obtain under applicable legislation, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the European Union and elsewhere may also result in clinical trial data submitted as part of an MAA becoming publicly available. Such developments could enable other companies to circumvent our intellectual property rights and use our clinical trial data to obtain marketing authorizations in the European Union and in other jurisdictions. Such developments may also require us to allocate significant resources to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology, products and product candidates, or limit the duration of the patent protection of our technology, products and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter such infringement or unauthorized use, we may be required to file claims, which can be expensive, time consuming and a distraction to management. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging our patents, trademarks, copyrights or other intellectual property are invalid or unenforceable or that we infringe their intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products, product candidates and technology, including interference, derivation, *inter partes* review or post-grant review proceedings before the USPTO. The risks of being involved in such litigation and proceedings may increase as our product candidates approach commercialization, and as we gain greater visibility as a public company with commercial products. Third parties may assert infringement claims against us based on existing or future intellectual property rights. We may not be aware of all such intellectual property rights potentially relating to our products and product candidates. Any freedom-to-operate search or analysis previously conducted may not have uncovered all relevant patents and patent applications, and there may be pending or future patent applications that, if issued, would block us from commercializing XENLETA®, CONTEPO™ or SIVEXTRO®.

Thus, we do not know with certainty whether XENLETA, CONTEPO, SIVEXTRO or any other product candidate, or our commercialization thereof, does not and will not infringe any third party's intellectual property.

If we are found to infringe a third party's intellectual property rights, or to avoid or settle litigation, we could be required to obtain a license to continue developing and marketing our technology, products and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us and could require us to make substantial payments. We could be forced, including by court order, to cease commercializing the infringing technology, products or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from commercializing our technology, products and product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our pleuromutilin business was founded as a spin-off from Sandoz. Although all patents and patent applications are fully owned by us and were either filed by Sandoz with all rights fully transferred to us, or filed in our sole name, because we acquired certain of our patent rights from Sandoz, we must rely on their prior practices, with regard to the assignment of such intellectual property. Similarly, for any patents and patent applications we acquired from Zavante in connection with the Acquisition, we must rely on Zavante's prior practices with regard to the assignment of intellectual property.

Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology, products and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, know-how, technology and other proprietary information, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, we cannot guarantee that we have executed these agreements with each party that may have or has had access to our trade secrets and other confidential information or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be obtained or independently developed by a competitor, our competitive position would be harmed.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary non-clinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, in particular in the United States or the European Union, we will not be able to commercialize our product candidates in those markets, and our ability to generate revenue will be materially impaired.

XENLETA, CONTEPO, and any other product candidates that we develop, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and, in the case of XENLETA, by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. On August 19, 2019, we received approval from the FDA to market the oral and intravenous formulations of XENLETA to treat CABP in the United States. Further, on July 28, 2020, the European Commission issued a legally binding decision for approval of the marketing authorization application for XENLETA for the treatment of community-acquired pneumonia in adults following a review by the European Medicines Agency. Sunovion Pharmaceuticals Canada Inc. additionally received approval from Health Canada to market oral and intravenous formulations of XENLETA for the treatment of community-acquired pneumonia in adults, with the Notice of Compliance from Health Canada dated July 10, 2020. We have entered into a license and commercialization agreement in March 2019 with Sunovion Pharmaceuticals Canada Inc. for XENLETA in Canada. In September 2021, we and Sumitomo Pharmaceuticals (Suzhou) announced the approval received by Sumitomo Pharmaceuticals (Suzhou) to market oral and intravenous formulations of XENLETA for the

treatment of community-acquired pneumonia in adults in Taiwan. We have not received approval to market XENLETA in any jurisdiction other than those mentioned above or for any other indication, and we have not received approval to market CONTEPO or any of our other product candidates from regulatory authorities in any jurisdiction, and we do not intend to seek approval to market CONTEPO outside the United States. In April 2019, the FDA issued a Complete Response Letter in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP, stating that it was unable to approve the application in its current form. Specifically, the Complete Response Letter requested us to address issues related to facility inspections and manufacturing deficiencies at our API contract manufacturer prior to the FDA approving the NDA. In December 2019, we resubmitted the NDA for CONTEPO. On June 19, 2020 we received a second Complete Response Letter from the FDA. Although our European contract manufacturing partners were prepared for regulatory authority inspections, the CRL cited observations at our manufacturing partners that could not be resolved due to FDA's inability to conduct onsite inspections because of travel restrictions. We do not have a forecasted date for the resubmission of our NDA for CONTEPO for the treatment of cUTI, including AP.

Even after obtaining marketing approval for XENLETA, we have limited experience in filing and supporting the applications necessary to obtain marketing approvals for product candidates and we have and expect to continue to rely on third parties to assist us in this process. Securing marketing approval requires the submission of extensive non-clinical and clinical data and supporting information to various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that XENLETA, CONTEPO or any of our other product candidates are not effective or only moderately effective, or have undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing approval or that prevent or limit commercial use.

The process of obtaining marketing approvals is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application.

The FDA and comparable regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from non-clinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Our failure to obtain marketing approval in jurisdictions other than the United States and Europe would prevent our product candidates from being marketed in these other jurisdictions, and any approval we are granted for our product candidates in the United States and Europe would not assure approval of product candidates in other jurisdictions.

In order to market and sell XENLETA and our other product candidates in jurisdictions other than the United States, Canada and Europe, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval process varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA approval or approvals from regulatory authorities in the European Union. The regulatory approval process outside the United States, Canada and Europe generally includes all of the risks associated with obtaining FDA approval or approvals from regulatory authorities in the European Union. In addition, some countries outside the United States, Canada and Europe require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement and a product may not be approved for sale in the country until it is also approved for reimbursement. We may not obtain marketing, pricing or reimbursement approvals outside the United States, Canada and Europe on a

timely basis, if at all. Approval by the FDA or regulatory authorities in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States and Europe does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA or regulatory authorities in the European Union. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Marketing approvals in countries outside the United States and Europe do not ensure pricing approvals in those countries or in any other countries, and marketing approvals and pricing approvals do not ensure that reimbursement will be obtained.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom and European Union entered into a Trade and Cooperation Agreement in connection with Brexit that sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any product candidates, which could significantly and materially harm our business.We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Any product candidate for which we obtain marketing approval will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

XENLETA and any other product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval. In addition, laws and regulations govern the distribution and tracing of prescription drugs and prescription drug samples, including the Prescription Drug Marketing Act of 1976 and the Drug Supply Chain Security Act, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the United States federal level and set minimum standards for the regulation of drug distributors by the states.

The FDA and other federal and state agencies, including the U.S. Department of Justice, or DOJ, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs subject to the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of such requirements may lead to investigations alleging violations of the Food, Drug and Cosmetic Act and other statutes, including the False Claims Act and other

federal and state health care fraud and abuse laws as well as state consumer protection laws. Accordingly, we may not promote XENLETA in the United States for use in any indications other than the treatment of CABP, and all promotional claims must be consistent with the FDA-approved labeling of XENLETA.

Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure;
- exclusion from participation in federal healthcare reimbursement programs or debarment or the imposition of Corporate Integrity Agreements; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Similar restrictions apply to the approval of our products in the EU. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the EU’s stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized

medicinal products, for which a separate manufacturer's license is mandator; and the marketing and promotion of authorized drugs, which are strictly regulated in the EU and are also subject to EU member state laws.

Accordingly, with respect to XENLETA and any other product candidates for which we receive marketing approval, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products, including XENLETA, withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies have delayed the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which has adversely affected our business. The FDA announced that in order to bring new therapies to patients sick with COVID-19 as quickly as possible, it has redeployed medical and regulatory staff from other areas to work on COVID-19 therapies. On June 19, 2020 we received a second Complete Response Letter in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP due to issues at our third party manufacturers that could not be inspected by the FDA owing to operational restrictions placed on the FDA by COVID-19. Additionally, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

A Fast Track or Priority Review designation by the FDA may not lead to a faster development or regulatory review or approval process and does not assure FDA approval of our product candidates.

If a product candidate is intended for the treatment of a serious or life threatening condition and the product candidate demonstrates the potential to address unmet medical need for this condition, the sponsor may apply to the FDA for fast track designation. For fast track products, sponsors may have greater interactions with the FDA, and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor,

that a fast track product may be effective. The FDA has designated the IV formulation of CONTEPO as a qualified infectious disease product, or QIDP, and granted a fast track designation for this formulation of CONTEPO.

Further, if FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. CONTEPO has been granted priority review by the FDA.

We may seek these and other expedited review designations for our product candidates. The FDA has broad discretion with respect to whether or not to grant these designations to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a fast track or breakthrough therapy designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. As a result, while we may seek and receive these designations for our product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw these designations if it believes that the designation is no longer supported by data from our clinical development program.

Designation of CONTEPO as a Qualified Infectious Disease Product does not assure FDA approval of this product candidate.

A QIDP is an antibacterial or antifungal drug intended to treat serious or life-threatening infections, including those caused by an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens or certain “qualifying pathogens”. Upon the approval of an NDA for a drug product designated by the FDA as a QIDP, the product is granted an additional period of five years of regulatory exclusivity. Even though we have received a QIDP designation for CONTEPO, there is no assurance that CONTEPO will be approved by the FDA.

If the FDA does not conclude that our product candidates satisfy the requirements under Section 505(b)(2) of the Federal Food Drug and Cosmetics Act, or if the requirements for such product candidates under Section 505(b)(2) are not as we expect, the approval pathway for those product candidates may take longer, cost more and entail greater complications and risks than anticipated, and may not be successful.

We submitted an NDA for marketing approval of CONTEPO for the treatment of cUTI in adults in the United States in October 2018, and we resubmitted the NDA in December 2019, utilizing Section 505(b)(2) of the Food, Drug and Cosmetic Act, or the FDCA, which was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, otherwise known as the Hatch-Waxman Act. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

For NDAs submitted under Section 505(b)(2) of the FDCA, the patent certification and related provisions of the Hatch-Waxman Act apply. In accordance with the Hatch-Waxman Act, such NDAs may be required to include certifications, known as Paragraph IV certifications, that certify any patents listed in the Orange Book publication in respect to any product referenced in the 505(b)(2) application are invalid, unenforceable and/or will not be infringed by the manufacture, use or sale of the product that is the subject of the 505(b)(2) application. Under the Hatch-Waxman Act, the holder of the NDA which the 505(b)(2) application references may file a patent infringement lawsuit after receiving notice of the Paragraph IV certification. Filing of a patent infringement lawsuit triggers a one-time automatic 30-month stay of the FDA’s ability to approve the 505(b)(2) application. We have not conducted a comprehensive freedom-to-operate review with regard to CONTEPO.

Accordingly, we may invest a significant amount of time and expense in the development of CONTEPO or any other product candidate we may develop and experience significant delays and patent litigation before such products may be commercialized, if at all. A Section 505(b)(2) application also may not be approved until any non-patent

exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired. The FDA may also require us to perform one or more additional clinical studies or measurements to support the change from the approved product. The FDA may then approve the new formulation for all or only some of the indications sought by us. The FDA may also reject our future Section 505(b)(2) submissions and may require us to file such submissions under Section 501(b)(1) of the FDCA, which could be considerably more expensive and time consuming.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, certain competitors and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2). It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. Thus, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to faster product development or earlier approval.

If the FDA does not conclude that CONTEPO, or any of our other product candidates for which we may utilize the 505(b)(2) pathway, satisfies the requirements for the 505(b)(2) regulatory approval pathway, or if the requirements for approval of any of our product candidates, including CONTEPO, under Section 505(b)(2) are not as we expect, the approval pathway for CONTEPO and any of our other product candidates for which we may utilize the 505(b)(2) pathway will likely take significantly longer, cost significantly more and encounter significantly greater complications and risks than anticipated, and in any case may not be successful.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which in the event of a violation could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any of our products, including SIVEXTRO, XENLETA, and product candidates, including CONTEPO, for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute SIVEXTRO, XENLETA, and any other products for which we obtain marketing approval. Restrictions under applicable federal, state, and foreign healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, with data collection beginning in August 2013; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, and foreign anti-corruption laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require product manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. We have developed and implemented a corporate compliance program designed to ensure that we will market and sell any approved products in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.

As a condition of reimbursement by various federal and state health insurance programs, pharmaceutical companies are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. Pharmaceutical companies are required to report any revisions to our calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect liability to federal and state payers and also adversely impact reported financial results of operations in the period of such restatement.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If a company becomes subject to investigations, restatements, or other inquiries concerning compliance with price reporting laws and regulations, it could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on the business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of products and thus have an adverse impact on financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in a company having to carry a liability on its consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, the company's financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if a pharmaceutical firm is found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to the Centers for Medicare & Medicaid Services, or CMS , it may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate the Medicaid drug rebate agreement, pursuant to which companies participate in the Medicaid program. In the event that CMS terminates a rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for covered outpatient drugs.

Additionally, if a pharmaceutical company overcharges the government in connection with the FSS program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, it is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against a company under the FCA 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.
Our collaborators are also subject to similar requirements outside of the U.S. and thus the attendant risks and uncertainties. If our collaborators suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material and adverse impact on our revenues.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our products and product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of CONTEPO or any of our other product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products, including SIVEXTRO, XENLETA, or product candidates, including CONTEPO, for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. Pursuant to subsequent legislation, however, these Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts for Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical

devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization, or PA, and step therapy, or ST, for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" in the regulations. It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in

response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In other countries, particularly the member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. Also, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to

individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to 4% of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by the GDPR, though the act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (i.e. “the Common Rule”). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

We cannot assure stockholders that our third-party service providers with access to our or our customers’, suppliers’, trial patients’ and employees’ personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure shareholders that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the Irish Criminal Justice (Corruption Offenses) Act, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in that existing laws might be administered or interpreted.

Compliance with the FCPA and other anti-corruption laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the trade control laws. For example, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

There is no assurance that we will be effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including trade control laws. If we are not in compliance with the FCPA and other anti-corruption laws or trade control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, other anti-corruption laws or trade control laws by U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations currently, and may in the future, involve the use of hazardous and flammable materials, including chemicals and medical and biological materials, and produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials or disposal of hazardous wastes, we could be held liable for any resulting damages, and any liability could exceed our resources.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We also maintain a general liability program for some of the risks, but our insurance program includes limited environmental damage coverage, which has an annual aggregate coverage limit of $2.0 million. Although we maintain an umbrella policy with an annual aggregate coverage limit of $10.0 million, which may provide some environmental coverage, we do not maintain a separate policy covering environmental damages.

In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Employee misconduct could also involve the improper use of information obtained during clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

We are increasingly dependent upon technology systems and data to operate our business. In particular, the COVID-19 pandemic has caused us to modify our business practices, including the requirement that our office-based employees work from home. As a result, we are increasingly dependent upon our technology systems to operate our business and our ability to effectively manage our business depends on the security, reliability and adequacy of our technology systems and data.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect the service reliability and threaten the confidentially, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our drug development programs and commercialization activities and business operations, in

addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our product research, development and commercialization efforts could be delayed.

We are subject to various laws protecting the confidentiality of certain patient health information, and our failure to comply could result in penalties and reputational damage.

Certain countries in which we operate have, or are developing, laws protecting the confidentiality of certain patient health information. European Union member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations.

For example, the European Union General Data Protection Regulation, or the GDPR, which came into force on May 25, 2018, introduced new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR imposes strict obligations and restrictions on controllers and processors of personal data including, for example, expanded disclosures about how personal data is to be used, increased requirements pertaining to health data and pseudonymised (i.e., key-coded) data, mandatory data breach notification requirements and expanded rights for individuals over their personal data. This could affect our ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting, or could cause our costs to increase, and harm our business and financial condition.

While the GDPR, as a directly effective regulation, was designed to harmonize data protection law across the European Union, it does permit member states to legislate in many areas (particularly with regard to the processing of genetic, biometric or health data), meaning that inconsistencies between different member states will still arise. European Union member states have their own regimes on medical confidentiality and national and European Union-level guidance on implementation and compliance practices is often updated or otherwise revised, which adds to the complexity of processing personal data in the European Union.

Risks Related to Our Acquisition of Zavante

We may fail to realize the anticipated benefits of our Acquisition of Zavante, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties.

On July 24, 2018, we completed the acquisition of Zavante pursuant to the Merger Agreement. Our ability to realize the anticipated benefits of the Acquisition is expected to entail numerous material potential difficulties, including, among others:

- any delay or failure in obtaining marketing approvals for CONTEPO, or any delay or failure to commercialize CONTEPO in the United States thereafter;
- increased scrutiny from third parties, including regulators, legislative bodies and enforcement agencies, including with respect to product pricing and commercialization matters;
- changes in laws or regulations that adversely impact the anticipated benefits of the Acquisition;
- challenges related to the perception by patients, the medical community and third-party payors of CONTEPO for the treatment of cUTIs;
- disruptions to our manufacturing arrangements with third-party manufacturers, including our manufacturing and supply arrangements with respect to CONTEPO and disruptions to our third-party distribution channel;

- difficulties in managing the expanded operations of a larger and more complex company following the Acquisition;
- difficulties in achieving the anticipated business opportunities and growth prospects from the Acquisition;
- the size of the treatable patient population for CONTEPO may be smaller than we believe it is;
- difficulties in attracting and retaining key personnel; and
- potential unknown liabilities, adverse consequences, unforeseen increased expenses or other unanticipated problems associated with the Acquisition.

Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially adversely impact our business, financial condition and results of operations.

The upfront consideration for the Acquisition was comprised of 815,209 of our ordinary shares, including the 81,518 ordinary shares that were initially held back but which were issued in July 2019 upon release of the Holdback Shares pursuant to the terms of the Merger Agreement. Pursuant to the Merger Agreement, former Zavante stockholders are also entitled to receive from us, subject to the terms and conditions of the Merger Agreement, up to $97.5 million in contingent consideration, of which $25.0 million would become payable upon the first approval of a new drug application from the FDA, for CONTEPO for any indication, or the Approval Milestone Payment, and an aggregate of up to $72.5 million would become payable upon the achievement of specified net sales milestones, or the Net Sales Milestone Payments, with the first commercial milestone becoming payable when CONTEPO exceeds $125.0 million in net sales in a calendar year. At our Extraordinary General Meeting of Shareholders held in October 2018, our shareholders approved the issuance of ordinary shares in settlement of potential milestone payment obligations that may become payable in the future to former Zavante stockholders, including the Approval Milestone Payment which will be settled in our ordinary shares. We also now have the right to settle the Net Sales Milestone Payments in ordinary shares, except as otherwise provided in the Merger Agreement. The issuance of our ordinary shares in connection with the closing of the Acquisition was dilutive to our existing shareholders, and the future issuance of our ordinary shares to satisfy our milestone payment obligations would be further dilutive to our then existing shareholders.

Also, following the Acquisition, we now possess certain liabilities and obligations, including contractual liabilities and obligations, that were assumed by us upon closing of the Acquisition. Prior to the Acquisition, former Zavante stockholders and SG Pharmaceuticals, Inc. entered into a stock purchase agreement, dated as of May 5, 2015, or the Stock Purchase Agreement, pursuant to which SG Pharmaceuticals, Inc. acquired all of the outstanding capital stock of Zavante from the Zavante selling stockholders and SG Pharmaceuticals, Inc., subsequently merged with and into Zavante, with Zavante as the surviving entity. Pursuant to the Stock Purchase Agreement, Zavante (as successor to SG Pharmaceuticals, Inc.) is obligated to make milestone payments payable in cash to the selling stockholders of $3.0 million upon marketing approval by the FDA with respect to any oral, intravenous or other form of fosfomycin, or the Zavante Products, and milestone payments that may be settled in ordinary shares of up to $26.0 million in the aggregate upon the occurrence of various specified levels of net sales with respect to the Zavante Products. In addition, Zavante is obligated to make annual royalty payments to the selling stockholders of a mid-single-digit percentage of net sales of Zavante Products, subject to adjustment based on net sales thresholds and with such percentage reduced to low single-digits if generic fosfomycin products account for half of the applicable market on a product-by-product and country-by-country basis. The Stock Purchase Agreement also provides that Zavante will pay to the selling stockholders a mid-single-digit percentage of transaction revenue in connection with the consummation of the grant, sale, license or transfer of market exclusivity rights for a qualified infectious disease product (within the meaning of the Cures Act) related to a Zavante Product.

In addition, we expect to incur expenses related to the continued development, regulatory approval process and commercialization with respect to CONTEPO. Zavante has entered into a manufacturing and supply agreement with Fisiopharma, pursuant to which Zavante has an obligation to purchase a minimum percentage of its commercial requirements of CONTEPO in the United States. Zavante has also entered into a manufacturing and exclusive supply

agreement with Laboratorios ERN, S.A., pursuant to which Laboratorios ERN, S.A. has agreed to supply Zavante with certain technical documentation and data as required for submission of an NDA, or an abbreviated new drug application for CONTEPO and certain regulatory support in connection with the commercial sale and use of CONTEPO in the United States, and which provides for payments to Laboratorios ERN, S.A. of a one-time cash payment upon the first commercial sale of CONTEPO and subsequent quarterly payments thereafter based on the number of vials of CONTEPO sold in the United States during each quarter. Zavante has also entered into a manufacturing and supply agreement with Ercros, S.A., pursuant to which Ercros, S.A. supplies to Zavante, on an exclusive basis, a blend of fosfomycin disodium and succinic acid, or API Mixture, for CONTEPO and, if CONTEPO is approved, will supply the commercial API Mixture for CONTEPO in the United States.

Because we have limited financial resources, by investing in the Acquisition, we may forgo or delay pursuit of other opportunities that may have proven to have greater commercial potential. Further, it is possible that undisclosed, contingent, or other liabilities or problems may arise in the future of which we were previously unaware. These undisclosed liabilities could have an adverse effect on our business, financial condition and results of operations.

All of these factors could decrease or delay the expected accretive effect of the Acquisition and negatively impact our share price. As a result, it cannot be assured that the Acquisition will result in the full realization of the benefits anticipated from the Acquisition or in the anticipated time frames or at all.

Risks Related to Employee Matters

Our future success depends on our ability to attract, retain and motivate key executives and qualified personnel.

We are highly dependent on the principal members of our management team. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain “key person” insurance on any of our executive officers. The unplanned loss of the services of any of these persons might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified personnel, including in the United States and Ireland where we have key business processes, will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. Our functional teams are small and therefore attrition can lead to gaps in institutional knowledge and risks to running the business. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by companies other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we cannot recruit and retain qualified personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

In 2020, we reduced the size of our organization, and we may encounter difficulties in managing our business as a result of this reduction, or the attrition that may occur following this reduction, which could disrupt our operations. In addition, we may not achieve anticipated benefits and savings from the reduction.

In April 2020, we announced a plan to restructure our hospital-based commercial sales force and transition to a community-based sales effort. Additional reductions in headcount occurred in the third quarter including the restructuring of the commercial organization, which led to the elimination of the role of the Chief Commercial Officer. Our commercial operations now report directly to our Chief Executive Officer. The restructuring was intended to reduce costs and to align the capabilities of our sales efforts with our strategic re-focus on making sales of XENLETA to community health care professionals, as well as our business development strategy to in-license additional community products, such as SIVEXTRO and additional community products. The restructuring resulted in the termination of long-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. Given the complexity and nature of our business, we must continue to implement and improve our managerial, operational and financial systems, manage our facilities and continue to recruit and retain qualified personnel. This will be made more challenging given

the restructuring described above and additional measures we may take to reduce costs. As a result, our management may need to divert a disproportionate amount of its attention away from our day-to-day strategic and operational activities and devote a substantial amount of time to managing these organizational changes. Further, the restructuring and possible additional cost containment measures may yield unintended consequences, such as attrition beyond our intended reduction in headcount and reduced employee morale. In addition, the restructuring may result in employees who were not affected by the reduction in headcount seeking alternate employment, which would result in us seeking contract support at unplanned additional expense. In addition, we may not achieve anticipated benefits from the restructuring. Due to our limited resources, we may not be able to effectively manage our operations or recruit and retain qualified personnel, which may result in weaknesses in our infrastructure and operations, risks that we may not be able to comply with legal and regulatory requirements, loss of business opportunities, loss of employees and reduced productivity among remaining employees. We may also determine to take additional measures to reduce costs, which could result in further disruptions to our operations and present additional challenges to the effective management of our company. If our management is unable to effectively manage this transition and restructuring and additional cost containment measures, our expenses may be more than expected, and we may not be able to implement our business strategy.

Risks Related to Ownership of Our Ordinary Shares

The price of our ordinary shares may be volatile and fluctuate substantially.

The trading price of our ordinary shares has been and is likely to continue to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced significant volatility that has often been unrelated to the operating performance of particular companies. The market price for our ordinary shares may be influenced by many factors, including:

- our ability to successfully commercialize the oral and IV formulations of XENLETA for the treatment of CABP and the IV formulation of CONTEPO, if approved;
- our ability to promote and distribute SIVEXTRO;
- our ability to obtain FDA approval of CONTEPO for the treatment of cUTIs, including AP;
- our ability to successfully implement our proposed business strategy;
- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory delays and greater government regulation of potential products due to adverse events;
- regulatory or legal developments in the United States, the European Union and other countries or regions;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products, including additional community products;
- one or more of our manufacturers or suppliers could have an event which causes an unforeseen disruption of the manufacture or supply of our product candidates;

- our ability to comply with the restrictive covenants under our Loan Agreement and avoid an event of default that may lead to an acceleration of the amounts due under the Loan Agreement;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- perception and market performance of companies that are perceived to be similar to us:
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- activism by any single large shareholder or combination of shareholders;
- our need to raise additional funds;
- the societal and economic impact of public health epidemics, such as the ongoing COVID-19 pandemic;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. We also may face securities class-action litigation if we cannot obtain regulatory approvals for or if we otherwise fail to successfully commercialize SIVEXTRO, XENLETA or, if approved, CONTEPO or any of our other product candidates or if our securities experience volatility for any reason. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources. For example, we and our Chief Executive Officer, our former Chief Medical Officer and former Chief Financial Officer were named as defendants in a purported class action lawsuit following our announcement in April 2019 that the FDA issued a CRL in connection with our NDA for CONTEPO for the treatment of cUTIs, including AP, stating that it was unable to approve the application in its current form.

The number of ordinary shares underlying our outstanding warrants is significant in relation to our currently outstanding ordinary shares, which could have a negative effect on the market price of our ordinary shares and make it more difficult for us to raise funds through future equity offerings.

As part of our March 2021 registered direct offering we issued warrants to purchase up to an aggregate of 5,180,505 ordinary shares at an exercise price of $2.39 per share. As part of our May 2020 registered direct offering, we issued warrants to purchase an aggregate of up to 4,144,537 ordinary shares at an exercise price of $7.92 per share. As part of our December 2019 registered direct offering, we issued warrants to purchase an aggregate of up to 1,379,310 ordinary shares at an exercise price of $19.00 per share. As of the date of this Annual Report on Form 10-K, there were 10,619,347 warrants outstanding from the three offerings and, upon exercise in full of these warrants, the shares issuable upon exercise would represent a significant portion of our outstanding ordinary shares. Each of the December 2019 warrants was initially exercisable six months following the date of issuance, which was December 24, 2019, and will expire on the three-year anniversary of the date on which such warrants became initially exercisable. Each of the May 2020 warrants was immediately exercisable and will expire on the two-year anniversary of the date of issuance. Each of the March 2021 warrants was immediately exercisable and will expire on the five-year anniversary of the date of issuance. We have registered the issuance of shares upon exercise of these warrants under a registration statement under the Securities Act of 1933, as amended, and, accordingly, such shares can be freely sold into the public market upon issuance, subject to volume limitations applicable to affiliates. Sales of these shares could cause the market price of our ordinary shares to decline significantly. Furthermore, if our share price rises, the holders of these warrants may be more

likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our ordinary shares and reduce or eliminate any appreciation in our share price that might otherwise occur.

We may also find it more difficult to raise additional equity capital while these warrants are outstanding. At any time during which these warrants are likely to be exercised, we may be unable to obtain additional equity capital on more favorable terms from other sources. In addition, the exercise of these warrants would result in a significant increase in the number of our outstanding ordinary shares, which could have the effect of significantly diluting the interest of our current shareholders, and following such exercise the former holders of such warrants could have significant influence over our company as a result of the ordinary shares they acquire upon such exercise.

If we fail to meet the requirements for continued listing on The Nasdaq Global Select Market, our ordinary shares could be delisted from trading, which would decrease the liquidity of our ordinary shares and our ability to raise additional capital.

Our ordinary shares are currently listed for quotation on The Nasdaq Global Select Market. We are required to meet specified requirements in order to maintain our listing on The Nasdaq Global Select Market, including, among other things, a minimum bid price of $1.00 per share.

On April 29, 2020, we received written notice from The Nasdaq Stock Market LLC, or Nasdaq, indicating that, based on the closing bid for the last 30 consecutive business days, we were not in compliance with the $1.00 minimum bid price requirement for continued listing on The Nasdaq Global Select Market, as set forth in Listing Rule 5450(a)(1), or the Bid Price Rule. On December 2, 2020, our board of directors effected a one-for-ten reverse stock split of our ordinary shares for the purpose of regaining compliance with the Bid Price Rule. On December 17, 2020, we received notification from Nasdaq that for 10 consecutive business days, the closing bid price of our ordinary shares had been at $1.00 per share or greater, confirming that we had regained compliance with the Bid Price Rule.

On January 4, 2022, we again received written notice from Nasdaq indicating that, based on the closing bid for the last 30 consecutive business days, we were not in compliance with the Bid Price Rule. The Notice does not result in the immediate delisting of our ordinary shares from The Nasdaq Global Select Market. In accordance with Listing Rule 5810(c)(3)(A), we have a period of 180 calendar days to regain compliance with the Bid Price Rule. As a result, we will have until July 5, 2022, or the Compliance Date, to regain compliance with the Bid Price Rule. To regain compliance, the closing bid price of our ordinary shares must be at least $1.00 per share for a minimum of ten consecutive business days on or before the Compliance Date. If we do not regain compliance with the Bid Price Rule by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would need to transfer the listing of our ordinary shares to the Nasdaq Capital Market, provided that we meet the continued listing requirement for market value of publicly held shares and all other initial listing standards, with the exception of the Bid Price Rule. To effect such a transfer, we would also need to pay an application fee to Nasdaq and provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period. If we do not qualify for the additional compliance period or fail to regain compliance during the additional 180-day period, then Nasdaq will notify us of its determination to delist our ordinary shares, at which point we would have an opportunity to appeal the delisting determination to a Nasdaq hearing panel. In addition to continuing to monitor the closing bid price of our ordinary shares, we expect to consider available options to regain compliance with the Bid Price Rule. However, there can be no assurance that we will be able to regain compliance with the Bid Price Rule.

If we do not regain compliance with the Bid Price Rule by the Compliance Date or if in the future we fail to satisfy The Nasdaq Global Select Market’s other continued listing requirements, we may transfer to The Nasdaq Capital Market, which generally has lower financial requirements for initial listing, to avoid delisting, or, if we fail to meet its listing requirements, the OTC Bulletin Board. A transfer of our listing to The Nasdaq Capital Market or having our ordinary shares trade on the OTC Bulletin Board could adversely affect the liquidity of our ordinary shares. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our ordinary shares, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our ordinary shares to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee

confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our share price.

There are many factors that may adversely affect our minimum bid price, including those described throughout this section titled “Risk Factors”. Many of these factors are outside our control. As a result, we may not be able to comply with the Bid Price Rule in the long term. Any potential delisting of our ordinary shares from The Nasdaq Global Select Market would likely result in decreased liquidity and increased volatility for our ordinary shares and would adversely affect our ability to raise additional capital or enter into strategic transactions. Any potential delisting of our ordinary shares from The Nasdaq Global Select Market would also make it more difficult for our shareholders to sell their ordinary shares in the public market.

Our ordinary shares do not trade on any exchange outside of the United States.

Our ordinary shares are listed only in the United States on The Nasdaq Global Select Market, and we have no plans to list our ordinary shares in any other jurisdiction. As a result, a holder of ordinary shares outside of the United States may not be able to effect transactions in our ordinary shares as readily as the holder may if our ordinary shares were listed on an exchange in that holder’s home jurisdiction.

Substantial future sales of our ordinary shares in the public market, or the perception that these sales could occur, could cause the price of our ordinary shares to decline significantly, even if our business is doing well.

Sales of a substantial number of our ordinary shares, or the perception in the market that these sales could occur, could reduce the market price of our ordinary shares. We had 56,715,306 ordinary shares outstanding as of December 31, 2021. To the extent any of these shares are sold into the market, particularly in substantial quantities, the market price of our ordinary shares could decline.

Future issuances of ordinary shares pursuant to our equity incentive plans could also result in a reduction in the market price of our ordinary shares. We have filed registration statements on Form S-8 registering all of the ordinary shares that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance and once vested, subject to volume, notice and manner of sale limitations applicable to affiliates. The majority of ordinary shares that may be issued under our equity compensation plans remain subject to vesting in tranches over a four-year period. As of December 31, 2021, an aggregate of 533,564 options to purchase our ordinary shares had vested and become exercisable although these options all have an exercise price that is higher than the recent market trading prices of our ordinary shares.

In addition, on June 25, 2019, we entered into the Jefferies ATM Agreement with Jefferies, pursuant to which, from time to time, we may offer and sell ordinary shares, for aggregate gross sale proceeds of up to $50.0 million through Jefferies by any method permitted that is deemed an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended.

On May 6, 2021, we entered into the New Sale Agreement with Jefferies, as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share for aggregate gross sale proceeds of up to $50.0 million, from time to time through Jefferies, by any method permitted that is deemed an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. Upon entry into the New Sale Agreement, our existing Jefferies ATM Agreement was terminated. We did not incur any termination penalties as a result of the replacement of the Jefferies ATM Agreement. As of the effective date of the termination of the Jefferies ATM Agreement, we had sold an aggregate of 5,925,699 of our ordinary shares pursuant to the Jefferies ATM Agreement for aggregate gross proceeds of $33.7 million and net proceeds to us of $31.9 million, after deducting commissions and offering expenses payable by us. The approximately $16.3 million of ordinary shares that had been available for sale pursuant to the Jefferies ATM Agreement remained unsold at the time of its replacement. The replacement of the Jefferies ATM Agreement terminated any future sales of ordinary shares through the Jefferies ATM Agreement.

As of December 31, 2021, we have issued and sold an aggregate of 18,232,689 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $30.5 million and net proceeds of $29.3 million, after deducting

commissions to Jefferies and other offering expenses. From January 1, 2022 and through the date of this filing, we have issued and sold an aggregate of 1,338,282 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $595,000 and net proceeds of $580,000, after deducting commissions to Jefferies and other offering expenses. As of the date of this filing, we may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the New Sale Agreement.

On September 24, 2021, we entered into a purchase agreement, or Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which, subject to the terms and conditions, provides that we have the right to sell to Lincoln Park and Lincoln Park is obligated to purchase up to $23.0 million of our Ordinary Shares. In addition, under the Purchase Agreement, we agreed to issue a commitment fee of 632,474 Ordinary Shares, or the Commitment Shares, as consideration for Lincoln Park entering into the Purchase Agreement and for the payment of $0.01 per Commitment Share. Under the Purchase Agreement, we may from time to time, at our discretion, direct Lincoln Park to purchase on any single business day, or a Regular Purchase up to (i) 400,000 Ordinary Shares if the closing sale price of our Ordinary Shares is not below $0.25 per share on Nasdaq, (ii) 600,000 Ordinary Shares if the closing sale price of our Ordinary Shares is not below $2.00 per share on Nasdaq or (iii) 800,000 Ordinary Shares if the closing sale price of our Ordinary Shares is not below $3.00 per share on Nasdaq. In any case, Lincoln Park's commitment in any single Regular Purchase may not exceed $2,500,000 absent a mutual agreement to increase such amount. As of December 31, 2021, we have issued and sold an aggregate of 2,400,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $2.4 million. From January 1, 2022 and through the date of this filing, we have issued and sold an aggregate of 3,600,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $1.6 million. As of the date of this filing, we may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the Purchase Agreement, subject to the Nasdaq rules which may limit our ability to make sales of our ordinary shares to Lincoln Park in excess of a specified amount without prior shareholder approval.

As part of our March 2021 registered direct offering we issued warrants to purchase up to an aggregate of 5,180,505 ordinary shares at an exercise price of $2.39 per share. As part of our May 2020 registered direct offering, we issued warrants to purchase an aggregate of up to 4,144,537 ordinary shares at an exercise price of $7.92 per share. As part of our December 2019 registered direct offering, we issued warrants to purchase an aggregate of up to 1,379,310 shares of ordinary shares at an exercise price of $19.00 per share. As of the date of this Annual Report on Form 10-K, there were 10,619,347 warrants outstanding from the three offerings and, upon exercise in full of these warrants, the shares issuable upon exercise would represent a significant portion of our outstanding ordinary shares. Each of the December 2019 warrants was initially exercisable six months following the date of issuance, which was December 24, 2019, and will expire on the three-year anniversary of the date on which such warrants became initially exercisable. Each of the May 2020 warrants was immediately exercisable and will expire on the two-year anniversary of the date of issuance. Each of the March 2021 warrants was immediately exercisable and will expire on the five-year anniversary of the date of issuance. We have registered the issuance of shares upon exercise of these warrants under a registration statements under the Securities Act of 1933, as amended, and, accordingly, such shares can be freely sold into the public market upon issuance, subject to volume limitations applicable to affiliates. The exercise of these warrants or sale of the shares issuable upon exercise of these warrants, or the perception that sales of these shares could occur, could cause the market price of our ordinary shares to decline significantly.

Furthermore, if our share price rises, the holders of these warrants may be more likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our ordinary shares and reduce or eliminate any appreciation in our share price that might have otherwise occurred.

If a large number of our ordinary shares are sold in the public market after they become eligible for sale, the sales could reduce the trading price of our ordinary shares and impede our ability to raise future capital.

The upfront consideration for the Acquisition was comprised of 815,209 of our ordinary shares, including 81,518 ordinary shares that were initially held back but which were issued in July 2019 upon release of the Holdback Shares pursuant to the terms of the Merger Agreement. Such shares are able to be freely sold in the public market, subject to any requirements and restrictions, including any applicable volume limitations, imposed by Rule 144 under the Securities Act. In addition, the Merger Agreement provides that we may issue up to an additional $97.5 million in our ordinary shares to former Zavante stockholders upon the achievement of specified regulatory and commercial

milestones in the future, and obligates us to provide registration rights with respect to the registration for resale of such additional ordinary shares that may become issuable upon the achievement of such milestones.

The sale or resale of these shares in the public market, or the market's expectation of such sales, may result in an immediate and substantial decline in our share price. Such a decline will adversely affect our investors and also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

We are a "smaller reporting company", and the reduced disclosure requirements applicable to smaller reporting companies may make our ordinary shares less attractive to investors.

We are a "smaller reporting company" as defined in Rule 12b-2 promulgated under the Exchange Act. We may remain a smaller reporting company until we have a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million, or a non-affiliate public float in excess of $700 million, each as determined on an annual basis. For so long as we remain a smaller reporting company, we are permitted and may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- an exemption from compliance with the auditor attestation requirement of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, on the design and effectiveness of our internal controls over financial reporting;
- an exemption from compliance with any requirement that the Public Company Accounting Oversight Board may adopt regarding mandatory audit firm rotation; and
- reduced disclosure about our executive compensation arrangements.

We cannot predict whether investors will find our ordinary shares less attractive if we rely on such exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and the market price of our ordinary shares may be more volatile.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, security holders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. As a growing company, implementing and maintaining effective controls may require more resources, and we may encounter internal control integration difficulties. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ordinary shares.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, as a smaller reporting company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm until we are no longer a smaller reporting company. To achieve compliance with Section 404 within the prescribed period, we document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a

continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

United States investors may have difficulty enforcing judgments against us, our directors and executive officers.

We are incorporated under the laws of Ireland, and our registered offices and a substantial portion of our assets are located outside of the United States. As a result, it may not be possible to effect service of process on our directors, executive officers, or us in the United States or to enforce judgments obtained in courts in the United States against such persons or us based on civil liability provisions of the securities laws of the United States.

There is no treaty between Ireland and the United States providing for the reciprocal enforcement of judgments obtained in the other jurisdiction and Irish common law rules govern the process by which a U.S. judgment may be enforced in Ireland. The following requirements must be met as a precondition before a U.S. judgment will be eligible for enforcement in Ireland:

- the judgment must be for a definite sum;
- the judgment must be final and conclusive, and the decree must be final and enforceable in the court which pronounces it;
- the judgment must be provided by a court of competent jurisdiction, and the procedural rules of the court giving the foreign judgment must have been observed;
- the U.S. court must have had jurisdiction in relation to the particular defendant according to Irish conflict of law rules; and
- jurisdiction must be obtained by the Irish courts over judgment debtors in enforcement proceedings by service in Ireland or outside Ireland in accordance with the applicable court rules in Ireland.

Even if the above requirements have been met, an Irish court may exercise its right to refuse to enforce the U.S. judgment if the Irish court is satisfied that the judgment (1) was obtained by fraud; (2) is in contravention of Irish public policy; (3) is in breach of natural justice; or (4) is irreconcilable with an earlier judgment. By way of example, a judgment of a U.S. court of liabilities predicated upon U.S. federal securities laws may not be enforced by Irish courts on the grounds of public policy if that U.S. judgment includes an award of punitive damages. Further, an Irish court may stay proceedings if concurrent proceedings are being brought elsewhere.

We do not expect to pay dividends in the foreseeable future.

We have not paid any dividends on our ordinary shares since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that earnings, if any, will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. If we propose to pay dividends in the future, we must do so in accordance with Irish law, which provides that distributions including dividend payments, share repurchases and redemptions be funded from “distributable reserves”. In addition, the terms of the Loan Agreement with Hercules currently, and the terms of any future debt agreements may in the future, preclude us from paying dividends. As a result, capital appreciation, if any, of our ordinary shares will be the sole source of gain for holders of our ordinary shares for the foreseeable future.

We are exposed to risks related to currency exchange rates*.*

A portion of our expenses are denominated in currencies other than the U.S. dollar. Because our consolidated financial statements are presented in U.S. dollars, changes in currency exchange rates have had and could have a

significant effect on our operating results. Exchange rate fluctuations between foreign currencies and the U.S. dollar create risk in several ways, including the following:

- weakening of the U.S. dollar may increase the U.S. dollar cost of overseas research and development expenses;
- strengthening of the U.S. dollar may decrease the value of our revenues denominated in other currencies; and
- the exchange rates on non-U.S. dollar transactions and cash deposits can distort our financial results.

As a holding company, our operating results, financial condition and ability to pay dividends or other distributions are entirely dependent on funding, dividends and other distributions received from our subsidiaries, which may be subject to restrictions.

Our ability to pay dividends or other distributions and to pay our obligations in the future will depend on the level of funding, dividends and other distributions, if any, received from our subsidiaries and any new subsidiaries we establish in the future. The ability of our subsidiaries to make loans or distributions (directly or indirectly) to us may be restricted as a result of several factors, including restrictions in financing agreements and the requirements of applicable law and regulatory and fiscal or other restrictions. In particular, our subsidiaries and any new subsidiaries may be subject to laws that restrict dividend payments, authorize regulatory bodies to block or reduce the flow of funds from those subsidiaries to us, or limit or prohibit transactions with affiliates. Restrictions and regulatory action of this kind could impede access to funds that we may need to make dividend payments or to fund our own obligations.

Furthermore, we may guarantee some of the payment obligations of certain of our subsidiaries from time to time. These guarantees may require us to provide substantial funds or assets to our subsidiaries or their creditors or counterparties at a time when we are in need of liquidity to fund our own obligations.

The ownership percentage of our shareholders may be diluted in the future which could dilute the voting power or reduce the value our outstanding ordinary shares.

As with any publicly traded company, the ownership percentage of our shareholders may be diluted in the future because of equity issuances for acquisitions, capital market transactions or otherwise, including equity awards that we intend to continue to grant to our directors, officers and employees. From time to time, we may issue additional options or other share awards to our directors, officers and employees under our benefits plans.

In addition, our articles of association authorize us to issue, without the approval of our shareholders, one or more classes or series of preferred shares having such designation, powers, preferences and relative, participating, optional and other special rights, including preferences over our ordinary shares respecting dividends and distributions, as our board of directors generally may determine. The terms of one or more classes or series of preferred shares could dilute the voting power or reduce the value of our ordinary shares. Similarly, the repurchase or redemption rights or liquidation preferences we could assign to holders of preferred shares could affect the residual value of the ordinary shares. Additionally, we may issue and sell our ordinary shares under our Jefferies ATM Agreement or the Purchase Agreement with Lincoln Park from time to time, and we may issue additional ordinary shares as contingent consideration upon the achievement of certain regulatory and commercialization milestones, subject to the terms and conditions of the Merger Agreement. See *"—Risks Related to Ownership of our Ordinary Shares—Substantial future sales of our ordinary shares in the public market, or the perception that these sales could occur, could cause the price of our ordinary shares to decline significantly, even if our business is doing well."*

The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation. We are incorporated as a public limited company under Irish law.

The rights of our shareholders are governed by our memorandum and articles of association and Irish law. The rights associated with our ordinary shares are different to the rights generally associated with shares held in a

U.S. corporation. Material differences between the rights of shareholders of a U.S. corporation and the rights of our shareholders include differences with respect to, among other things, distributions, dividends, repurchases and redemptions, bonus issues, the election of directors, the removal of directors, the fiduciary and statutory duties of directors, conflicts of interests of directors, the indemnification of directors and officers, limitations on director liability, the convening of annual meetings of shareholders and special shareholder meetings, notice provisions for meetings, the quorum for shareholder meetings, the adjournment of shareholder meetings, the exercise of voting rights, shareholder suits, rights of dissenting shareholders, anti-takeover measures and provisions relating to the ability to amend the articles of association.

As an Irish public limited company, certain capital structure decisions require shareholder approval, which may limit our flexibility to manage our capital structure.

Under Irish law, our board of directors may issue new ordinary or preferred shares up to a maximum amount equal to the authorized but unissued share capital, without shareholder approval, once authorized to do so by our articles of association or by an ordinary resolution of our shareholders. Additionally, subject to specified exceptions, Irish law grants statutory preemption rights to existing shareholders where shares are being issued for cash consideration but allows shareholders to disapply such statutory preemption rights either in our articles of association or by way of special resolution. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. Accordingly, our articles of association contain, as permitted by Irish company law, provisions authorizing our board of directors to issue new shares, and to disapply statutory preemption rights. The authorization of our board of directors to issue shares and the disapplication of statutory preemption rights must both be renewed by the shareholders at least every five years.

We asked our shareholders to renew the authorization of our board of directors to issue shares and the disapplication of statutory preemption rights at our 2021 Annual General Meeting of Shareholders, or the 2021 Annual Meeting, and to extend that authorization to the increase in authorized share capital that was approved by our shareholders at the 2021 Annual Meeting. Our shareholders renewed the authorization of our board of directors to issue shares; however, although we received over 67% support of the votes cast on renewing the pre-emption rights opt-out authority, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions. We originally convened an Extraordinary General Meeting of Shareholders, or EGM, on December 22, 2021 but was ultimately adjourned to March 24, 2022 to allow us to solicit from our shareholders the additional proxies necessary to obtain approval of the sole proposal to grant the board of directors authority under Irish law to allot and issue ordinary shares (including rights to acquire ordinary shares) for cash without first offering those ordinary shares to our existing shareholders pursuant to the statutory pre-emption right that would otherwise apply. On March 24, 2022, our shareholders approved the dis-application of statutory pre-emption rights for an additional five year term.

The authorization of our board of directors to issue shares and the disapplication of statutory preemption rights must both be renewed by the shareholders at least every five years, or at the time our shareholders approve an increase in our authorized share capital. We cannot provide any assurance that these authorizations will always be approved, which could limit our ability to issue equity and thereby adversely affect the holders of our ordinary shares. As a result of this limitation, we may be limited in the amount of ordinary shares we may sell in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. In the event we are not able to obtain such shareholder approval of the disapplication of pre-emption rights, when needed, we will be limited in the amount of ordinary shares we may sell in any capital raising transaction without first offering those shares to all of our existing shareholders.

Irish law differs from the laws in effect in the U.S. with respect to defending unwanted takeover proposals and may give our board less ability to control negotiations with hostile offerors.

We are subject to the Irish Takeover Panel Act, 1997, Takeover Rules, 2013. Under those Irish Takeover Rules, the board is not permitted to take any action that might frustrate an offer for our ordinary shares once the board has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of ordinary shares, options or convertible

securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which the board has reason to believe an offer is or may be imminent. These provisions may give the board less ability to control negotiations with hostile offerors and protect the interests of holders of ordinary shares than would be the case for a corporation incorporated in a jurisdiction of the United States.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Rules, if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of a company, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for our outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company if the effect of such acquisition were to increase that person's percentage of the voting rights by 0.05% within a 12-month period. The Irish Takeover Rules could therefore discourage an investor from acquiring 30% or more of our outstanding ordinary shares, unless such investor was prepared to make a bid to acquire all outstanding ordinary shares.

Certain separate concert parties will also be presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of the company. The application of these presumptions may result in restrictions upon the ability of any of the concert parties and members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. We may consult with the Irish Takeover Panel with respect to the application of this presumption and the restrictions on the ability to acquire further securities if necessary, although we are unable to provide any assurance as to whether the Irish Takeover Panel would overrule this presumption.

We will be exposed to the risk of future changes in law, which could materially adversely affect us.

We are subject to Irish law. As a result, we are subject to the risk of future adverse changes in Irish law (including Irish corporate and tax law). In addition, we and our subsidiaries are also subject to the risk of future adverse changes in Austrian and U.S. law, as well as changes of law in other countries in which we and our subsidiaries operate.

Future adverse changes in law could result in our not being able to maintain a worldwide effective corporate tax rate that is competitive in our industry.

While we believe that being incorporated in Ireland should not affect our ability to maintain a worldwide effective corporate tax rate that is competitive in our industry, we cannot give any assurance as to what our effective tax rate will be because of, among other things, uncertainty regarding the tax policies of the jurisdictions where we will operate. The tax laws of Ireland, Austria, the United States, and other jurisdictions could change in the future, and such changes could cause a material change in our worldwide effective corporate tax rate. In particular, legislative action could be taken by Ireland, Austria, the United States or other jurisdictions which could override tax treaties upon which we expect to rely and adversely affect our effective tax rate. As a result, our actual effective tax rate may be materially different from our expectation.

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 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. New statutory and/or regulatory provisions under Section 7874 of the Code or otherwise could be enacted that 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 and our shareholders.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity by certain significant shareholders over a rolling three year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income and taxes may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our share ownership, some of which would be outside our control. If our ability to use our net operating losses and other tax attributes is limited by ownership changes, we may be unable to utilize a material portion of our net operating losses and other tax attributes to offset our future taxable income. In addition, there is also a risk that due to changes in laws and regulations, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities.

U.S. persons who own 10 percent or more of our shares may be subject to U.S. federal income taxation on certain of our foreign subsidiaries' income even if such income is not distributed to such U.S. persons.

A foreign corporation is treated as a "controlled foreign corporation", or CFC, for U.S. federal income tax purposes if, on any day during a taxable year, "United States shareholders" (as defined below) own (directly, indirectly or constructively within the meaning of Section 958 of the Code) more than 50% of the total combined voting power of all classes of our voting shares or more than 50% of the total value of all of our shares. A "United States shareholder" of a foreign corporation is a U.S. person who owns (directly, indirectly or constructively within the meaning of Section 958 of the Code) at least 10% of the total combined voting power of voting shares of such non-U.S. corporation or at least 10% of the total value of shares of all classes of stock of such non-U.S. corporation.

As a result of the Tax Act, all of our non-U.S. subsidiaries will be treated as CFCs.

Any United States shareholder who owns our shares (directly or indirectly within the meaning of Section 958(a) of the Code) on the last day in such taxable year must include in its gross income for U.S. federal income tax purposes its pro rata share (based on direct or indirect ownership of value) of the non-U.S. subsidiaries' "subpart F income", regardless of whether that income was actually distributed to such U.S. person (with certain adjustments). "Subpart F income" of a CFC generally includes among other items passive income, such as dividends, interest, royalties, rents, annuities and net gains from commodities, foreign currency and securities transactions and from sales of property that produced, or was held for the production of, passive income (or no income).

United States shareholders must also include in their gross income for U.S. federal income tax purposes their pro rata share of a CFC's "global intangible low tax income", or GILTI. In general terms, GILTI is the net income of the CFCs (other than income already included in United States shareholders' taxable income) that exceeds 10% of the CFCs' bases in depreciable tangible assets. GILTI is treated in a manner similar to subpart F income.

In addition, if a U.S. person disposes of shares in a non-U.S. corporation and the U.S. person was a United States shareholder at any time when the corporation was a CFC during the five-year period ending on the date of disposition, any gain from the disposition will generally be treated as a dividend to the extent of the U.S. person's share of the corporation's undistributed earnings and profits that were accumulated during the period or periods that the U.S. person owned the shares while the corporation was a CFC (with certain adjustments). Also, a U.S. person may be required to comply with specified reporting requirements, regardless of the number of shares owned.

A transfer of our ordinary shares, other than a transfer effected by means of the transfer of book-entry interests in the Depository Trust Company, may be subject to Irish stamp duty.

Transfers of our ordinary shares effected by means of the transfer of book entry interests in the Depository Trust Company, or DTC, will not be subject to Irish stamp duty. However, if you hold our ordinary shares directly rather than beneficially through DTC, any transfer of your ordinary shares could be subject to Irish stamp duty (currently at the rate of 1% of the higher of the price paid or the market value of the shares acquired). Payment of Irish stamp duty is generally a legal obligation of the transferee. The potential for stamp duty could adversely affect the price of our ordinary shares.

Our ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax, or CAT, could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT. Gifts and inheritances passing between spouses are exempt from CAT. Children have a tax-free threshold of €335,000 in respect of taxable gifts or inheritances received from their parents.

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

Shareholder activism, which takes many forms and arises in a variety of situations, has been increasingly prevalent. If we become the subject of certain forms of shareholder activism, such as proxy contests, the attention of our management and our board of directors may be diverted from execution of our business 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 share price could be subject to significant fluctuation or otherwise be adversely affected by the events, risks and uncertainties of any shareholder activism.

We may be classified as a passive foreign investment company for one or more of our taxable years, which may result in adverse U.S. federal income tax consequence to U.S. holders.

A corporation organized outside the United States generally will be classified as a “passive foreign investment company”, or PFIC, for U.S. federal income tax purposes (1) in any taxable year in which (A) at least 75% of its gross income is passive income or (B) on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held for the production of passive income, and (2) as to a given holder who was a holder in such taxable year and regardless of such corporation’s income or asset composition, in any subsequent taxable year, unless certain elections are made by that holder that allow the holder to discontinue that classification as to that holder, generally at a substantial tax cost to that holder. Passive income for this purpose generally includes dividends, interest, royalties, rents, annuities and net gains from commodities, foreign currency and securities transactions and from sales of property that produced, or was held for the production of, passive income (or no income).

Based on our gross income and average value of our gross assets for each relevant taxable year, and given the nature of our business, we do not believe that we were a PFIC for any such taxable year from our initial public offering through the year ended December 31, 2021, although there is no assurance that the IRS will agree with this conclusion. Our status in any taxable year (determined without regard to our status in any prior taxable year) will depend on our assets and activities in that year, and because this is a factual determination made annually after the end of the year, there can be no assurance that we will not be considered a PFIC for the current taxable year or any other taxable year. In particular, in many cases the gross value of our assets may be inferred from the market price of our ordinary shares, which may fluctuate considerably given that market prices of biotechnology companies can be especially volatile. In other cases, factors external to our specific circumstances may make the presumptive relationship between the gross value of our assets and our market capitalization unreliable, in which case the gross value of our individual assets, based upon valuation methods suitable for use in U.S. federal tax matters (the choice of which may vary from taxable year to

taxable year), will govern the determination of our status. While, based on the market price of our ordinary shares, we would be treated as a PFIC in 2021, we believe that the market price renders an unreliable valuation of our gross assets. Based on our valuation of our gross assets taking into account our specific circumstances, we believe that we were not a PFIC in 2021. There is no assurance, however, that the IRS will agree with our valuation.

If we are treated as a PFIC for the taxable year ending December 31, 2022, or any other taxable year during which a U.S. holder held or holds our ordinary shares, certain adverse U.S. federal income tax consequences generally will apply to the U.S. holder. We currently intend to make available, upon request, the information necessary to permit a U.S. holder to make a valid qualified electing fund, or QEF, election, which may mitigate some of the adverse U.S. federal income tax consequences applicable to a U.S. holder of ordinary shares if we are a PFIC for a given taxable year. However, we may choose not to provide such information at a future date.

General Risk Factors

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter such infringement or unauthorized use, we may be required to file claims, which can be expensive, time consuming and a distraction to management. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging our patents, trademarks, copyrights or other intellectual property are invalid or unenforceable or that we infringe their intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

We have broad discretion in the use of our funds and may not use them effectively.

We have broad discretion in the application of our available funds and could spend the funds in ways that do not improve our results of operations or enhance the value of our ordinary shares. Our failure to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our ordinary shares to decline and delay the development of our product candidates. Pending their use, we may invest funds in a manner that does not produce income or that loses value.

We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company we incur, and particularly after we are no longer a smaller reporting company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations have made it more expensive for us to obtain director and officer liability insurance, and if such insurance becomes prohibitively expensive, this could make it more difficult for us to attract and retain qualified members of our board.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Facilities

Our facilities consist of approximately 2,900 square meters of leased laboratory and office space in Vienna, Austria, approximately 8,000 square feet of subleased office space in Fort Washington, Pennsylvania and we also lease office space in Dublin, Ireland and San Diego, California. We believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

We are not currently subject to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our ordinary shares have been listed on the Nasdaq Global Select Market since June 26, 2017 and trade under the symbol "NBRV".

Stockholders

As of January 31, 2022, there were 25 holders of record of our ordinary shares. The number of record holders may not be representative of the number of beneficial owners because many of our ordinary shares are held by depositories, brokers or other nominees.

Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding securities authorized for issuance under our equity compensation plans is contained in Part III, Item 12 of this Annual Report on Form 10-K.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. In addition, the terms of the Loan Agreement with Hercules preclude us from paying dividends. We do not intend to pay cash dividends on our ordinary shares for the foreseeable future.

Recent Sales of Unregistered Securities

We did not sell any of our equity securities or any options, warrants, or rights to purchase our equity securities during the year ended December 31, 2021 that were not registered under the Securities Act of 1933, as amended, or the Securities Act, and that have not otherwise been described in a Current Report on Form 8-K or a Quarterly Report on Form 10-Q.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

ITEM 6. [Reserved]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our historical consolidated financial statements and the related notes thereto appearing elsewhere in this Annual Report. The objective of the following discussion and analysis is to provide material information relevant to your assessment of the financial condition and results of operations of our company, including an evaluation of the amounts and certainty of cash flows from operations and from outside sources, and to better allow you to view our company from management's perspective. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in "Risk Factor Summary and"Risk Factors" in Part I, Item 1A of this Annual Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company engaged in the commercialization and research and development of novel anti-infective agents to treat serious infections. We have the commercial rights to two approved products, SIVEXTRO and XENLETA, as well as one development product candidate, CONTEPO. In August 2019, our first product was approved by the U.S. Food and Drug Administration, or FDA, and we made it available in the United States in September 2019 under the brand name XENLETA. XENLETA (lefamulin) is a first-in-class semi-synthetic pleuromutilin antibiotic for systematic administration in humans discovered and developed by our team. XENLETA is designed to inhibit the synthesis of bacterial protein, that is required for bacteria to grow, by binding with high affinity, high specificity and at molecular targets that are different than other antibiotic classes. Based on results from two global, Phase 3 clinical trials, we believe that XENLETA is well-positioned for use as a first-line monotherapy for the treatment of community-acquired bacterial pneumonia, or CABP, due to its novel mechanism of action, targeted spectrum of activity, resistance profile, achievement of substantial drug concentration in lung tissue and fluid, availability of oral and intravenous, or IV, formulations and a generally well-tolerated safety profile. We believe XENLETA represents a potentially important new treatment option for the five million adults in the United States diagnosed with CABP each year.

Since inception, we have incurred significant operating losses. As of December 31, 2021, we had an accumulated deficit of $595.7 million. To date, we have financed our operations primarily through equity offerings, convertible and term debt financings and research and development support from governmental grants and proceeds from our licensing agreements. We have devoted substantially all of our efforts to research and development, including clinical trials, as well as commercializing SIVEXTRO and XENLETA. Our ability to generate profits from operations and become and remain profitable depends on our ability to successfully develop and commercialize drugs that generate significant revenue.

We expect to continue to incur significant expenses and have negative cash flows for at least the next several years. Our expenses will increase if we suffer any regulatory delays or are required to conduct additional clinical trials to satisfy regulatory requirements. If we obtain marketing approval for CONTEPO or any other product candidate that we develop, in-license or acquire, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. In light of the COVID-19 pandemic, a substantial decrease of non-COVID-19 respiratory infections, the associated disruption to the healthcare delivery and the uncertainty of resuming full direct physician promotion, the timing and amount of sales of SIVEXTRO, XENLETA or any product candidates are uncertain. Based on our current forecasts and plans, we will need to obtain substantial additional funding in connection with our continuing operations. Adequate additional capital may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs and commercialization efforts.

Business Update Regarding COVID-19

On March 11, 2020, the World Health Organization declared the outbreak of COVID-19 as a pandemic. The outbreak had an impact on the global economy, resulting in rapidly changing market and economic conditions. National and local governments around the world instituted certain measures, including travel bans, prohibitions on group events and gatherings, shutdowns of certain non-essential businesses, curfews, shelter-in-place orders and recommendations to practice social distancing. The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and financial markets.

The extent of the impact of COVID-19 on our business will depend on the length and severity of the pandemic, including the extent there is any resurgence of the COVID-19 virus or any variant strains of the virus, the availability and effectiveness of vaccines and the impact of the foregoing on our business. The full extent to which the COVID-19 pandemic will continue to directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted. The full impact of COVID-19 is unknown and may continue as the rates of infection have increased in many states in the U.S., thus additional restrictive measures may be necessary. Federal, state and local governmental policies and initiatives designed to reduce the transmission of COVID-19 have resulted in, among other things, a significant reduction in physician office visits, the cancellation of elective medical procedures, and the adoption of hybrid-remote-working policies, all of which have had, and we believe will continue to have, an impact on our consolidated results of operations, financial position and cash flows.

In response to the COVID-19 pandemic, we closed our administrative offices and shifted to a remote working business model. We have implemented a hybrid-remote-working policy for all of our employees, and we may take further actions that alter our operations as may be required by federal, state, or local authorities, or which we determine are in our best interests. The commercial and medical organizations suspended in-person interactions with physicians and customers and were restricted to conducting educational and promotional activities virtually. The impact of the COVID-19 pandemic could continue to have a material adverse effect on our business, results of operations, financial condition, liquidity and prospects in the near-term and beyond 2022. While we have used all currently available information in our forecasts, the ultimate impact of the COVID-19 pandemic and our product sales for SIVEXTRO and XENLETA, on our results of operations, financial condition and cash flows is highly uncertain, and cannot currently be accurately predicted. According to the Centers for Disease Control and Prevention, or CDC, there have been lower incidences of influenza-like illness cases within the United States from a median of 49,696 per week during the period of September 2019 through February 2020, to 19,537 during the period of March through May 2020, which are largely responsible for the seasonality observed with community-acquired bacterial pneumonia and which lead to the decrease in bacterial respiratory tract infection rates, indicated by the decrease in the number of physician office visits, hospitalizations and antibiotic prescriptions. Data from clinical laboratories in the United States indicated a 61% decrease in the number of specimens submitted and a 98% decrease in influenza activity as measured by percentage of submitted specimens testing positive. Our results of operations, financial condition and cash flows are dependent on future developments, including the duration of the pandemic and the related length of its impact on the global economy or any other negative trend in the U.S. or global economy and any new information that may emerge concerning the COVID-19 pandemic and the actions to contain it or treat its impact, which at the present time are highly uncertain and cannot be predicted with any accuracy.

SIVEXTRO is approved for the treatment of ABSSSIs caused by certain susceptible Gram-positive microorganisms. Before we were permitted to sell SIVEXTRO under the Distribution Agreement, we were required to secure a sales force of a certain size and the restrictions related to COVID-19 needed to be eased in a sufficient manner to permit us to promote and distribute SIVEXTRO. Re-securing a sales force of a certain size for the promotion and distribution of SIVEXTRO has resulted in significant additional expense and our efforts to maintain a sales force may not be successful. We have secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace our hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. We expanded this effort to 60 sales representatives in 2021 and may expand it further. We also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

XENLETA is approved for the treatment of CABP in adults in the United States. The National Institute for Allergy and Infectious Diseases, or NIAID, has identified that secondary bacterial pneumonia caused by common upper respiratory tract bacteria plays a predominant role in the cause of death in pandemic influenza. NIAID recommends that the prevention, diagnosis, prophylaxis, and treatment of secondary bacterial pneumonia, as well as the stockpiling of antibiotics and bacterial vaccines, be high priorities for pandemic planning. We believe there is a potential for XENLETA to be considered for U.S. government stockpiling for pandemic preparedness.

Two ongoing pediatric Phase 1 clinical trials for lefamulin and IV fosfomycin were temporarily closed for enrollment as hospitals suspended access and non-essential clinical research to focus on health care delivery to COVID-19 patients. As of July 2020, both trials started to re-open, where allowed by the institution, and initiated screening of potential subjects at sites.

Financial Operations Overview

Revenue

In September 2019 we launched XENLETA and in April 2021 we began exclusive distribution of SIVEXTRO in the United States and certain of its territories. For the year ended December 31, 2021, we recorded $23.8 million of SIVEXTRO product revenue, net of gross-to-net accruals and adjustments for returns, and $(0.4) million of XENLETA product revenue, net of gross-to-net accruals and adjustments for returns. Our distribution partners had primarily utilized their existing inventory from the initial launch to satisfy product demand for XENLETA, which in turn impacted sales during the year ended December 31, 2021. Given the fact that the launch lot inventory had 36 month dating, and has a near term shelf life expiration, we recorded a $1.3 million returns reserve adjustment during 2021. We launched a new 10-count blister pack of XENLETA in the fourth quarter of 2021, which has four year dating for expiry. Future product revenues will be subject to the amount and frequency of reorders from our wholesale customers based on the ultimate consumption patterns from the end users of SIVEXTRO and XENLETA.

Collaboration revenues for the year ended December 31, 2021 included $2.6 million related to the restructured China Region License Agreement, a portion of which is recognized over the estimated period the manufacturing collaboration and regulatory support will be provided to Sumitomo Pharmaceuticals (Suzhou), as well as $1.2 million of our share of revenues through April 11, 2021 associated with the SIVEXTRO distribution agreement with Merck & Co., Inc. which commenced at the end of September 2020.

Our revenues for the year ended December 31, 2021 included governmental research premiums, non-refundable government grants, collaboration revenues and the benefit of government loans at below-market interest rates.

Cost of Revenues

Cost of revenues represented 17.0%, 1.1% and 0.1% of our total operating expenses for the years ended December 31, 2021, 2020 and 2019, respectively. Cost of revenues primarily represent the cost of the product itself, labor and overhead, and any reserve for excess or obsolete inventory. Other cost of revenues include costs associated with the manufacturing collaboration and regulatory support under our licensing agreements. The increase in cost of revenue for the year ended December 31, 2021 was primarily due to the launch of SIVEXTRO under our own National Drug Code, or NDC, on April 12, 2021.

Research and Development Expenses

Research and development expenses represented 16.3%, 21.2% and 29.7% of our total operating expenses for the years ended December 31, 2021, 2020 and 2019, respectively.

For each of our research and development programs, we incur both direct and indirect expenses. Direct expenses include third-party expenses related to these programs such as expenses for manufacturing services (prior to our products receiving FDA approval, after which time these costs are capitalized in inventory until product is sold),

non-clinical and clinical studies and other third party development services. Indirect expenses include salaries and related costs, including stock-based compensation, for personnel in research and development functions, infrastructure costs allocated to research and development operations, costs associated with obtaining and maintaining intellectual property associated with our research and development operations, laboratory consumables, consulting fees related to research and development activities and other overhead costs. We utilize our research and development staff and infrastructure resources across multiple programs, and many of our indirect costs historically have not been specifically attributable to a single program. Accordingly, we cannot state precisely our total indirect costs incurred on a program-by-program basis.

The following table summarizes our direct research and development expenses by program and our indirect costs.

	Year Ended Ended December 31,		
(in thousands)	**2021**	**2020**	**2019**
Direct Costs			
XENLETA	$ 2,891	$ 2,119	$ 7,765
CONTEPO	340	450	2,977
FDA filing fee refund	—	—	(2,589)
Other programs and initiatives	1,383	1,347	1,412
Indirect Costs	8,016	11,186	16,850
Total research and development expenses	**$ 12,630**	**$ 15,102**	**$ 26,415**

We expect to continue to incur research and development expenses in connection with required regulatory activities, our activities related to our ongoing pediatric studies of lefamulin for the treatment of CABP and of CONTEPO for the treatment of cUTI, and may incur costs related to the pursuit of the clinical development of lefamulin and CONTEPO for additional indications including the treatment of resistant bacterial infections in patients with cystic fibrosis, or CF and engagement in earlier stage research and development activities. We initiated screening of our Phase 1 clinical trial of XENLETA for the treatment of resistant bacterial infections in patients with CF in March 2022, and are on track to begin dosing in April 2022. Given the ongoing COVID-19 pandemic and the high risk it puts CF patients under, it is difficult to estimate recruitment timelines at this time. It is difficult to estimate the duration and completion costs of our research and development programs.

The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the efficacy and potential advantages of our product candidates compared to alternative treatments, including any standard of care, and our ability to achieve market acceptance for any of our product candidates that receive marketing approval;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- the costs, timing and outcome of regulatory review of our product candidates;
- the scope, progress, costs and results of clinical trials and other research and development activities; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining, enforcing and protecting our intellectual property rights and defending against any intellectual property-related claims.

A change in the outcome of any of these variables with respect to the development of our product candidates could result in a significant change in the costs and timing associated with the development of that product candidate.

For example, if the FDA or another regulatory authority were to require us to conduct clinical trials or other testing beyond those that we have completed or currently contemplate will be required for the completion of clinical development of any product candidate, we could be required to expend significant additional resources and time on the completion of clinical development of that product candidate.

Selling, General and Administrative Expenses

Selling, general and administrative expenses represented 66.7%, 77.7%, and 70.2% of our total operating expenses for the years ended December 31, 2021, 2020 and 2019, respectively.

Selling, general and administrative expenses consist primarily of salaries and related costs, including stock-based compensation not related to research and development activities for personnel in our commercial, medical affairs, finance, information technology and administrative functions, as well as costs related to our contract commercial organization, to provide community-based commercial and sales services. Selling, general and administrative expenses also include costs related to professional fees for auditors, lawyers and tax advisors and consulting fees not related to research and development operations, as well as functions that are partly or fully outsourced by us, such as accounting, payroll processing and information technology.

We expect selling, general and administrative expenses in 2022 to be comparable to 2021.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP. The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the end of the reporting period, as well as the reported revenues and expenses during the reporting periods and how our estimates and assumptions have changed over each relevant reporting period. However, these estimates and assumptions are subject to uncertainty, due to unknown trends and events and various other factors that we believe to be reasonably likely under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies and estimates are described in more detail in the notes to our consolidated financial statements appearing at the end of this filing. However, we believe that the following accounting policies and estimates are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

Under Accounting Standards Codification, or ASC, 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied as services are rendered.

The transaction price that we recognize as revenue reflects the amount we expect with the sale and transfer of control of the product to our customers. Once the customer takes control of the product, our performance obligation under the sale contract is complete and revenue is recorded net of applicable reserves for various types of variable consideration. The types of variable consideration are as follows and are further described in Note 2 in our Consolidated Financial Statements.

- Fees-for-service

- Product returns
- Chargebacks and rebates
- Government rebates
- Commercial payer and other rebates
- Group Purchasing Organizations, or GPO, administration fees
- Voluntary patient assistance programs

In determining the amounts of variable consideration, we must make significant judgments and estimates. In assessing the amount of net revenue to record, we consider both the likelihood and the magnitude of the revenue reversal. Actual amounts of consideration ultimately received may differ significantly from our estimates. If actual results in the future vary from our estimates, we adjust our estimates which would affect net product revenue and earnings in the period such variances become known.

XENLETA Inventory and Purchase Commitments

Our XENLETA inventory is stated at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis, and consists primarily of material costs, third-party manufacturing costs, and related transportation costs in our supply chain. Our inventory is subject to expiration dating, which can be extended in certain circumstances. We also have non-cancellable purchase commitments for XENLETA active pharmaceutical ingredient, or API. We continually evaluate forecasted product sales for XENLETA which is used in estimating the need to reserve for estimated excess, slow-moving and obsolete inventory on hand and potential accrued losses on firm purchase committments. During the years ended December 31, 2021 and 2020, we recorded $0.3 million and $0.7 million, respectively, of non-cash reserves for excess and obsolete inventory due to timing of expiry dating of expiring inventory.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

(in thousands)	Year Ended December 31, 2021	2020	Change
Consolidated operations data:			
Product revenue, net	$ 23,386	$ 108	$ 23,278
Collaboration revenue	3,830	2,756	1,074
Research premium and grant revenue	1,679	2,163	(484)
Total revenue	28,895	5,027	23,868
Costs and expenses:			
Cost of revenues	(13,148)	(766)	(12,382)
Research and development expenses	(12,630)	(15,102)	2,472
Selling, general and administrative expenses	(51,645)	(55,285)	3,640
Total operating expenses	(77,423)	(71,153)	(6,270)
Loss from operations	**(48,528)**	**(66,126)**	**17,598**
Other income (expense):			
Other income (expense), net	469	1,187	(718)
Interest income (expense), net	(901)	(1,649)	748
Loss on extinguishment of debt	—	(2,757)	2,757
Loss before income taxes	**(48,960)**	**(69,345)**	**20,385**
Income tax expense	(490)	(139)	(351)
Net loss	**$ (49,450)**	**$ (69,484)**	**$ 20,034**

Revenues

Revenues for the year ended December 31, 2021 were $28.9 million compared to $5.0 million for the year ended December 31, 2020. The $23.9 million increase was primarily due to $23.8 million in SIVEXTRO product revenue, net since the launch of SIVEXTRO under our own NDC on April 12, 2021.

Cost of Revenues

Cost of revenues for the year ended December 31, 2021 was $13.1 million compared to $0.8 million for the year ended December 31, 2020. The $12.4 million increase was primarily due to the launch of SIVEXTRO under our own NDC on April 12, 2021. Cost of revenues for XENLETA primarily represents direct and indirect manufacturing costs, while cost of revenues for SIVEXTRO represent the actual purchase cost for the finished product from Merck. Prior to the FDA approval of XENLETA on August 19, 2019, the inventory costs for XENLETA were expensed as research and development expenses since the approval was outside of our control and therefore not considered probable. As such, the majority of the expenses incurred for our initial inventories of XENLETA has been previously expensed. For the years ended December 31, 2021 and 2020, cost of revenues include $0.3 million and $0.7 million, respectively, of a non-cash reserve adjustment for excess and obsolete inventory due to timing of expiring inventory.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2021 were $12.6 million compared to $15.1 million for the year ended December 31, 2020. The $2.5 million decrease was primarily due to a $0.7 million decrease in stock-based compensation expense, a $1.0 million decrease in staff costs, and a $0.7 million decrease in study costs.

Selling, General and Administrative Expenses

Selling, general and administrative expense for the year ended December 31, 2021 were $51.6 million compared to $55.3 million for the year ended December 31, 2020. The $3.6 million decrease was primarily due to a $5.9

million decrease in staff costs due to the reduction of headcount, a $1.2 million decrease in stock-based compensation expense, a $0.7 million decrease in travel costs, a $0.6 million decrease in infrastructure costs, and a $2.5 million decrease in professional fees, partly offset by a $7.4 million increase in advisory and external consultancy expenses primarily related to commercialization activities and professional service fees for the relaunch of SIVEXTRO and XENLETA.

Other Income (Expense), net

Other income (expense), net, decreased by $0.7 million for the year ended December 31, 2021 primarily due to remeasurements of our foreign currency account balances.

Interest Income (Expense), net

Interest income (expense), net decreased by $0.7 million due the repayment of indebtedness under our Loan Agreement with Hercules in March 2020. See Note 7 to our consolidated financial statements included elsewhere in this Form 10-K for further information.

Loss on Extinguishment of Debt

In connection with the third amendment to our Loan Agreement with Hercules, we recognized a non-cash $2.8 million loss on the extinguishment of debt during the year ended December 31, 2020, which represents the excess of the reacquisition price of the $30.0 million debt repaid over the net carrying amount of the extinguished debt. We did not have a loss on the extinguishment of debt during the year ended December 31, 2021.

Income Tax Expense

Our income tax expense was $0.5 million for the year ended December 31, 2021 compared to $139,000 for the year ended December 31, 2020.

Comparison of Years Ended December 31, 2020 and 2019

(in thousands)	Year Ended December 31, 2020	2019	Change
Consolidated operations data:			
Product revenue, net	$ 108	$ 1,538	$ (1,430)
Collaboration revenue	2,756	6,210	(3,454)
Research premium and grant revenue	2,163	1,733	430
Total revenue	5,027	9,481	(4,454)
Costs and expenses:			
Cost of revenues	(766)	(70)	(696)
Research and development expenses	(15,102)	(26,415)	11,313
Selling, general and administrative expenses	(55,285)	(62,485)	7,200
Total operating expenses	(71,153)	(88,970)	17,817
Loss from operations	**(66,126)**	**(79,489)**	**13,363**
Other income (expense):			
Other income (expense), net	1,187	215	972
Interest income (expense), net	(1,649)	(3,389)	1,740
Loss on extinguishment of debt	(2,757)	—	(2,757)
Loss before income taxes	**(69,345)**	**(82,663)**	**13,318**
Income tax expense	(139)	(101)	(38)
Net loss	**$ (69,484)**	**$ (82,764)**	**$ 13,280**

Revenues

Revenues for the year ended December 31, 2020 were $5.0 million compared to $9.5 million for the year ended December 31, 2019. The $4.5 million decrease was primarily due to a $3.5 million decrease in collaboration revenue and a $1.4 million decrease in product revenue, net, partially offset by a $0.4 million increase in research premiums and government grants provided to us by the Austrian government. The decrease in collaboration revenues was primarily due to the $5.0 million recognized in 2019 under our China Region License Agreement, partially offset by $1.8 million recognized in 2020 under our SIVEXTRO distribution agreement with Merck & Co., Inc.

Cost of Revenues

Cost of revenues primarily represents direct and indirect manufacturing costs of our XENLETA product. Prior to the FDA approval of XENLETA on August 19, 2019, the inventory costs for the product were expensed as research and development expenses since the approval was outside of our control and therefore not considered probable. As such, the majority of the expenses incurred for our initial inventories of XENLETA has been previously expensed. As a result, we anticipate that our cost of revenues for XENLETA will remain at relatively low levels for a period of time until our initial pre-launch inventory stock has been distributed by our customers based on end user consumption demand. For the year ended December 31, 2020, cost of revenues include a $0.7 million non-cash reserve for excess and obsolete inventory due to timing of expiring inventory.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2020 were $15.1 million compared to $26.4 million for the year ended December 31, 2019. The $11.3 million decrease was primarily due to a $7.2 million decrease in research materials and purchased services related to the development of lefamulin, a $2.9 million decrease in staff costs due to the reduction of employees, a $2.0 million decrease in research consulting fees, a $0.9 million decrease in stock-based compensation expense and $0.4 million decrease in travel expenses, partly offset by a $2.0 million increase in other fees due to a $2.6 million NDA filing fee refund for CONTEPO in 2019.

Selling, General and Administrative Expenses

Selling, general and administrative expense for the year ended December 31, 2020 were $55.3 million compared to $62.5 million for the year ended December 31, 2019. The $7.2 million decrease was primarily due to a $4.2 million decrease in staffing expense related to the termination of our sales force in early 2020, $3.7 million decrease in stock-based compensation expense, a $1.6 million decrease in travel expenses, a $0.7 million decrease in advisory and external consultancy expenses primarily related to commercialization activities and professional service fees, and a $0.1 million decrease in other corporate costs, partly offset by a $1.2 million increase in insurance costs, a $1.5 million increase in professional fees.

Other Income (Expense), net

Other income (expense), net was $1.2 million for the year ended December 31, 2020 compared to a $0.2 million for the year ended December 31, 2019. The $1.0 million increase was primarily from $0.6 million income from the sublease of our laboratory and office space in Vienna, Austria.

Interest Income (Expense), net

Interest income (expense), net decreased by $1.7 million due to the repayment of $30.0 million of indebtedness under our Loan Agreement with Hercules in March 2020. See Note 7 to our consolidated financial statements included elsewhere in this Form 10-K for further information.

Loss on Extinguishment of Debt

In connection with the repayment of our Loan Agreement with Hercules, we recognized a non-cash $2.8 million loss on the extinguishment of debt during the year ended December 31, 2020, which represents the excess of the reacquisition price of the $30.0 million debt repaid over the net carrying amount of the extinguished debt.

Income Tax Expense

Our income tax expense was $139,000 for the year ended December 31, 2020 compared to $101,000 for the year ended December 31, 2019.

Liquidity and Capital Resources

Since our inception, we have incurred net losses and generated negative cash flows from our operations. To date, we have financed our operations through the sale of equity securities, convertible and term debt financings, research and development support from governmental grants and loans and proceeds from licensing agreements. As of December 31, 2021, we had cash and cash equivalents, restricted cash and short-term investments of $47.9 million. We will need to obtain substantial additional funding to achieve our business objectives during the next 12 months and beyond. If we are unable to raise additional funds when needed, including through the sale of our ordinary shares for cash, we may be unable to pursue our business plans and strategy, and we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Additionally, our inability to raise funds when needed may cause investors to lose confidence in us and raise substantial doubt about our ability to continue as a going concern, which may cause our share price to decline.

In September 2021, we entered into a purchase agreement, or Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which, subject to the terms and conditions, provides that we have the right to sell to Lincoln Park and Lincoln Park is obligated to purchase up to $23.0 million of our ordinary shares. In addition, under the Purchase Agreement, we agreed to issue a commitment fee of 632,474 ordinary shares, or the Commitment Shares, as consideration for Lincoln Park entering into the Purchase Agreement and for the payment of $0.01 per Commitment Share. Under the Purchase Agreement, we may from time to time, at our discretion, direct Lincoln Park to purchase on any single business day, or a Regular Purchase, up to (i) 400,000 ordinary shares if the closing sale price of our ordinary shares is not below $0.25 per share on Nasdaq, (ii) 600,000 ordinary shares if the closing sale price of our ordinary shares is not below $2.00 per share on Nasdaq or (iii) 800,000 ordinary shares if the closing sale price of our ordinary shares is not below $3.00 per share on Nasdaq. In addition to Regular Purchases, we may also direct Lincoln Park to purchase other amounts as accelerated purchases or as additional accelerated purchases on the terms and subject to the conditions set forth in the Purchase Agreement. In any case, Lincoln Park's commitment in any single Regular Purchase may not exceed $2.5 million absent a mutual agreement to increase such amount. As of December 31, 2021, we have issued and sold an aggregate of 2,400,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $2.4 million. From January 1, 2022 and through the date of this filing, we have issued and sold an aggregate of 3,600,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $1.6 million. As of the date of this filing, we may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the Purchase Agreement, subject to the Nasdaq rules which may limit our ability to make sales of our ordinary shares to Lincoln Park in excess of a specified amount without prior shareholder approval.

In May 2021, we entered into an Open Market Sale Agreement[SM], or the New Sale Agreement, with Jefferies, as agent, pursuant to which we may offer and sell ordinary shares for aggregate gross sale proceeds of up to $50.0 million, from time to time through Jefferies, by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. Upon entry into the New Sale Agreement, our existing Jefferies ATM Agreement entered into in June 2019 was terminated. We did not incur any termination penalties as a result of the replacement of the Jefferies ATM Agreement. As of December 31, 2021, we have issued and sold an aggregate of 18,232,689 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $30.5 million and net proceeds of $29.3 million, after deducting commissions to Jefferies and other offering expenses. From January 1, 2022 and through the date of this filing, we have issued and sold an aggregate of 1,338,282

ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $595,000 and net proceeds of $580,000, after deducting commissions to Jefferies and other offering expenses.

In March 2021, we entered into a securities purchase agreement with certain institutional investors pursuant to which we agreed to issue and sell in a registered direct offering (1) an aggregate of 9,761,010 ordinary shares, $0.01 nominal value per share, and accompanying warrants to purchase up to an aggregate of 4,880,505 ordinary shares and (2) pre-funded warrants to purchase up to an aggregate of 600,000 ordinary shares and accompanying ordinary share warrants to purchase up to an aggregate of 300,000 ordinary shares. Each share was issued and sold together with an accompanying ordinary share warrant at a combined price of $2.4525, and each pre-funded warrant was issued and sold together with an accompanying ordinary share warrant at a combined price of $2.4425. The proceeds to us from the offering were $25.4 million gross and $23.4 million net after deducting the placement agent's fees and estimated offering expenses. Each pre-funded warrant had an exercise price per ordinary share equal to $0.01 and each pre-funded warrant was exercised in full on the issuance date. Each ordinary share warrant has an exercise price per ordinary share equal to $2.39, was exercisable on the date of issuance and will expire on the five-year anniversary of the date of issuance.

In December 2020, we completed a registered public offering in which we sold 6,000,000 ordinary shares at a public offering price of $2.50. The proceeds to us from the offering were $15.0 million gross and $13.3 million net, after deducting the placement agent's fees and offering expenses. In December 2018, we announced the closing of up to a $75.0 million term loan with Hercules, or the Loan Agreement, $25.0 million of which was funded on the day of closing. Under the terms of the loan, in addition to the $25.0 million received at closing, we borrowed an additional $10.0 million in connection with the approval by the FDA of the NDA for XENLETA. In March 2020, we repaid Hercules $30.0 million of the $35.0 million in aggregate principal amount of debt outstanding under the Loan Agreement. See Note 7 to the consolidated financial statements included elsewhere in this Form 10-K for additional information on the terms associated with the remaining term loans potentially available to us and the costs and other conditions associated with this funding source.

Cash Flows

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our cash flows for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
(in thousands)	**2021**	**2020**
Net cash (used in) provided by:		
Operating activities	$ (59,557)	$ (71,331)
Investing activities	(81)	(274)
Financing activities	66,366	26,924
Effects of foreign currency translation on cash	(484)	(140)
Net increase/(decrease) in cash, cash equivalents and restricted cash	**$ 6,244**	**$ (44,821)**

Operating Activities

Cash flow used in operating activities decreased by $11.8 million from $71.3 million for the year ended December 31, 2020 to $59.6 million for the year ended December 31, 2021 primarily due to a $15.2 million decrease in net loss, after adjustments for non-cash amounts included in net loss, offset by a higher working capital of $3.5 million primarily due to increases in inventory and accounts receivable driven by the launch of SIVEXTRO under our own NDC in April 2021.

Investing Activities

Cash flow used in investing activities decreased by $0.2 million from $0.3 million cash used for the year ended December 31, 2020 to $0.1 million cash used for the year ended December 31, 2021 primarily due to changes in restricted cash and lower investments in property, plant and equipment.

Financing Activities

Cash flow generated from financing activities for the year ended December 31, 2021 was $66.4 million from our March 2021 financing, our Purchase Agreement with Lincoln Park, as well as our New Sale Agreement. Cash flow generated from financing activities for the year ended December 31, 2020 was $26.9 million, primarily from total net proceeds of approximately $56.9 million from the securities purchase agreements entered into in May 2020 and December 2020, warrant exercises, as well as our Jefferies ATM Agreement, partly offset by the repayment of $30.0 million of long-term borrowings on our debt facility in the year ended December 31, 2020.

Comparison of Years Ended December 31, 2020 and 2019

The following table summarizes our cash flows for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
(in thousands)	**2020**	**2019**
Net cash (used in) provided by:		
Operating activities	$ (71,331)	$ (71,892)
Investing activities	(274)	331
Financing activities	26,924	56,075
Effect of foreign currency translation on cash	(140)	(106)
Net decrease in cash, cash equivalents and restricted cash	**$ (44,821)**	**$ (15,592)**

Operating Activities

Cash flow used in operating activities decreased by $0.6 million from $71.9 million for the year ended December 31, 2019 to $71.3 million for the year ended December 31, 2020 primarily due to a $11.8 million decrease in net loss, after adjustments for non-cash amounts included in net loss and higher working capital of $11.2 million primarily due to a decrease in accrued expenses and other current liabilities and an increase in inventory.

Investing Activities

Cash flow provided by investing activities decreased by $0.6 million from $0.3 million cash provided for the year ended December 31, 2019 to $0.3 million cash used for the year ended December 31, 2020 primarily due to changes in restricted cash.

Financing Activities

Cash flow provided by financing activities decreased by $29.2 million from $56.1 million for the year ended December 31, 2019 to $26.9 million for the year ended December 31, 2020 primarily due to the repayment of $30.0 million of long-term borrowings on our debt facility and lower net proceeds of $20.4 million related to sales of our ordinary shares under our ATM Agreements , partly offset by higher net proceeds of $33.3 million from our May 2020 and December 2020 equity offerings of ordinary shares, as well as the exercise of warrants.

Material Cash Requirements

We anticipate that our expenses will increase as we expect to incur significant additional commercialization expenses related to product sales, marketing, distribution and manufacturing. In addition, our expenses will increase if we suffer any regulatory delays or are required to conduct additional clinical trials to satisfy regulatory requirements.

In addition, our expenses will increase if and as we:

- initiate or continue the research and development of XENLETA and CONTEPO for additional indications and of our other product candidates;
- seek to develop additional product candidates;
- seek marketing approval for any product candidates that successfully complete clinical development;
- are required by the FDA, EMA or other regulators to conduct additional clinical trials prior to or after approval;
- continue to build or re-build a medical affairs, sales, marketing and distribution infrastructure and scale up manufacturing capabilities to commercialize SIVEXTRO, XENLETA and any other product candidates for which we receive marketing approval;
- in-license or acquire other products, product candidates or technologies, including additional community products;
- maintain, expand and protect our intellectual property portfolio;
- expand our physical presence in the United States and Ireland;
- incur additional debt;
- establish and expand manufacturing arrangements with third parties; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and our operations as a public company in addition to our commercialization efforts.

As described above, on March 11, 2020, we entered into a Third Amendment to our Loan Agreement with Hercules. Pursuant to the Third Amendment, we repaid to Hercules in March 2020, $30.0 million of the $35.0 million in aggregate principal amount of debt outstanding under the Loan Agreement, which we refer to as the Prepayment. Under the Third Amendment, we and Hercules agreed to defer the end of term loan charge payment in the amount of approximately $2.1 million that would have otherwise become payable on the date of the Prepayment and to reduce the prepayment charge with respect to the Prepayment from $600,000 to $300,000 and to defer its payment, in each case, until June 1, 2023 or such earlier date on which all loans under the Loan Agreement are repaid or become due and payable. The Third Amendment also reset the revenue performance covenant to 70% of targeted revenue based on a revised net product revenue forecast and lowered our minimum liquidity requirement to $3.0 million in cash and cash equivalents, in each case, following the Prepayment. The new minimum liquidity requirement will not apply if CONTEPO receives regulatory approval from the U.S. Food and Drug Administration and we achieve at least 70% of our revised net product revenue targets under the Loan Agreement. On June 2, 2021, we entered into a further amendment, or the Fourth Amendment, to our Loan Agreement with Hercules. Pursuant to the Fourth Amendment, the date on which we must commence repaying principal under the Loan Agreement was extended to April 1, 2022, which date may be extended until July 1, 2022, subject to our receipt of a specified amount of additional net financing proceeds and the achievement of a specified product revenue milestone. Additionally, the time during which the Tranche Advance (as defined in Note 7 to our consolidated financial statements) may be requested by us under the Loan Agreement was extended until the Amortization Date. In addition, pursuant to the Fourth Amendment, the minimum liquidity requirement of $3.0 million in cash and cash equivalents will be waived at any time we have recognized $15.0 million of net product revenue during the applicable trailing three months. Based on our current operating plans, we expect that our existing cash resources as of the date of this Annual Report on Form 10-K will be sufficient to enable us to fund our operations, debt service obligations and capital expenditure requirements well into the fourth quarter of 2022. We have

based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not obtain any additional funding through grants and clinical trial support, collaboration agreements, or equity or debt financings. This estimate also assumes that we remain in compliance with the covenants and no event of default occurs under the Loan Agreement.

We expect to continue to invest in critical commercial promotion and distribution, medical affairs and other commercialization activities, as well as investing in our supply chain for the commercialization of SIVEXTRO, XENLETA and, if approved, CONTEPO. We expect to seek additional funding in future periods to support these activities.

Our future capital requirements will depend on many factors, including:

- the costs and timing of process development and manufacturing scale-up activities associated with XENLETA and CONTEPO;
- the costs to secure supply of SIVEXTRO and costs to sell and market the product in the U.S.;
- the costs, timing and outcome of regulatory review of lefamulin in Europe and for any other indications and CONTEPO;
- the costs of commercialization activities for SIVEXTRO, XENLETA and potentially CONTEPO if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and outsourced manufacturing capabilities, including the costs of building finished product inventory and its components in preparation of initial marketing of CONTEPO, if approved;
- the commercial success of SIVEXTRO and XENLETA and the amount and frequency of reorders or product returns by our wholesale customers;
- subject to the resubmission of our NDA for CONTEPO and potential receipt of marketing approval, revenue received from commercial sales of CONTEPO;
- the costs of developing XENLETA and CONTEPO for the treatment of additional indications;
- the impact of the COVID-19 pandemic;
- our ability to establish collaborations on favorable terms, if at all;
- the scope, progress, results and costs of product development of any other product candidates that we may develop;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies, including additional community products;
- the costs related to the promotion, sale and distribution of the products under our Distribution Agreement with Merck & Co., Inc.;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property-related claims;
- the continued availability of Austrian governmental grants;
- the need to satisfy interest and principal obligations under our Loan Agreement with Hercules as well as the covenants contained in our Loan Agreement;

- the rate of the expansion of our physical presence in the United States and Ireland; and
- the costs of operating as a public company in the United States.

Our commercial revenues, if any, will be derived from sales of SIVEXTRO, XENLETA, and if approved, CONTEPO or any other products that we successfully develop, in-license or acquire. In addition, SIVEXTRO, XENLETA and, if approved, CONTEPO or any other product candidate that we develop, in-license or acquire may not achieve commercial success. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, and funding from local and international government entities and non-government organizations in the disease areas addressed by our product candidates and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity, warrants or convertible debt securities, the ownership interest of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing shareholders. Additional debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

In addition, as part of our corporate strategy, we continue to evaluate business development opportunities and potential collaborations. We may further expand our product pipeline through opportunistically in licensing or acquiring the rights to complementary products, product candidates and technologies for the treatment of a range of infectious diseases or other products that we would market with our commercial infrastructure, including additional community products, which could involve an acquisition of or combination or other strategic transaction with another operating business. To the extent any additional business development opportunity is consummated, our capital expenditures may increase significantly.

We have contractual commitments related primarily to contracts entered into with contract manufacturing organizations and contract research organizations in connection with the commercial manufacturing of XENLETA, the purchase of SIVEXTRO finished product and other research and development activities. The contractual commitments are further described in Note 15 to our consolidated financial statements included elsewhere in this Form 10-K.

Capital Expenditures

Capital expenditures were $25,000 and $0.1 million for the year ended December 31, 2021 and 2020, respectively. Currently, there are no material capital projects planned in 2022.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET

We are exposed to a variety of financial risks in the ordinary course of our business: market risk, credit risk and liquidity risk. Our overall risk management program focuses on preservation of capital given the unpredictability of financial markets. These market risks are principally limited to interest rate and foreign currency fluctuations.

Market Risk

We do not have any significant credit risk exposure to any single counterparty or any group of counterparties having similar characteristics. The credit risk on liquid funds (bank accounts, cash balances, marketable securities and term deposits) is limited because the counterparties are banks with high credit ratings from international credit rating agencies. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We do not enter into investments for trading or speculative purposes.

We are exposed to foreign exchange risk arising from various currency exposures, primarily with respect to the euro and the British pound. Our functional currency is the U.S. dollar, but we receive payments and acquire materials, in each of these other currencies. We have not established any formal practice to manage the foreign exchange risk against our functional currency. However, we attempt to minimize our net exposure by buying or selling foreign currencies at spot rates upon receipt of new funds to facilitate committed or anticipated foreign currency transactions.

Interest rate risk may arise from short-term or long-term debt. Our outstanding indebtedness with Hercules bears interest at the greater of 9.80% and 9.80% plus the prime rate of interest minus 5.50%. Based on the current prime rate, our outstanding indebtedness with Hercules bears interest at 9.80%. If the prime rate increases to over 5.50%, the interest on our loan with Hercules will increase.

Inflation generally affects us by increasing our cost of labor and research, manufacturing and development costs. We believe that inflation has not had a material effect on our financial statements included elsewhere in this Annual Report on Form 10-K. However, our operations may be adversely affected by inflation in the future.

Liquidity Risk

Since our inception, we have incurred net losses and generated negative cash flows from our operations. We anticipate based on our current operating plans, that our existing cash, cash equivalents, restricted cash and short-term investments as of the date of this Annual Report on Form 10-K will be sufficient to enable us to fund our operating expenses, debt service obligations and capital expenditure requirements well into the fourth quarter of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not obtain any additional funding through grants and clinical trial support, collaboration agreements or equity or debt financings.

We expect to continue to invest in critical commercial and medical affairs activities, as well as investing in our supply chain for the commercialization of SIVEXTRO, XENLETA and the potential launch of CONTEPO. We expect to seek additional funding in future periods to support these activities.

If we obtain marketing approval for CONTEPO or any other product candidate that we develop, in-license or acquire, we expect to incur significant additional commercialization expenses related to distribution and manufacturing. Our expenses will increase if we suffer any delays in our clinical programs, including regulatory delays, or are required to conduct additional clinical trials to satisfy regulatory requirements.

There can be no assurance that we will be successful in acquiring additional capital at a level sufficient to fund our operations or on terms favorable to us. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-33 of this Annual Report on Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

We have carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) under the supervision and the participation of the company's management, which is responsible for the management of the internal controls, and which includes our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively). The term "disclosure controls and procedures", as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms.

Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act of 1934 is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives. Based upon our evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable level of assurance.

Management's Annual Report on Internal Control Over Financial Reporting

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

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(e) under the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we

conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled "*Internal Control—Integrated Framework (2013)"* published by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2021, the end of our most recent fiscal year.

Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain a "smaller reporting company" as defined in Rule 12b-2 under the Exchange Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f)) that occurred during the three months ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Board of Directors

Set forth below are the names and certain biographical information about each member of our board of directors, including their ages as of March 1, 2022. The information presented includes each director's principal occupation and business experience for at least the past five years and the names of other public companies of which he or she has served as a director during the past five years.

Name	Age	Position
Daniel Burgess(1)(3)	60	Director, Chairman of the Board
Theodore Schroeder	66	Director, Chief Executive Officer
Colin Broom, MD	66	Director
Carrie Bourdow(2)(3)	59	Director
Mark Corrigan(1)	64	Director
Lisa Dalton(2)	49	Director
Charles Rowland, Jr.(2)	63	Director
Stephen Webster(1)(3)	61	Director
Steven Gelone	54	Director, President and Chief Operating Officer

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the nominating and corporate governance committee.

Daniel Burgess has served on our board of directors since June 23, 2017. Mr. Burgess was a member of the supervisory board of Nabriva Austria and served as its chairman from October 2016 until the redomiciliation to Ireland. Mr. Burgess has been a venture partner at SV Health Investors (SV) since 2014. Mr. Burgess is currently the chairman of the board and chief executive officer of Pulmocide Ltd., a private biopharmaceutical company, a position he has held since May 2021. Mr. Burgess served as the part-time president and chief executive officer of Therini Bio, Inc., a private therapeutics company, from May 2019 to December 2021. He was previously president and chief executive officer of Rempex Pharmaceuticals, an antibiotics company he co-founded in 2011 and that was subsequently sold to The Medicines Company (now Novartis AG) in 2013. Prior to this, Mr. Burgess was president and chief executive officer of Mpex Pharmaceuticals from 2007 until its acquisition by Aptalis Inc. (now AbbVie Inc.) in 2011. Prior to his time at Mpex, Mr. Burgess served in various senior operating roles for other biotechnology companies. In addition, he serves as a member of the boards of directors of Cidara Therapeutics, Inc., a public biotechnology company; Arbutus Biopharma Corp., a public biotechnology company; and several private healthcare companies. Mr. Burgess was a member of the board of directors of Santarus, Inc., from 2004 until its acquisition in 2014 by Salix Pharmaceuticals Inc., a publicly traded pharmaceutical company. He received his B.A. in economics from Stanford University and an M.B.A. from Harvard University. We believe Mr. Burgess is qualified to serve as a director because of his expertise and experience as an executive in the pharmaceutical industry, his service on other boards of directors and his educational background.

Theodore Schroeder has served on our board of directors and as chief executive officer since July 24, 2018. During the last 30 years, Mr. Schroeder has been focused on drug development and commercialization in both large and small pharmaceutical companies. Most recently, he served as president, chief executive officer and director of Zavante Therapeutics from June 2015 until its acquisition by Nabriva Therapeutics in July 2018. Mr. Schroeder co-founded Cadence Pharmaceuticals in 2004 and previously held leadership roles at Elan Pharmaceuticals, Dura Pharmaceuticals and earlier in his career, Bristol-Myers Squibb. He currently serves on the board of Cidara Therapeutics, and Otonomy, Inc. and formerly was a member of the board of Collegium Pharmaceutical. He is a former chair of BIOCOM, the California life sciences trade association and in 2014, he was named the EY Entrepreneur of the Year for the San Diego region and was listed as a national finalist. He received a bachelor's degree in management from Rutgers University. We

believe Mr. Schroeder is qualified to serve as a director because of his expertise and experience as an executive in the pharmaceutical industry, his service on other boards of directors and his educational background.

Colin Broom has served on our board of directors since June 23, 2017. Dr. Broom has served as the chief executive officer and a member of the board of directors of Pulmotect, Inc., a private biotechnology company, since September 2019. Dr. Broom was previously our chief executive officer from April 12, 2017 until July 24, 2018, and the chief executive officer of Nabriva Austria from August 2014 until the redomiciliation to Ireland. Prior to joining Nabriva Austria, he served as chief scientific officer at ViroPharma Incorporated from 2004 until it was acquired by Shire plc in 2014. Dr. Broom served as vice president of clinical development and medical affairs in Europe for Amgen Inc. from 2000 to 2003 and previously held several leadership positions with Hoechst Marion Roussel (now Sanofi), SmithKline Beecham and Glaxo (now GlaxoSmithKline) . Dr. Broom served as a member of the board of directors of NPS Pharmaceuticals, Inc. from 2009 until its acquisition by Shire in 2015. He is a member of the U.K. Royal College of Physicians and a fellow of the Faculty of Pharmaceutical Medicine. Dr. Broom received his B.Sc. from University College, London and M.B.B.S. from St. George's Hospital Medical School, London. We believe that Dr. Broom is qualified to serve as a director due to his extensive experience in all stages of drug development and commercialization.

Carrie Bourdow has served on our board of directors since June 23, 2017. Ms. Bourdow has been the president, the chief executive officer, and member of the board of directors of Trevena, Inc., a publicly-traded biopharmaceutical company, since October 2018. She has served in various senior positions at Trevena since May 2015. She joined Trevena as chief commercial officer and was appointed executive vice president and chief operating officer in January 2018. Prior to joining Trevena, Ms. Bourdow was vice president of marketing at Cubist Pharmaceuticals, Inc., from 2013 until its acquisition by Merck & Co., Inc. in January 2015. At Cubist, Ms. Bourdow led launch strategy, marketing, reimbursement, and operations for acute care hospital pharmaceuticals. Prior to Cubist, Ms. Bourdow served for more than 20 years at Merck & Co., Inc., where she held positions of increasing responsibility across multiple therapeutic areas. Ms. Bourdow also serves as a director of Sesen Bio, Inc., a publicly traded pharmaceutical company. Ms. Bourdow holds a B.A. degree from Hendrix College and an M.B.A. from Southern Illinois University. We believe Ms. Bourdow is qualified to serve as a director due to her extensive experience in the biopharmaceutical industry, including her experience with anti-infectives and with the commercialization of new drugs.

Mark Corrigan has served on our board of directors since June 2, 2021. Dr. Corrigan previously served on our board of directors from June 23, 2017 to May 26, 2020, and prior to the redomiciliation to Ireland, Dr. Corrigan served on the supervisory board of Nabriva Austria from October 2016 until the redomiciliation to Ireland. Dr. Corrigan was most recently the chief executive officer of Correvio Pharma Corporation (formerly Cardiome Pharma), a public biopharmaceutical company, from March 2019 until May 2021. From April 2016 until March 2019, Dr. Corrigan was founder and president of research and development of Tremeau Pharmaceuticals. Dr. Corrigan served as president and chief executive officer of Zalicus, Inc. from January 2010 until July 2014. Previously, Dr. Corrigan was executive vice president of research and development at the specialty pharmaceutical company Sepracor Inc., and prior to this, he spent 10 years with Pharmacia & Upjohn, most recently as group vice president of Global Clinical Research and Experimental Medicine. Dr. Corrigan currently serves on the boards of directors of Wave Biosciences, a public biopharmaceutical company, Tremeau Pharmaceuticals, a private company, and Exacis BioTherapeutics, a private biopharmaceutical company. He previously served on the boards of directors of Correvio Pharma Corporation, Novelin Therapeutics, Inc., BlackThorn Therapeutics, Inc., Cubist Pharmaceuticals, Inc., CoLucid Pharmaceuticals, Inc., Avanair Pharmaceuticals, Inc., and EPIRUS Biopharmaceuticals, Inc., where he served as chairman of the board of directors. Dr. Corrigan holds an M.D. from the University of Virginia and received specialty training in psychiatry at Maine Medical Center and Cornell University. We believe Dr. Corrigan is qualified to serve as a director due to his extensive experience in the biopharmaceutical industry as both an executive and a board member and because of his education and training.

Lisa Dalton has served on our board of directors since June 2, 2021. Ms. Dalton has served as the chief people officer at Spark Therapeutics, a member of the Roche Group, since July 2014. She previously served as vice president, human resources at Shire. Ms. Dalton received her M.B.A. from Rutgers University School of Business and B.A. from Pennsylvania State University. We believe Ms. Dalton is qualified to serve as a director because of her expertise and experience as an executive in the pharmaceutical industry.

Steven Gelone has served on our board of directors since March 10, 2021 and as our president and chief operating officer since July 24, 2018. Dr. Gelone previously served as Nabriva Austria's chief development officer and head of business development from 2014 until the redomiciliation to Ireland, our chief development officer from the redomiciliation to Ireland until June 30, 2017 and our chief scientific officer from June 30, 2017 until July 24, 2018. Prior to joining Nabriva Austria, he served as head of clinical research and development at Spark Therapeutics, Inc. in 2014 and vice president of clinical and preclinical development at ViroPharma Incorporated from 2005 to 2014. Dr. Gelone also served as director of medical affairs at Vicuron Pharmaceuticals from 2002 to 2003 and director of clinical pharmacology and experimental medicine at GlaxoSmithKline Pharmaceuticals from 2000 to 2002. Dr. Gelone received his B.S. Pharm. and Pharm.D. from Temple University. We believe Dr. Gelone is qualified to serve as a director due to his extensive experience in the biopharmaceutical industry as an executive and because of his education and training.

Charles A. Rowland, Jr. has served on our board of directors since June 23, 2017. Mr. Rowland previously served on the supervisory board of Nabriva Austria from January 2015 until the redomiciliation to Ireland. Mr. Rowland served as chief executive officer of Aurinia Pharmaceuticals Inc. from April 2016 to January 2017. Mr. Rowland previously served as vice president and chief financial officer of ViroPharma Incorporated from 2008 until it was acquired by Shire plc in 2014. Prior to joining ViroPharma, Mr. Rowland served as executive vice president and chief financial officer, as well as interim co-chief executive officer, for Endo Pharmaceuticals Inc. from 2006 to 2008 and chief financial officer at Biovail Corporation from 2004 to 2006. He previously held finance and operational positions of increasing responsibility at Breakaway Technologies, Inc., Pharmacia, Novartis International AG and Bristol-Myers Squibb Company. Mr. Rowland currently serves as a member of the board of directors for Blueprint Medicines Corporation, a public biopharmaceutical company, Viking Therapeutics, a public, clinical-stage biopharmaceutical company, and Orchard Therapeutics, a public, clinical-stage biopharmaceutical company. In addition, Mr. Rowland serves as a member of the board of directors for Generation Bio, a public biopharmaceutical company. Previously, he served on the board of directors at Idenix Pharmaceuticals, Inc., Vitae Pharmaceuticals, Inc., Bind Therapeutics Inc. and Aurinia Pharmaceuticals Inc. Mr. Rowland received his B.S. from Saint Joseph's University and M.B.A. from Rutgers University. We believe that Mr. Rowland is qualified to serve as a director due to his extensive experience in pharmaceutical operations and all areas of finance and accounting.

Stephen Webster has served on our board of directors since June 23, 2017. Mr. Webster previously served on the supervisory board of Nabriva Austria from October 2016 until the redomiciliation to Ireland. Mr. Webster served as the chief financial officer of Spark Therapeutics from July 2014 until its acquisition by Roche Holdings, Inc. in December 2019. He was previously senior vice president and chief financial officer of Optimer Pharmaceuticals, Inc. from June 2012 until its acquisition by Cubist Pharmaceuticals in November 2013. Prior to this, Mr. Webster served as senior vice president and chief financial officer of Adolor Corporation, also acquired by Cubist, from 2008 to 2011. Previously, Mr. Webster served as managing director, Investment Banking Division, Health Care Group for Broadpoint Capital Inc. (formerly First Albany Capital) . He also was a co-founder and served as president and chief executive officer of Neuronyx, Inc. Prior to this, Mr. Webster held positions of increasing responsibility, including as director, Investment Banking Division, Health Care Group, for PaineWebber Incorporated. Mr. Webster is currently a member of the board of directors of TCR^2 Therapeutics, Inc., Cullinan Oncology, Inc., and NextCure, Inc. He was a member of the board of directors of Viking Therapeutics, Inc., a public biopharmaceutical company, from 2014 to 2020. Mr. Webster holds an A.B. in economics from Dartmouth College and an M.B.A. from the University of Pennsylvania. We believe that Mr. Webster is qualified to serve as a director due to his extensive experience in the biopharmaceutical industry, particularly his service as a chief financial officer and in other executive management roles.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates under a charter that has been approved by our board. Copies of the committee charters are posted under the heading "Corporate Governance" on the Investor section of our website, which is located at http://investors.nabriva.com.

Audit Committee

Our audit committee consists of Mark Corrigan, Daniel Burgess and Stephen Webster. Stephen Webster is the chair of the audit committee. The audit committee oversees our accounting and financial reporting processes and the audits of our consolidated financial statements. The audit committee is responsible for, among other things:

- making recommendations to our board regarding the ratification by the annual general meeting of shareholders of our independent auditors;
- overseeing the work of the independent auditors, including resolving disagreements between management and the independent auditors relating to financial reporting;
- pre-approving all audit and non-audit services permitted to be performed by the independent auditors;
- reviewing the independence and quality control procedures of the independent auditors;
- reviewing and approving all proposed related-party transactions;
- discussing the annual audited consolidated and statutory financial statements with management;
- annually reviewing and reassessing the adequacy of our audit committee charter;
- meeting separately with the independent auditors to discuss critical accounting policies, recommendations on internal controls, the auditor's engagement letter and independence letter and other material written communications between the independent auditors and the management; and
- attending to such other matters as are specifically delegated to our audit committee by our board from time to time.

Our Board has determined that Stephen Webster is an "audit committee financial expert" as defined in the applicable SEC rules.

Compensation Committee

Our compensation committee consists of Charles A. Rowland, Jr., Lisa Dalton and Carrie Bourdow. Charles A. Rowland, Jr. is the chair of the compensation committee. The compensation committee assists the board in reviewing and approving or recommending our compensation structure, including all forms of compensation relating to our directors and management. The compensation committee is responsible for, among other things:

- reviewing and making recommendations to the board with respect to compensation of our board of directors and management;
- reviewing and approving the compensation, including equity compensation, change-of-control benefits and severance arrangements, of our chief executive officer, chief financial officer and such other members of our management as it deems appropriate;
- overseeing the evaluation of our management;
- reviewing periodically and making recommendations to our board with respect to any incentive compensation and equity plans, programs or similar arrangements;
- exercising the rights of our board under any equity plans, except for the right to amend any such plans unless otherwise expressly authorized to do so; and

- attending to such other matters as are specifically delegated to our compensation committee by our board from time to time.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Daniel Burgess, Carrie Bourdow and Stephen Webster. Daniel Burgess is the chair of the nominating and corporate governance committee. The nominating and corporate governance committee assists the board in selecting individuals qualified to become our directors and in determining the composition of the board and its committees. The nominating and corporate governance committee is responsible for, among other things:

- recommending to the board persons to be nominated for election or re-election to the board at any meeting of shareholders;
- overseeing the board's annual review of its own performance and the performance of its committees; and
- developing and recommending to the board a set of corporate governance guidelines.

Executive Officers

The following table sets forth certain information regarding our executive officers, including their ages as of March 1, 2022:

Name	Age	Position
Theodore Schroeder	66	Chief Executive Officer
J. Christopher Naftzger	54	General Counsel and Secretary
Steven Gelone	54	President and Chief Operating Officer
Christine Guico-Pabia	59	Chief Medical Officer
Daniel Dolan	45	Chief Financial Officer

In addition to the biographical information for Mr. Schroeder and Dr. Gelone, which is set forth above under "Board of Directors", set forth below is certain biographical information about Dr. Guico-Pabia, and Messrs. Naftzger and Dolan:

J. Christopher Naftzger has served as our general counsel and secretary since September 1, 2021. Previously, Mr. Naftzger served as General Counsel and Corporate Secretary of Krystal Biotech, an emerging-stage, gene therapy company, from February 2020 to May 2021. Before joining Krystal, he was Vice President, Deputy General Counsel and Assistant Secretary of Nabriva Therapeutics from January 2017 to January 2020. Prior to Nabriva, Mr. Naftzger served as Vice President, General Counsel, Chief Compliance Officer, and Secretary of Unilife Medical Solutions, a developer and manufacturer of innovative drug delivery systems. Mr. Naftzger also held senior in-house counsel positions with Chesapeake Corporation and Koch Industries, and was a corporate partner with Blank Rome LLP in Washington, DC. Mr. Naftzger obtained his undergraduate degree from Hampden-Sydney College and his law degree from the Willamette University College of Law.

Christine Guico-Pabia has served as our chief medical officer since October 1, 2021. Dr. Guico-Pabia brings over 30 years of global biopharmaceutical experience and extensive expertise in every stage of drug development, pharmacoeconomics and outcomes research, and medical affairs. Most recently, she was Vice President, Head of Clinical Development and Medical Affairs of Metagenics from 2014 to 2021. Dr. Guico-Pabia previously held leadership positions at small startups and large multinational companies including McKesson, Merck, Wyeth, and Pfizer. Dr. Guico-Pabia completed her MD at the University of Santo Tomas Medical School in Manila, Philippines, obtained her MBA from Temple University Fox School of Business, and her MPH from Johns Hopkins University Bloomberg School of Public Health.

Daniel Dolan has served as our chief financial officer since March 2021. Mr. Dolan previously served as Vice President of Finance at Radius Health, Inc., or Radius, a commercial-stage biopharmaceutical company, from July 2017 to January 2021. He also acted as principal financial officer and principal accounting officer of Radius from September 2020 to December 2020. Prior to joining Radius, Mr. Dolan worked at Shire plc from September 2005 to July 2017, where he held financial management positions of increasing responsibility, including Vice President of Finance, Global Product Strategy from May 2016 to July 2017 and Senior Finance Director, GI/Internal Medicine from May 2013 to May 2016. Mr. Dolan received his M.B.A. and B.S. from Widener University.

Code of Business Conduct and Ethics

Our Code of Business Conduct and Ethics is applicable to all of our directors, officers and employees and is available on our website at http://investors.nabriva.com/corporate-governance/governance-overview. Our Code of Business Conduct and Ethics provides that our directors, officers and employees are expected to avoid any action, position or interest that conflicts with the interests of our company or gives the appearance of a conflict. We expect that any amendment to this code, or any waivers of its requirements, will be disclosed on our website. Information contained on, or that can be accessed through, our website is not incorporated by reference into this document, and you should not consider information on our website to be part of this document.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, executive officers and persons who own more than 10% of our ordinary shares to file an initial report of ownership on Form 3 and changes in ownership on Form 4 or Form 5 with the SEC. Such officers, directors and 10% shareholders are also required by SEC rules to furnish us with copies of any Forms 3, 4 or 5 that they file. The SEC rules require us to disclose late filings of initial reports of stock ownership and changes in share ownership by our directors, executive officers and 10% shareholders.

Based solely on a review of copies of Forms 3, 4 and 5 furnished to us by reporting persons and any written representations furnished by certain reporting persons, we believe that during the fiscal year ended December 31, 2021, all Section 16(a) filing requirements applicable to our directors, executive officers and 10% shareholders were completed in a timely manner other than (1) Forms 4 for each of Theodore Schroeder, Steven Gelone and Robert Crotty, in each case filed on April 8, 2021 and relating to the withholding of securities for tax purposes on February 6, 2021 and March 6, 2021 in connection with the vesting of restricted stock units and (2) a Form 3 for J. Christopher Naftzger, filed on September 15, 2021.

ITEM 11. EXECUTIVE COMPENSATION

The following discussion provides the amount of compensation paid, and benefits in-kind granted, by us and our subsidiaries to the members of our board of directors and certain executives for services provided in all capacities to us and our subsidiaries for the year ended December 31, 2021.

Executive and Director Compensation Processes

Our executive compensation program is administered by the compensation committee of our board of directors, subject to the oversight and approval of our full board of directors. Our compensation committee reviews our executive compensation practices on an annual basis and based on this review approves, or, as appropriate, makes recommendations to our board of directors for approval of our executive compensation program.

In designing our executive compensation program, our compensation committee considers publicly available compensation data for national and regional companies in the biotechnology/pharmaceutical industry to help guide its executive compensation decisions at the time of hiring and for subsequent adjustments in compensation. Since 2016, our compensation committee has retained Radford, a part of Aon Hewitt, a business unit of Aon plc, as its independent compensation consultant, to provide comparative data on executive compensation practices in our industry and to advise on our executive compensation program generally. The committee also has retained Radford for guidelines and review

of non-employee director compensation. Although our compensation committee considers the advice and guidelines of Radford as to our executive compensation program, our compensation committee ultimately makes its own decisions about these matters. In the future, we expect that our compensation committee will continue to engage independent compensation consultants to provide additional guidance on our executive compensation programs and to conduct further competitive benchmarking against a peer group of publicly traded companies.

Our director compensation program is administered by our board of directors with the assistance of the compensation committee. The compensation committee conducts an annual review of director compensation and makes recommendations to the board of directors with respect thereto.

Summary Compensation Table

Our "named executive officers" for the year ended December 31, 2021 were as follows: Mr. Schroeder, our chief executive officer, Dr. Gelone, our president and chief operating officer and Mr. Dolan, our chief financial officer. The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers for the periods presented.

Name and principal position	Year	Salary($)	Bonus ($)(1)	Share Awards ($)(2)	Option Awards ($)(2)	Non-Equity Incentive Plan Compensation ($) (3)	All Other Compensation ($)(4)	Total ($)
Theodore Schroeder(5)	2021	594,170	—	307,850	—	302,993	32,287	1,237,300
Chief Executive Officer	2020	576,800	—	464,130	339,625	242,256	31,759	1,654,570
Steven Gelone	2021	500,947	225,000	611,349	—	191,590	14,138	1,543,024
President and Chief Operating Officer	2020	486,300	—	270,863	231,493	153,185	12,675	1,154,516
Daniel Dolan(6)	2021	271,250	—	—	110,000	93,500	26,690	501,440
Chief Financial Officer								

(1) The amount reported in the "Bonus" column represents a $225,000 retention bonus awarded to Dr. Gelone in 2021, which shall be paid in March 2022.

(2) The amounts reported in the "Share Awards" and "Option Awards" columns reflect the aggregate grant-date fair value of share-based compensation awarded during the year computed in accordance with the provisions of ASC Topic 718. See Note 10 to the consolidated financial statements regarding assumptions underlying the valuation of equity awards.

(3) The amounts reported in the "Non-Equity Incentive Plan Compensation" column represent awards to our named executive officers under our annual cash bonus program.

(4) The compensation included in the "All Other Compensation" column consists of amounts we contributed to our 401(k) plan and medical insurance premiums paid by us on behalf of such individual.

(5) Mr. Schroeder declined to accept his bonus payout for 2021.

(6) Mr. Dolan commenced employment with us in March 2021.

Narrative Disclosure to Summary Compensation Table

Base Salary

In 2021, we paid annualized base salaries of $594,104 to Mr. Schroeder, $500,889 to Dr. Gelone and $330,000 to Mr. Dolan. In 2020, we paid annualized base salaries of $576,800 to Mr. Schroeder and $486,300 to Dr. Gelone.

In January 2022, our board of directors, following approval and recommendation from the compensation committee and consistent with the recommendations of the compensation committee's independent compensation consultant, approved an increase to the base salaries of our named executive officers for 2022 as follows: $515,916 for Dr. Gelone and $363,000 for Mr. Dolan. Our board of directors also approved of an increase in base salary for Mr. Schroeder, who declined to accept an increase to his base salary. The board also approved the 2022 base salary for Mr. Naftzger, our general counsel and secretary, of $367,500, and Dr. Guico-Pabia, our chief medical officer, of $428,480, which was also consistent with the recommendation of the compensation committee's independent consultant.

None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Annual Performance-Based Compensation

Our executive officers, which include the named executive officers, participate in our performance-based bonus program. All annual cash bonuses for our executives under the performance-based bonus program are tied to the achievement of strategic and operational corporate goals for the company, which are set by the compensation committee and approved by the board. There are no discretionary individual goals under the bonus program. The 2021 strategic and operational goals for Nabriva related to the following objectives:

- commercialization of our products;
- finance, specifically fundraising;
- regulatory approvals;
- business development; and
- chemistry, manufacturing, and control (CMC).

Under their respective employment agreements, the annual target bonus for Mr. Schroeder is 60% of his current base salary, the annual target bonus for Dr. Gelone is 45% of his current base salary and the annual target bonus for each of Dr. Guico-Pabia, Mr. Naftzger and Mr. Dolan is 40% of their respective current base salaries.

At a meeting held in January 2022, our compensation committee reviewed the accomplishments of the named executive officers as measured against the aforementioned 2021 goals. The compensation committee reviewed whether each goal had been obtained and the weight such goals should be given in determining the bonus payout for 2021 performance. Based on its review, the compensation committee recommended a 85% payout of the target bonuses for 2021 for Mr. Schroeder, Dr. Gelone and Mr. Dolan. Mr. Schroeder declined to accept his bonus payout for 2021. Accordingly, the 2021 bonus payouts which were paid in February 2022, were $191,590 for Dr. Gelone and $93,500 for Mr. Dolan.

Equity Incentive Awards

We believe that equity grants provide our executive officers with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executive officers and our shareholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our executive officers, which includes the named executive officers, and from time to time may grant equity incentive awards to them in the form of stock options or restricted stock units, or RSUs. We also generally make stock option grants to new executive officers in connection with the commencement of their employment.

Since our initial public offering, we have granted stock options with exercise prices that are set at no less than the fair market value of the underlying award on the date of grant, as determined by reference to the trading price of our ordinary shares on Nasdaq, and approved by our compensation committee or our board.

The following table sets forth the number of our ordinary shares issuable upon vesting of the share awards granted to our named executive officers in 2022:

Name	Option Award (#)	RSU Award (#)
Theodore Schroeder	239,800	119,900
Steven Gelone	93,400	46,700
Daniel Dolan	83,200	41,600

On January 28, 2021, our board of directors granted share option awards, as well as restricted share share units, or RSUs, under the 2020 Share Incentive Plan to Mr. Schroeder, Dr. Gelone and Mr. Dolan, in each case, subject to shareholder approval of an amendment to increase the number of ordinary shares authorized for issuance under our 2020 Share Incentive Plan. The share option awards and RSUs vest over a four year period beginning on January 28, 2022, with 25% of the option vesting upon the first anniversary of the grant date and on a monthly pro rata basis thereafter over the remaining three years. Twenty five percent (25%) of the RSUs vest annually over the four year vesting period. If shareholder approval of the amendment to the 2020 Share Incentive Plan is not obtained, the options will remain outstanding and will convert into cash-settled share appreciation rights. If shareholder approval of the amendment to the 2020 Share Incentive Plan is not obtained, each of the RSUs will represent the right to receive the economic equivalent of one ordinary share in cash on the applicable vesting date.

The following table sets forth the number of our ordinary shares issuable upon exercise or vesting of the share awards granted to our named executive officers in 2021:

Name	Option Award (#)	RSU Award (#)
Theodore Schroeder	—	117,500
Steven Gelone	—	333,197
Daniel Dolan	100,000	—

On January 29, 2021, our board of directors granted RSUs under the 2020 Share Incentive Plan to Mr. Schroeder and Dr. Gelone. The RSUs vest over a four year period beginning on January 29, 2021. Twenty five percent (25%) of the RSUs vest annually over the four year vesting period. Mr. Dolan´s option to purchase 100,000 of our ordinary shares vests over four years, with 25% of the options vesting on March 31, 2022, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period. The option was awarded to Mr. Dolan in connection with the commencement of his employment.

As previously disclosed, our board of directors in 2020 awarded Dr. Gelone 23,250 options and 11,625 RSUs that were subject to performance conditions related to the commercial performance of the company and life cycle management of our product and product candidate portfolio. The vesting of these awards continues to be subject to the achievement of performance conditions, which, due to business disruption caused by the COVID-19 global pandemic, were extended and modified in March 2022.

Outstanding Equity Awards as of December 31, 2021

The following table sets forth information regarding outstanding stock options and RSUs held by our named executive officers as of December 31, 2021:

	Option Awards				Equity incentive plan awards:	Equity incentive plan awards:
Name	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price ($)	Option expiration date	Number of unearned shares, units or other rights that have not vested (#)	Market or payout value of unearned shares, units or other rights that have not vested ($)
Theodore Schroeder	72,603	12,397 (1)	35.30	07/25/2028	4,761 (12)	2,852
	31,339	11,641 (2)	19.00	01/31/2029	18,623 (13)	11,155
	24,348	44,402 (3)	13.50	02/06/2030	117,500 (14)	70,383
Steven Gelone	8,879	— (4)	72.05	07/05/2025	3,084 (12)	1,847
	5,590	— (5)	83.40	02/05/2026	8,396 (13)	5,029
	11,300	— (6)	85.00	02/07/2027	42,500 (14)	25,458
	9,791	209 (7)	64.70	01/31/2028	11,625 (15)	6,963
	6,619	1,131 (8)	35.30	07/25/2028	290,697 (16)	174,128
	624	126 (9)	24.90	08/02/2028	—	—
	20,299	7,541 (2)	19.00	01/31/2029	—	—
	10,979	20,021 (3)	13.50	02/06/2030	—	—
	—	23,250 (10)	5.30	09/25/2030	—	—
Daniel Dolan	—	100,000 (11)	1.66	03/31/2031	—	—

(1) Mr. Schroeder's option to purchase 85,000 of our ordinary shares vests over four years, with 25% of the options vesting on July 25, 2019, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period.

(2) Mr. Schroeder's and Dr. Gelone's option to purchase ordinary shares vests over four years, with 25% of the options vesting on January 31, 2020, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period.

(3) Mr. Schroeder's and Dr. Gelone's option to purchase ordinary shares vests over four years, with 25% of the options vesting on February 6, 2021, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period.

(4) Dr. Gelone's option to purchase 8,879 of our ordinary shares vests over four years, with 25% of the options vesting on May 31, 2016, and the remaining 75% of the option vesting on a monthly pro-rata basis over the remaining three years of the vesting period.

(5) Dr. Gelone's option to purchase 5,590 of our ordinary shares vests over four years, with 25% of the options vesting on February 28, 2017, and the remaining 75% of the option vesting on a monthly pro-rata basis over the remaining three years of the vesting period.

(6) Dr. Gelone's option to purchase 11,300 of our ordinary shares vests over four years, with 25% of the options vesting on February 28, 2018, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period.

(7) Dr. Gelone's option to purchase 10,000 of our ordinary shares vests over four years, with 25% of the options vesting on January 31, 2019, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period.

(8) Dr. Gelone's option to purchase 7,750 of our ordinary shares vests over four years, with 25% of the options vesting on July 25, 2019, and the remaining 75% of the option vesting on a monthly pro-rata basis over the remaining three years of the vesting period.

(9) Dr. Gelone's option to purchase 750 of our ordinary shares vests over four years, with 25% of the options vesting on August 2, 2019, and the remaining 75% of the option vesting on a monthly pro-rata basis over the remaining three years of the vesting period.

(10) Dr. Gelone's option to purchase ordinary shares is subject to the commercial performance and life cycle management of the product and product candidate portfolio.

(11) Mr. Dolan´s option to purchase 100,000 of our ordinary shares vests over four years, with 25% of the options vesting on March 31, 2022, and the remaining 75% of the option vesting on a monthly pro rata basis over the remaining three years of the vesting period.

(12) Mr. Schroeder's and Dr. Gelone's RSUs vest over four years, with 25% of the RSUs vesting on January 31, 2020, and the remaining 75% of the RSUs vesting on a monthly pro-rata basis over the remaining three years of the vesting period.

(13) Mr. Schroeder's and Dr. Gelone's RSUs vest over four years, with 25% of the RSUs vesting on February 6, 2021, and the remaining 75% of the RSUs vesting on a monthly pro-rata basis over the remaining three years of the vesting period.

(14) Mr. Schroeder's and Dr. Gelone's RSUs vest over four years, with 25% of the RSUs vesting on January 29, 2022 and 25% of the RSUs vesting annually over the remainder of the vesting period.

(15) Dr. Gelone's vesting of the RSUs is subject to the commercial performance and life cycle management of the product and product candidate portfolio.

(16) Dr. Gelone's RSUs vest over two years, with 100% of the RSUs vesting on April 28, 2023.

Employment Agreements with Executive Officers

Agreement with Theodore Schroeder, Chief Executive Officer and Director

Mr. Schroeder was appointed our chief executive officer and entered into an employment agreement dated and effective as of July 23, 2018. He was appointed to our board on August 1, 2018. On March 10, 2021, we entered into an amended and restated employment agreement with Mr. Schroeder, or the Schroeder Employment Agreement. The Schroeder Employment Agreement continues until terminated in accordance with its terms, as described below.

Pursuant to the Schroeder Employment Agreement, Mr. Schroeder receives an annual base salary of $594,104 and is eligible to receive an annual performance bonus targeted at 60% of his annual base salary, with the actual amount of such bonus, if any, to be determined by the Board. Mr. Schroeder is also (1) eligible to receive equity awards at such times and on such terms and conditions as the Board may determine and (2) entitled to participate in any and all benefit programs that we make available to our executive officers, for which he may be eligible, under the plan documents governing such programs.

The employment agreement, and Mr. Schroeder's employment, may be terminated as follows: (1) upon Mr. Schroeder's death or "disability" (as disability is defined in his employment agreement); (2) at our election, with or without "cause" (as cause is defined in his employment agreement); and (3) at Mr. Schroeder's election, with or without "good reason" (as good reason is defined in his employment agreement).

In the event of the termination of Mr. Schroeder's employment by us without cause, including as a result of a termination of his employment for good reason prior to, or more than twelve months following, a "change in control" (as change in control is defined in the Schroeder Employment Agreement), Mr. Schroeder will be entitled to his base salary that has accrued and to which he is entitled as of the termination date. In addition, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with his proprietary rights, non-disclosure and developments agreement with us, he is entitled to (1) continued payment of his base salary, in accordance with our regular payroll procedures, for a period of 18 months (2) provided he is eligible for and timely elects to continue receiving group medical insurance under COBRA and the payments would not result in the violation of nondiscrimination requirements of applicable law, payment by us of the portion of health coverage premiums we pay for similarly-situated, active employees who receive the same type of coverage, for a period of up to 18 months following his date of termination, (3) a lump sum payment equal to any earned but unpaid annual bonus for a previously completed calendar year, (4) a lump sum payment equal to a prorated annual bonus for the year in which Mr. Schroeder's employment is terminated based on the number of days he provided services to us during the year in which his employment is terminated and (5) accelerated vesting of his then-unvested equity awards that are subject to time-based vesting and that would have vested within twelve months of the termination date, whether granted under the 2017 Share Incentive Plan, 2020 Share Incentive Plan or any successor equity incentive plan or as an inducement to his employment.

In the event of the termination of Mr. Schroeder's employment by us without cause, including as a result of a termination of his employment for good reason prior to, or by him for good reason within twelve months following a change in control, subject (as described above with respect to certain payments), to his execution and nonrevocation of a release of claims in our favor and his continued compliance with his proprietary rights, non-disclosure and developments agreement with us, Mr. Schroeder would be entitled to the same payments and benefits as described in the preceding paragraph, except that, in lieu of a pro-rated annual bonus payment, he would be entitled to receive a lump sum payment equal to 100% of his target bonus for the year in which his employment is terminated and he shall also be entitled to full vesting acceleration of his then-unvested equity awards, whether granted under the 2017 Share Incentive Plan, 2020 Share Incentive Plan or any successor equity incentive plan or as an inducement to his employment, such that his equity awards become fully exercisable and non-forfeitable as of the termination date, except as otherwise determined by the Board in the case of awards subject to performance conditions.

If Mr. Schroeder's employment is terminated for any other reason, including as a result of his death or disability, for cause, or voluntarily by Mr. Schroeder without good reason, our obligations under the Schroeder Employment Agreement cease immediately, and Mr. Schroeder is only entitled to his base salary that has accrued and to which he is entitled as of the termination date and solely if his employment is terminated as a result of his death or disability, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with his proprietary rights, non-disclosure and developments agreement with us, he or his estate, as applicable, is entitled to any earned but unpaid annual bonus from a previously completed calendar year.

As a condition of his employment, Mr. Schroeder signed a proprietary rights, non-disclosure and developments agreement.

Agreements with Daniel Dolan, Chief Financial Officer, Steven Gelone, President, Chief Operating Officer and Director, Christine Guico-Pabia, Chief Medical Officer and Christopher Naftzger, General Counsel and Secretary

Mr. Dolan was appointed our chief financial officer effective as of March 12, 2021, and entered into an employment agreement dated and effective as of March 10, 2021, or the Dolan Employment Agreement. Dr. Gelone was appointed our chief development officer and entered into an employment agreement dated and effective as of December 1, 2014, which was amended and restated as of May 26, 2016 and further amended on restated on July 24, 2018. Dr. Gelone was subsequently appointed our chief scientific officer on June 30, 2017 and our president and chief operating officer on July 24, 2018. Dr. Gelone was appointed to our board on March 10, 2021. On March 10, 2021, we entered into an amended and restated employment agreement with Dr. Gelone, or the Gelone Employment Agreement. Dr. Guico-Pabia was appointed as our chief medical officer and entered into an employment agreement dated and effective as of October 1, 2021, or the Guico-Pabia Employment Agreement. Mr. Naftzger was appointed as our general counsel and secretary and entered into an employment agreement dated and effective as of September 1, 2021, or the Naftzger Employment Agreement. Each of the Dolan Employment Agreement, Gelone Employment Agreement, Guico-Pabia Employment Agreement and Naftzger Employment Agreement, or the Executive Employment Agreements, provides that such executive officer is an at will employee, and his employment with us can be terminated by the respective executive officer or us at any time and for any reason.

Pursuant to the Dolan Employment Agreement, Mr. Dolan receives an annual base salary of $330,000 and is eligible to receive an annual performance bonus targeted at 40% of his annual base salary, with the actual amount of such bonus, if any, to be determined by the Board. Pursuant to the Gelone Employment Agreement, Dr. Gelone receives an annual base salary of $509,888 and is eligible to receive an annual performance bonus targeted at 45% of his annual base salary, with the actual amount of such bonus, if any, to be determined by the Board. Pursuant to the Guico-Pabia Employment Agreement, Dr. Guico-Pabia receives an annual base salary of $416,000 and is eligible to receive an annual performance bonus targeted at 40% of her annual base salary, with the actual amount of such bonus, if any, to be determined by the Board. Pursuant to the Naftzger Employment Agreement, Mr. Naftzger receives an annual base salary of $350,000 and is eligible to receive an annual performance bonus targeted at 40% of his annual base salary, with the actual amount of such bonus, if any, to be determined by the Board. Each of Mr. Dolan, Dr. Gelone, Dr. Guico-Pabia and Mr. Naftzger are also (1) eligible to receive equity awards at such times and on such terms and conditions as the Board may determine and (2) entitled to participate in any and all benefit programs that we make available to our executive officers, for which he may be eligible, under the plan documents governing such programs.

In addition, pursuant to the Dolan Employment Agreement, subject to approval by the compensation committee of the Board or a majority of our independent directors as defined in Nasdaq Listing Rule 5605(a)(2), Mr. Dolan shall receive a nonqualified share option to purchase 100,000 ordinary shares at an exercise price per share equal to the closing price per share of the ordinary shares on the Nasdaq Global Select Market on the date of grant, to vest over a period of four (4) years, subject to the terms and conditions of our 2021 Inducement Share Incentive Plan and a nonqualified share option agreement between us and Mr. Dolan, and awarded outside of our equity incentive plans as an "inducement grant" within the meaning of Nasdaq Listing Rule 5635(e)(4).

Each Executive Employment Agreement and the employment of each of Mr. Dolan, Dr. Gelone, Dr. Guico-Pabia and Mr. Naftzger may be terminated in one of three ways: (1) upon the death or "disability" (as disability is defined in the applicable Executive Employment Agreement) of such executive officer; (2) at our election, with or

without “cause” (as cause is defined in the applicable Executive Employment Agreement); and (3) at such executive officer’s election, with or without “good reason” (as good reason is defined in the applicable Executive Employment Agreement).

In the event of the termination of such executive officer’s employment by us without cause or by him for good reason prior to, or more than twelve months following, a “change in control” (as change in control is defined in the applicable Executive Employment Agreement), such executive officer will be entitled to his or her base salary that has accrued and to which he is entitled as of the termination date. In addition, subject to such executive officer’s execution and nonrevocation of a release of claims in our favor and his or her continued compliance with his or her proprietary rights, non-disclosure and developments agreement with us, such executive officer is entitled to (1) continued payment of such executive officer’s base salary, in accordance with our regular payroll procedures, for, in the case of Mr. Dolan, Dr. Guico-Pabia and Mr. Naftzger, a period of 12 months, and in the case of Dr. Gelone, a period of 15 months, (2) provided he or she is eligible for and timely elects to continue receiving group medical insurance under COBRA and the payments would not result in the violation of nondiscrimination requirements of applicable law, payment by us of the portion of health coverage premiums we pay for similarly-situated, active employees, who receive the same type of coverage, for, in the case of Mr. Dolan, Dr. Guico-Pabia and Mr. Naftzger, a period of up to 12 months and, in the case of Dr. Gelone, a period of 15 months, following the date of termination, (3) a lump sum payment equal to any earned but unpaid annual bonus for a previously completed calendar year and (4) a lump sum payment equal to a prorated annual bonus for the year in which such executive officer’s employment is terminated based on the number of days such executive officer provided services to us during the year in which such executive officer’s employment is terminated.

In the event of the termination of the executive officer’s employment by us without cause or by him or by her for good reason within twelve months following a change in control, subject (as described above with respect to certain payments) to such executive officer’s execution and nonrevocation of a release of claims in our favor and his or her continued compliance with his or her proprietary rights, non-disclosure and developments agreement with us, such executive officer will be entitled to the same payments and benefits as described in the preceding paragraph, except that, in lieu of a pro-rated annual bonus payment, such executive officer will be entitled to receive a lump sum payment equal to 100% of such executive officer’s target bonus for the year in which his or her employment is terminated, and such executive officer shall also be entitled to full vesting acceleration of his or her then-unvested equity awards, whether granted under the 2017 Share Incentive Plan, 2020 Share Incentive Plan or any successor equity incentive plan, such that his or her equity awards become fully exercisable and non-forfeitable as of the termination date, except as otherwise determined by the Board in the case of awards subject to performance conditions.

If such executive officer’s employment is terminated for any other reason, including as a result of his or her death or disability, for cause, or voluntarily by such executive officer without good reason, our obligations under the applicable Executive Employment Agreements cease immediately, and such executive officer is only entitled to his or her base salary that has accrued and to which he is entitled as of the termination date and, solely if such executive officer’s employment is terminated as a result of his or her death or disability and subject to his or her execution and nonrevocation of a release of claims in our favor and his or her continued compliance with his or her proprietary rights, non-disclosure and developments agreement with us, such executive officer or the estate of such executive officer, as applicable, is entitled to any earned but unpaid annual bonus from a previously completed calendar year.

As a condition to their employment, each of Mr. Dolan, Dr. Gelone, Dr. Guico-Pabia and Mr. Naftzger signed a proprietary rights, non-disclosure and developments agreement.

Equity Incentive Plans

In this section, we describe our 2020 Share Incentive Plan, 2017 Share Incentive Plan and Stock Option Plan 2015. Prior to the redomiciliation to Ireland, or Redomiciliation, Nabriva Austria granted awards to eligible recipients under the Stock Option Plan 2015. In connection with the Redomiciliation, both plans were amended to take account of certain requirements under Irish law and assumed by us, with each option to acquire one Nabriva Austria common share becoming an option to acquire ten of our ordinary shares on the same terms and conditions. We currently make share awards to eligible recipients solely under our 2020 Share Incentive Plan.

2020 Share Incentive Plan

On March 4, 2020, our board of directors adopted the 2020 Share Incentive Plan, or the 2020 Plan, which was approved by our shareholders at the 2020 Annual General Meeting of Shareholders in July 2020, or the AGM. As of the date of the 2020 AGM, the total number of ordinary shares reserved for issuance under the 2020 Plan was for the sum of 9,300,000 ordinary shares, plus the number of our ordinary shares that remained available for grant under the 2017 Plan as of immediately prior to the AGM and the number of ordinary shares subject to awards granted under the 2017 Plan and our Amended and Restated Stock Option Plan 2015, that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right. Following shareholder approval of the 2020 Plan, no further awards will be made under the 2017 Plan.

The 2020 Plan provides for the grant of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units, other share-based and cash-based awards and performance awards.

As of January 31, 2022, under our 2020 Share Incentive Plan, there were options to purchase an aggregate of 418,730 of our ordinary shares at a weighted average exercise price of $4.72 per share, 734,938 restricted stock units outstanding with a weighted average grant date fair value of $2.10 per share, and 271,080 ordinary shares available for future issuance under the plan.

The 2020 Plan is administered by the board of directors. The exercise or measurement prices, vesting periods, performance goals and other award restrictions are determined at the discretion of the board of directors, except that the exercise price or measurement price per share of options or share appreciation rights may not be less than 100% of the fair market value of the ordinary shares on the date of grant, provided that if the board of directors approves the grant of an option or a share appreciation right with an exercise or measurement price to be determined on a future date, the exercise or measurement price may not be less than 100% of the fair market value of the ordinary shares on such future date. No share option or share appreciation right will be granted under the 2020 Plan with a term in excess of ten years.

If, during the term of the 2020 Plan, there is a change in our share capital or a restructuring measure which has an effect on our share capital, such as a share split or reverse share split, the board of directors will make equitable adjustments to the price or the amount of outstanding awards.

The 2020 Plan also contains provisions addressing the consequences of any reorganization event. A reorganization event is defined as (a) any merger or consolidation of ours with or into another entity as a result of which all of our ordinary shares are converted into or exchanged for the right to receive cash, securities or other property, or are canceled, (b) any transfer or disposition of all of our ordinary shares for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of ours; any one of which, (a), (b) or (c), may be effected pursuant to the laws of the Republic of Ireland.

The 2020 Plan provides that, if a reorganization event occurs, the board of directors may take one or more of the following actions with respect to all or any outstanding awards other than restricted shares on such terms as the board of directors determines: (1) provide that such awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (2) upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited immediately prior to the consummation of such reorganization event and/or that all of the participant's unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice, (3) provide that outstanding awards will become exercisable, realizable, or deliverable, or restrictions applicable to an award will lapse, in whole or in part prior to or upon such reorganization event, (4) in the event of a reorganization event under the terms of which holders of our ordinary shares will receive, upon consummation thereof, a cash payment for each share surrendered in the reorganization event, or the Acquisition Price, make or provide for a cash payment to participants with respect to each award held by a participant equal to (A) the number of ordinary shares subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award, (5) provided that, in connection with our

liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (6) any combination of the foregoing. Our board of directors is not obligated to treat all awards, all awards held by a participant, or all awards of the same type, identically.

No award may be granted under the 2020 Plan after the date that is ten years from the date the 2020 Plan is approved by our shareholders. Our board of directors may, at any time, amend, suspend or terminate the 2020 Plan or any portion thereof. However, if shareholder approval is required, including by application of Irish law or the terms of the 2020 Plan, the board of directors may not effect such modification or amendment without such approval.

2017 Share Incentive Plan

The 2017 Share Incentive Plan permits the award of share options, share appreciation rights, or SARs, restricted shares, restricted share units or RSUs, and other share-based awards to our employees, officers, directors, consultants and advisers. With the approval of the 2020 Share Incentive Plan, there were no further shares available for issuance under the 2017 Plan. However, all outstanding awards under 2017 Plan will remain in effect and continue to be governed by the terms of the 2017 Plan. As of January 31, 2022, under our 2017 Share Incentive Plan, there were options to purchase an aggregate of 389,497 of our ordinary shares at a weighted average exercise price of $31.04 per share and 54,800 restricted stock units outstanding with a weighted average grant date fair value of $13.85 per share. Unless the context specifically indicates otherwise, references to our 2017 Share Incentive Plan in this Annual Report on Form 10-K refer to the 2017 Share Incentive Plan, as amended and adopted by us.

If, during the term of the 2017 Share Incentive Plan, there is a change in our capital or a restructuring measure which has an effect on our capital, such as a share split or reverse share split, which change or measure results in a change in the value of the share-based awards outstanding under the 2017 Share Incentive Plan, the board will make appropriate adjustments to the price or the amount of such outstanding awards.

The 2017 Share Incentive Plan also contains provisions addressing the consequences of any reorganization event. A reorganization event is defined as (a) any merger or consolidation of us with or into another entity as a result of which all of our ordinary shares are converted into or exchanged for the right to receive cash, securities or other property, or are cancelled, (b) any transfer or disposition of all of our ordinary shares for cash, securities or other property pursuant to a share exchange or other transaction or (c) our liquidation or dissolution; any one of which, (a), (b) or (c), may be effected pursuant to the laws of the Republic of Ireland.

The 2017 Share Incentive Plan provides that, if a reorganization event occurs, the board of directors may take one or more of the following actions to all or any outstanding awards other than restricted shares on such terms as the board of directors determines: (1) provide that such awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (2) upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited immediately prior to the consummation of such reorganization event and/or that all of the participant's unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice, (3) provide that outstanding awards will become exercisable, realizable, or deliverable, or restrictions applicable to an award will lapse, in whole or in part prior to or upon such reorganization event, (4) in the event of a reorganization event under the terms of which holders of our ordinary shares will receive, upon consummation thereof, a cash payment for each share surrendered in the reorganization event, which we refer to as the Acquisition Price, make or provide for a cash payment to participants with respect to each award held by a participant equal to (A) the number of ordinary shares subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award, (5) provide that, in connection with our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (6) any combination of the foregoing. Our board is not obligated to treat all awards, all awards held by a participant, or all awards of the same type, identically.

No additional awards may be granted under the 2017 Share Incentive Plan. The board of directors may, at any time, amend, suspend or terminate the 2017 Share Incentive Plan or any portion thereof. However, if shareholder approval is required, including by application of Irish law, the board may not effect such modification or amendment without such approval.

Stock Option Plan 2015

The Stock Option Plan 2015 provided for the grant of options to purchase our ordinary shares to our employees, including executive officers, and to directors. With the approval of the 2017 Share Incentive Plan, there were no further shares available for issuance under the Stock Option Plan 2015. However, all outstanding awards under Stock Option Plan 2015 will remain in effect and continue to be governed by the terms of the Stock Option Plan 2015. As of January 31, 2021, under our Stock Option Plan 2015, there were options to purchase an aggregate of 160,205 of our ordinary shares at a weighted average exercise price of $80.17 per share and no ordinary shares are available for issuance under the plan. Unless the context specifically indicates otherwise, references to our Stock Option Plan 2015 in this Annual Report on Form 10-K refer to the Stock Option Plan 2015, as amended and adopted by us.

Options granted under the Stock Option Plan 2015 entitle beneficiaries thereof to purchase our ordinary shares at an exercise price equal to 100% of the fair market value per share on the beneficiary's date of participation, which following the Redomiciliation was derived from the closing sale price of our ordinary shares on the Nasdaq Global Select Market. Options granted under the Stock Option Plan 2015 generally vest over four years from the beneficiary's date of participation. Typically, 25% of the options subject to a particular grant vest on the last day of the last calendar month of the first year of the vesting period, and the remaining 75% vests on a monthly pro-rata basis over the second, third and fourth years of the vesting period (i.e., 2.083% per month). Any alternative vesting period determined by us is subject to approval by our executive officers, board of directors or shareholders, in accordance with any applicable voting requirements.

The Stock Option Plan 2015 provides that, if a liquidity event (as defined below) occurs, all options outstanding under the Stock Option Plan 2015 will be assumed (or substantially equivalent awards will be substituted by an acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation)), and any then-unvested options shall continue to vest in accordance with the beneficiary's original vesting schedule. If a beneficiary is terminated due to a good leaver event (within the meaning of the Stock Option Plan 2015), on or prior to the first anniversary of the date of the liquidity event, the beneficiary's options will be immediately exercisable in full as of the date of such termination. If the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation) refuses to assume the options outstanding under the Stock Option Plan 2015 or to substitute substantially equivalent options therefor, all then-unvested options under the Stock Option Plan 2015 will automatically vest in full upon the liquidity event. For purposes of the Stock Option Plan 2015, a liquidity event generally refers to an exclusive license of or the sale, lease or other disposal of all or substantially all of our assets, a sale or other disposal (but not a pledge) of 50% or more of our shares, a merger or consolidation of us with or into any third party, or our liquidation, winding up or other form of dissolution of us.

Unless otherwise specifically permitted in an option agreement or resolved upon by the board of directors, the exercise of vested options is permitted under the Stock Option Plan 2015 only during specified periods and on specified terms in the case of a liquidity event or following an initial public offering occurring during the term of the option. A beneficiary is entitled to exercise vested options at any time during the remaining term of the option while the beneficiary is providing services to us, and within the three-month period following a termination of the beneficiary's services due to a good leaver event. Options granted under the Stock Option Plan 2015 will have a term of no more than ten years from the beneficiary's date of participation.

If, during the term of the Stock Option Plan 2015, there is a change in our capital or a restructuring measure which has an effect on our capital, such as a stock split or reverse stock split, which change or measure results in a change in the value of the options outstanding under the Stock Option Plan 2015, the board may make appropriate adjustments to the price or the amount of such outstanding options.

The board of directors may, at any time, amend, suspend or terminate the Stock Option Plan 2015 in whole or in part. However, if shareholder approval is required, including by application of Irish law, the board may not effect such modification or amendment without such approval.

401(k) Plan

We maintain a defined contribution employee retirement plan for our U.S.-based employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Internal Revenue Code, so that contributions to our 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan. Our 401(k) plan provides that each participant may contribute up to 100% of his or her pre-tax compensation, up to a statutory limit, which is $19,500 for 2021. Participants who are at least 50 years old can also make "catch-up" contributions, which in 2021 may be up to an additional $6,500 above the statutory limit. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan's trustee, subject to participants' ability to give investment directions by following certain procedures. We generally match 100.0% of the first 3.0% of the employee's voluntary contribution to the 401(k) plan and 50.0% of the next 2.0% contributed by the employee. Our 401(k) matching policy was temporarily suspended during a portion of 2020.

Risk Considerations in Our Compensation Program

Our compensation committee has reviewed and evaluated the philosophy and standards on which our compensation plans have been developed and implemented across our company. It is our belief that our compensation programs do not encourage inappropriate actions or risk taking by our executive officers. We do not believe that any risks arising from our employee compensation policies and practices are reasonably likely to have a material adverse effect on our company. In addition, we do not believe that the mix and design of the components of our executive compensation program encourage management to assume excessive risks.

DIRECTOR COMPENSATION

Summary Compensation Table

The following table sets forth a summary of the compensation earned by the non-employee members of the board of directors for the year ended December 31, 2021.

Name	Fees Earned or Paid in Cash ($)(1)	Option Awards ($)(2)	Share Awards ($)(2)	Total ($)
Daniel Burgess	89,509	24,185 (3)	18,900 (5)	132,594
Colin Broom	39,781	24,185 (3)	18,900 (5)	82,866
Lisa Dalton(6)	26,309	33,635 (4)	18,900 (5)	78,844
Charles Rowland, Jr.	60,396	24,185 (3)	18,900 (5)	103,481
Stephen Webster	68,917	24,185 (3)	18,900 (5)	112,002
Carrie Bourdow	49,364	24,185 (3)	18,900 (5)	92,449
Mark Corrigan(6)	27,370	33,635 (4)	18,900 (5)	79,905
George Talbot(7)	25,644	—	—	25,644

(1) Fees earned consist of gross director retainer fees which were subject to income tax withholdings in Ireland.

(2) The amounts reported in the “Option Awards” and “Share Awards” columns reflect the aggregate fair value of share-based compensation awarded during 2021 computed in accordance with the provisions of ASC Topic 718. See Note 10 to the consolidated financial statements regarding assumptions underlying the valuation of equity awards.

(3) Represents the grant of an option to purchase 35,000 of our ordinary shares vesting with respect to all of the shares on the last date of the month of the first anniversary of the grant date.

(4) Represents the grant of an option to purchase 35,000 of our ordinary shares vesting with respect to all of the shares on the last date of the month of the first anniversary of the grant date, as well as the grant of an option to purchase 10,500 shares vesting on a monthly pro-rata basis over three years of the vesting period.

(5) Represents the grant of 17,500 RSUs vesting with respect to all of the shares on the last date of the month of the first anniversary of the grant date.

(6) Lisa Dalton and Mark Corrigan joined as directors on June 2, 2021.

(7) George Talbot resigned as a director on July 28, 2021.

Director Compensation Arrangements

Effective as of October 31, 2018, our board of directors adopted a non-employee director compensation policy, which provided for the following:

- each new non-employee director receives an initial grant of an option to purchase 7,000 of our ordinary shares upon his or her initial election to the board of directors;
- each non-employee director receives an annual grant of an option to purchase 3,500 of our ordinary shares on the date of our annual general meeting of shareholders;
- each non-employee director receives an annual cash fee of $40,000;
- the chairman of our board of directors receives an additional annual cash fee of $30,000;

- each non-employee director who is a member of the audit committee receives an additional annual cash fee of $10,000 ($20,000 for the audit committee chair);

- each non-employee director who is a member of the compensation committee receives an additional annual cash fee of $7,500 ($15,000 for the compensation committee chair); and

- each non-employee director who is a member of the nominating and corporate governance committee receives an additional annual cash fee of $5,000 ($10,000 for the nominating and corporate governance committee chair).

On December 16, 2019, our board of directors approved an amendment to our non-employee director compensation policy. Effective as of December 16, 2019, the amendment increased the initial grant of an option to purchase our ordinary shares to new non-employee directors upon their initial election to the board of directors to 10,500 ordinary shares and increased the annual grant of an option to purchase our ordinary shares to 3,500 ordinary shares and 1,750 restricted stock units. Effective as of July 29, 2021, a subsequent amendment increased the initial grant of an option to purchase our ordinary shares to new non-employee directors upon their initial election to the board of directors to 105,000 ordinary shares and increased the annual grant of an option to purchase our ordinary shares to 35,00 ordinary shares and 17,500 restricted stock units.

The stock options to be granted to our non-employee directors under our non-employee director compensation policy have an exercise price equal to the fair market value of our ordinary shares on the date of grant and will expire ten years after the date of grant. The initial stock options granted to newly elected director vest, subject to such director's continued service on the board, over a three-year period on a monthly pro-rata basis at the end of each successive month following the date of the initial grant. The annual stock options granted to directors will vest, subject to such director's continued service on the board, fully on the last date of the month of the first anniversary of the grant date. The annual restricted stock units awarded to directors will vest, subject to such director's continued service on the board, fully on the last date of the month of the first anniversary of the grant date.

Under our non-employee director compensation policy, the annual cash fees are payable in arrears in four equal quarterly installments payable the week following the end of each quarter. Each non-employee director is also entitled to reimbursement for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors and any committee on which he or she serves or otherwise in direct service of the company.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of January 31, 2022 by:

- each of our directors and director nominees;

- each of our "named executive officers";

- all of our directors and executive officers as a group; and

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our ordinary shares.

The percentages in the columns entitled "Percentage of Shares Beneficially Owned" are based on a total of 56,715,965 ordinary shares outstanding as of January 31, 2022.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our ordinary shares. Our ordinary shares subject to options that are currently exercisable or exercisable within 60 days of January 31, 2022 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the ordinary shares beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Nabriva Therapeutics plc, 25-28 North Wall Quay, Dublin 1, Ireland.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Directors and Named Executive Officers:		
Daniel Burgess(1)	19,665	* %
Stephen Webster(2)	15,713	* %
Charles A. Rowland, Jr.(3)	20,793	* %
Carrie Bourdow(4)	13,903	* %
Colin Broom(5)	100,359	* %
Lisa Dalton(6)	2,336	* %
Mark Corrigan(6)	2,336	* %
Steven Gelone(7)	107,069	* %
Theodore Schroeder(8)	343,002	* %
Daniel Dolan(9)	25,000	* %
All current directors and executive officers as a group (12 individuals)(10)	657,176	1.16 %
5% Shareholders:		
Lincoln Park Capital Fund, LLC (11)	4,512,589	7.96 %

* Less than one percent.

(1) Consists of (i) 4,225 ordinary shares and (ii) 15,440 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(2) Consists of (i) 1,773 ordinary shares and (ii) 13,940 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(3) Consists of (i) 6,273 ordinary shares and (ii) 14,520 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(4) Consists of (i) 973 ordinary shares and (ii) 12,930 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(5) Consists of (i) 22,094 ordinary shares directly owned by Dr. Broom and (ii) 78,265 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(6) Consists of 2,336 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(7) Consists of (i) 29,097 ordinary shares, (ii) 76,887 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022 and (iii) 1,085 ordinary shares issuable upon the vesting of restricted stock units within 60 days of January 31, 2022.

(8) Consists of (i) 204,403 ordinary shares, (ii) 136,486 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022 and (iii) 2,113 ordinary shares issuable upon the vesting of restricted stock units within 60 days of January 31, 2022.

(9) Consists of (i) 275,838 ordinary shares and (ii) 378,140 ordinary shares issuable upon exercise of stock options within 60 days of January 31, 2022 and (iii) 3,198 ordinary shares issuable upon the vesting of restricted stock units within 60 days of January 31, 2022.

(10) Consists of 25,000 ordinary shares issuable upon exercise of stock options exercisable within 60 days of January 31, 2022.

(11) Based solely upon a Schedule 13G filed on November 19, 2021, which sets forth beneficial ownership as of November 18, 2021. Consists of 4,512,589 ordinary shares held by Lincoln Park Capital Fund, LLC, or LPC Fund. Lincoln Park Capital, LLC, or LPC, is the Managing Member of LPC Fund. Rockledge Capital Corporation, or RCC, and Alex Noah Investors, Inc., or Alex Noah are the Managing Members of LPC. Josh Scheinfeld is the president and sole shareholder of RCC, as well as a principal of LPC. Jonathan Cope is the president and sole shareholder of Alex Noah, as well as a principal of LPC. As a result of the foregoing, each of LPC, RCC LPC, RCC, Mr. Scheinfeld, Alex Noah, and Mr. Cope (i) may be deemed to beneficially own and (ii) have shared voting and shared dispositive power over the 4,512,589 ordinary shares directly held by LPC Fund. Each of LPC, RCC, Mr. Scheinfeld, Alex Noah and Mr. Cope disclaims beneficial ownership of the ordinary shares directly held by LPC Fund, except to the extent of its or his pecuniary interest therein, if any. LPC Funds' address is 440 N. Wells Street, Suite 410, Chicago, Illinois 60654.

Securities Authorized for Issuance under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2021. As of December 31, 2021, we had four equity compensation plans: the 2020 Share Incentive Plan, the 2017 Share Incentive Plan, the Stock Option Plan 2015 and the 2018 Employee Share Purchase Plan, each of which were approved by our shareholders. In addition, from time to time, the compensation committee grants inducement equity awards to individuals as an inducement material to the individual's entry into employment with us within the meaning of Nasdaq Listing Rules, including pursuant to our 2021 Inducement Share Incentive Plan, or the Inducement Plan, that was adopted by our board of directors without shareholder approval. We also previously made such inducement awards pursuant to our 2019 Inducement Share Incentive Plan.

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column(a)) (c)
Equity compensation plans approved by security holders	1,673,170 (1)	$ 27.07 (3)	290,218 (5)
Equity compensation plans not approved by security holders	465,045 (2)	7.91 (3)	128,120
Total	2,138,215	$ 20.46 (4)	418,338

(1) Includes ordinary shares underlying awards outstanding under our 2020 Share Incentive Plan, 2017 Share Incentive Plan and our Stock Option Plan 2015.

(2) Represents an option award and a performance-based restricted share unit award granted to Mr. Schroeder on July 25, 2018, as an inducement material to Mr. Schroeder's acceptance of employment with the company in accordance with Nasdaq Listing Rule 5635(c)(4) and other inducement awards made in accordance with Nasdaq

Listing Rule 5635(c)(4) under our 2019 Inducement Share Incentive Plan and 2021 Inducement Share Incentive Plan.

(3) Only share option awards were used in computing the weighted-average exercise price.

(4) Only share option awards were used in computing the weighted-average exercise price.

(5) Includes ordinary shares available for issuance under our 2020 Share Incentive Plan and 2018 Employee Share Purchase Plan.

2021 Inducement Share Incentive Plan

On December 9, 2020, our board of directors adopted without stockholder approval the 2021 Inducement Share Incentive Plan, or the 2021 Inducement Plan and, subject to the adjustment provisions of the 2021 Inducement Plan, reserved 200,000 oridnary shares for issuance purusant to equity awards granted under the 2021 Inducement Plan. In accordance with Nasdaq Listing Rule 5635(c)(4), awards under the 2021 Inducement Plan may only be made to individuals who were not previously employees or non-employee directors of the company (or following such individuals' bona fide period of non-employment with the company), as an inducement material to the individuals' entry into employment with the company. In September 2021, our board of directors adopted an amendment to the 2021 Inducement Plan that increased the amount of shares reserved for issuance under the plan from 200,000 shares to 500,000 shares.

Options and SARs granted will be exercisable at such times and subject to such terms and conditions as the board may specify in the applicable option agreement; provided, however, that no option or SAR will be granted with a term in excess of ten years. The board will also determine the terms and conditions of restricted shares and RSUs, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Board Determination of Independence

Applicable Nasdaq rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. To be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting, advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In April 2021, our board of directors undertook a review of the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board determined that each of our directors, with the exception of Colin Broom, Theodore Schroeder and Steven Gelone, is an "independent director" as defined under applicable Nasdaq rules, including, in the case of all the members of our audit committee, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all the members of our compensation committee, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determination, our board considered the relationships that each such director has with us, including each of the transactions described below in "—Board Policies—Related Person Transactions—Certain Relationships and Related Transactions", and all other facts and circumstances that our board deemed relevant in make such independence determination. Mr. Schroeder is not an independent director because he is our chief executive officer, and Dr. Broom is not an independent director because he was employed as our chief executive officer during the past three years. In addition, Dr. Gelone is not an independent director because he is our president and chief operating officer.

Board Policies

Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which the company is a participant, the amount involved exceeds the lesser of $120,000 and one percent of the average of the our total assets at year-end for the last two completed fiscal years and one of our executive officers, directors, director nominees or 5% shareholders, or their immediate family members, each of whom we refer to as a "related person", has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction", the related person must report the proposed related person transaction to our chief financial officer or general counsel. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its

discretion, may ratify the related person transaction. The policy also permits the chair of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of such transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of the entity, that is a participant in the transaction where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our memorandum and articles of association.

The policy provides that transactions involving compensation of our executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee's charter.

In addition, under our Code of Business Conduct and Ethics, our directors, executive officers and employees have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

Certain Relationships and Related Transactions

Since January 1, 2020, we have engaged in the following transactions with our executive officers, directors and holders of more than 5% of our voting securities, and affiliates of our executive officers, directors and 5% shareholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties:

Consulting Agreement with Sender Consulting LLC

On March 9, 2021, Sender Consulting LLC, a single-member limited liability company of which Gary Sender is the principal, entered into a two-year consulting agreement with us, effective March 15, 2021, to provide financially related advice and actively manage projects as requested. In addition to an hourly service fee, Mr. Sender is entitled to receive an award of 7,000 RSUs as of the effective date of the consulting agreement, which vests as to 50% of the shares underlying the RSUs each year over the term of the consulting agreement.

Consulting Agreement with Jennifer Schranz

On May 3, 2021, we entered into a two-year consulting agreement with Jennifer Schranz, our former chief medical officer. Pursuant to the consulting agreement, Dr. Schranz has agreed to provide expert scientific advisory services to us in connection with the advancement of our pipeline programs and product candidates in consideration for our agreement to forego the repayment of any and all amounts owed by Dr. Schranz to us pursuant her retention agreement following her resignation from the company on March 19, 2021. In addition, Dr. Schranz received an award of 7,000 RSUs as of the date of the consulting agreement, which vests as to 50% of the shares underlying the RSUs on each annual anniversary of the consulting agreement over two years.

June 2020 Financing

In June 2020, we entered into a securities purchase agreement with certain institutional investors pursuant to which we agreed to issue and sell in a registered direct offering an aggregate of 4,144,537 ordinary shares and accompanying warrants to purchase up to an aggregate of 4,144,537 ordinary shares. Each share in the offering was issued and sold together with an accompanying warrant at a combined price of $9.1686. Each warrant has an exercise price of $7.92 per share, was immediately exercisable following the date of issuance and expires on the two-year anniversary of the date of issuance. In connection with such offering, entities affiliated with FMR LLC, a beneficial owner of more than 5% of our voting securities, purchased an aggregate of 872,498 ordinary shares and accompanying warrants to purchase up to 872,498 ordinary shares at a purchase price of $9.1686 per ordinary share and accompanying warrant for an aggregate purchase price of $7,999,601.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The following table sets forth, for each of the years indicated, the aggregate fees billed or expected to be billed to us for services rendered by KPMG LLP, or KPMG.

	Year Ended December 31,	
(in thousands)	**2021**	**2020**
Audit Fees(1)	$ 813	$ 724
Tax Fees(2)	9	9
All Other Fees	—	—
Total	$ 822	$ 733

(1) This category includes fees related to services associated with our at-the-market facility and December 2020 public offering.

(2) This category includes fees related to services rendered on tax compliance, tax advice and tax planning.

Pre-Approval Policies and Procedures

Our audit committee has adopted policies and procedures relating to the approval of all audit and non-audit services that are to be performed by our independent registered public accounting firm. This policy generally provides that we will not engage our independent registered public accounting firm to render audit or non-audit services unless the service is specifically approved in advance by our audit committee or the engagement is entered into pursuant to a de minimis exception in accordance with applicable SEC rules.

All of the services provided to us by KPMG during the last two fiscal years were approved by the audit committee.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) (1) Financial Statements: See Index to Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K.

(2) No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our financial statements or notes thereto.

(3) The exhibits listed on the Exhibit Index set forth immediately following Item 16 are filed or furnished as part of this Annual Report. The Exhibit Index is incorporated herein by reference.

ITEM 16. FORM 10-K SUMMARY

None

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
2.1*	Agreement and Plan of Merger dated as of July 23, 2018, by and among Nabriva Therapeutics plc, Zuperbug Merger Sub I, Inc., Zuperbug Merger Sub II, Inc., Zavante Therapeutics, Inc. and Cam Gallagher, solely in his capacity as Stockholder Representative	8-K	001-37558	07/25/2018	2.1	
3.1	Amended and Restated Memorandum and Articles of Association of Nabriva Therapeutics plc	10-Q	001-37558	8/5/2021	3.1	
4.1	Description of the Registrant's Securities Registered under Section 12 of the Exchange Act	10-K	001-37558	03/11/2021	4.1	
4.2	Form of December 2019 Warrant	8-K	001-37558	12/20/2019	4.1	
4.3	Form of May 2020 Warrant	8-K	001-37558	06/01/2020	4.1	
4.4	Form of March 2021 Warrant	8-K	001-37558	03/01/2021	4.1	
4.5	Registration Rights Agreement dated September 24, 2021 between Nabriva Therapeutics plc and Lincoln Park Capital Fund, LLC	8-K	001-37558	09/27/2021	4.1	
10.1	Form of Indemnification Agreement	8-K	001-38132	06/26/2017	10.1	
10.2#	2017 Share Incentive Plan, as Amended	10-Q	001-37558	11/09/2017	10.2	
10.3#	Stock Option Plan 2007, as Amended	8-K	001-38132	06/26/2017	10.2	
10.4#	Stock Option Plan 2015, as Amended	8-K	001-38132	6/26/2017	10.3	
10.5	Lease Agreement, dated March 16, 2007, by and between Nabriva Therapeutics AG and CONTRA Liegenschaftsverwaltung GmbH	F-1	333-205073	06/18/15	10.4	
10.6#	Form of Restricted Share Unit Agreement under the 2017 Share Incentive Plan (Share Withholding)	10-K	001-37558	03/12/2019	10.10	
10.7#	Form of Restricted Share Unit Agreement under the 2017 Share Incentive Plan (Automatic Sale)	8-K	001-37558	02/02/2018	10.1	
10.8#	Form of Share Option Agreement under the 2017 Share Incentive Plan	8-K	001-37558	02/02/2018	10.2	
10.9**	Manufacturing Services Agreement, dated May 8, 2017, by and between Patheon UK Limited and Nabriva Therapeutics AG	10-K	03/16/2018	03/16/2018	10.16	

10.10**	Master Agreement for the Manufacture, Packaging and Supply of Products, dated August 7, 2017, by and between ALMAC Pharma Services Limited and Nabriva Therapeutics Ireland DAC	10-K	03/16/2018	03/16/2018	10.17
10.11**	Key Intermediate Supply Agreement, dated of August 28, 2017 by and among Nabriva Therapeutics Ireland DAC, and SEL Biochem Xinjiang Co., Ltd, and Fountain International Development Holding Limited	10-K	03/16/2018	03/16/2018	10.18
10.12**	License Agreement, dated March 26, 2018, by and among Nabriva Therapeutics Ireland DAC, Sinovant Sciences, Ltd., Nabriva Therapeutics GmbH and Roivant Sciences, Ltd.	10-Q	001-37558	05/08/2018	10.2
10.13	Transition, Separation and Release of Claims Agreement, by and between Nabriva Therapeutics US, Inc. and Colin Broom, dated as of July 23, 2018	8-K	001-37558	07/25/2018	10.1
10.14#	Amended and Restated Employment Agreement, by and between Nabriva Therapeutics US, Inc. and Theodore Schroeder, dated as of March 10, 2021	10-K	001-37558	03/11/2021	10.18
10.15	Consulting Agreement, by and between Nabriva Therapeutics US, Inc. and Colin Broom, dated as of July 24, 2018 (included as Attachment A to Exhibit 10.1)	8-K	001-37558	07/25/2018	10.1
10.16	Form of Inducement Option Award Agreement.	S-8	333-226330	07/25/2018	99.2
10.17	Form of Inducement Performance-Based Share Award Agreement.	S-8	333-226330	07/25/2018	99.3
10.18	Stock Purchase Agreement by and among SG Pharmaceuticals, Inc., the Sellers named on Annex A, and Julia Feliciano, as Sellers' Representative, dated as of May 5, 2015	10-Q	001-37558	11/06/2018	10.4
10.19**	License Agreement by and between ICPD Holdings, LLC and Evelyn J. Ellis-Grosse and Zavante Therapeutics, Inc., dated as of March 1, 2014	10-Q	001-37558	11/06/2018	10.5
10.20**	Manufacturing and Supply Agreement by and between Zavante Therapeutics, Inc. and Ercros, S.A., dated as of July 28, 2016	10-Q	001-37558	11/06/2018	10.7

10.21**	Amended and Restated Three-Way Agreement by and between Laboratorios ERN, S.A, Ercros, S.A., and Zavante Therapeutics, Inc., dated as of July 28, 2016	10-Q	001-37558	11/06/2018	10.8
10.22**	Amended and Restated Pharmaceutical Manufacturing and Exclusive Supply Agreement by and between Laboratorios ERN, S.A. and Zavante Therapeutics, Inc. dated as of July 28, 2016, as amended	10-Q	001-37558	11/06/2018	10.9
10.23**	Manufacturing and Supply Agreement by and between Zavante Therapeutics, Inc. and Fisiopharma, S.r.l., dated as of April 25, 2017	10-Q	001-37558	11/06/2018	10.10
10.24**	Commercial Packaging Agreement by and between Zavante Therapeutics, Inc. and AndersonBrecon Inc., d/b/a PCI of Illinois, dated as of December 26, 2017	10-Q	001-37558	11/06/2018	10.11
10.25**	Packaging and Supply Agreement by and between Sharp Corporation and Nabriva Therapeutics US, Inc., dated as of August 30, 2018	10-Q	001-37558	11/06/2018	10.12
10.26#	Third Amended and Restated Employment Agreement by and between Nabriva Therapeutics US, Inc. and Steven Gelone, dated as of March 10, 2021	10-K	001-37558	03/11/2021	10.31
10.27#	2018 Employee Share Purchase Plan	DEF 14A	001-37558	06/19/2018	99.1
10.28**	Loan and Security Agreement, dated as of December 20, 2018, by and among Nabriva Therapeutics plc, Nabriva Therapeutics Ireland DAC, certain other subsidiaries of Nabriva Therapeutics plc from time to time party thereto, any bank and other financial institution or entity from time to time party thereto and Hercules Capital, Inc, as administrativeagent and collateral agent.	10-K	001-37558	3/12/2019	10.35
10.29**	Agreement for the Commercial Supply of Products by and between Arran Chemical Company Limited and Nabriva Therapeutics Ireland DAC, dated as of November 12, 2018	10-K	001-37558	3/12/2019	10.37
10.30**	Active Pharmaceutical Ingredient Supply Agreement by and between Nabriva Therapeutics Ireland DAC and Hovione Limited, dated as of November 23, 2018.	10-K	001-37558	3/12/2019	10.38

10.31	2019 Inducement Share Incentive Plan	S-8	333-230216	3/12/2019	99.1
10.32	First Amendment to Loan and Security Agreement, dated as of September 26, 2019, by and among Nabriva Therapeutics Public Limited Company, Nabriva Therapeutics Ireland Designated Activity Company, Nabriva Therapeutics GmbH, Nabriva Therapeutics US, Inc., Zavante Therapeutics, Inc., and Hercules Capital, Inc.	10-Q	001-37558	11/12/2019	10.1
10.33	Second Amendment to Loan and Security Agreement, dated as of January 8, 2020, by and among Nabriva Therapeutics Public Limited Company, Nabriva Therapeutics Ireland Designated Activity Company, Nabriva Therapeutics GmbH, Nabriva Therapeutics US, Inc., Zavante Therapeutics, Inc., and Hercules Capital, Inc.	10-K	001-37558	03/12/2020	10.40
10.34	Third Amendment to Loan and Security Agreement, dated as of March 11, 2020, by and among Nabriva Therapeutics Public Limited Company, Nabriva Therapeutics Ireland Designated Activity Company, Nabriva Therapeutics GmbH, Nabriva Therapeutics US, Inc., Zavante Therapeutics, Inc., and Hercules Capital, Inc.	10-K	001-37558	03/12/2020	10.41
10.35#	Form of Share Option / Cash Settled Share Appreciation Right Agreement under the 2020 Share Incentive Plan	10-K	001-37558	03/12/2020	10.43
10.36#	2020 Share Incentive Plan, as amended	8-K	001-37558	07/29/2020	99.1
10.37	Sales Promotion and Distribution Agreement, dated as of July 15, 2020, by and among Nabriva Therapeutics Ireland Designated Activity Company, MSD International GmbH and Merck Sharp & Dohme Corp.	10-Q	001-37558	08/6/2020	10.2
10.38	Sublease Agreement, dated as of February 8, 2021, by and between Professional Payroll Solutions, LLC and Nabriva Therapeutics US, Inc.	8-K	001-37558	02/12/2021	10.1
10.39#	2021 Inducement Share Incentive Plan, as amended	S-1	333-260146	10/08/2021	10.43
10.40#	Employment Agreement, by and between Nabriva Therapeutics US, Inc. and Daniel Dolan, dated as of March 10, 2021	10-K	001-37558	03/11/2021	10.47

10.41***	First Amendment to License Agreement, dated October 29, 2021, by and among Nabriva Therapeutics Ireland DAC, Sinovant Sciences, Ltd., Nabriva Therapeutics GmbH and Roivant Sciences, Ltd.	10-K	001-37558	03/11/2021	10.48
10.42	Consulting Agreement, by and between Nabriva Therapeutics US, Inc. and Sender Consulting LLC, dated as of March 9, 2021.	10-K	001-37558	03/11/2021	10.49
10.43#	Employment Agreement dated August 24, 2021 by and between Nabriva Therapeutics US, Inc. and J. Christopher Naftzger	10-Q	001-37558	11/09/2021	10.1
10.44#	Employment Agreement dated August 23, 2021 by and between Nabriva Therapeutics US, Inc. and Christine Guico-Pabia	10-Q	001-37558	11/09/2021	10.2
10.45	Purchase Agreement dated September 24, 2021 between Nabriva Therapeutics plc and Lincoln Park Capital Fund, LLC	8-K	001-37558	9/24/2021	10.1
10.46	Fourth Amendment to Loan and Security Agreement, dated as of June 2, 2021, by and among Nabriva Therapeutics Public Limited Company, Nabriva Therapeutics Ireland Designated Activity Company, Nabriva Therapeutics GmbH, Nabriva Therapeutics US, Inc., Zavante Therapeutics, Inc., and Hercules Capital, Inc.	10-Q	001-37558	08/05/2021	10.1
10.47	Assignment, Assumption and Novation agreement, by and among Nabriva Therapeutics Ireland Designated Activity Company, Nabriva Therapeutics GmbH, Roivant Sciences Ltd., Roivant China Holdings Ltd., Sinovant Sciences HK Limited, Sinovant Sciences Co., Ltd., Sumitomo Dainippon Pharma Co., Ltd. and Sumitomo Pharmaceuticals (Suzhou) Co., Ltd.	10-Q	001-37558	08/05/2021	10.2
10.48	First Amendment to Sales Promotion and Distribution Agreement, dated as of July 15, 2020, by and among Nabriva Therapeutics Ireland Designated Activity Company, MSD International GmbH and Merck Sharp & Dohme Corp.	10-Q	001-37558	08/05/2021	10.3

10.49	Second Amendment to Sales Promotion and Distribution Agreement, dated as of April 12, 2021, by and among Nabriva Therapeutics Ireland Designated Activity Company, MSD International GmbH and Merck Sharp & Dohme Corp.	10-Q	001-37558	08/05/2021	10.4	
10.50	First Amendment to API Supply Agreement, dated August 4, 2021, by and between Nabriva Therapeutics Ireland Designated Activity Company and Hovione Limited	10-Q	001-37558	08/05/2021	10.5	
10.51	Consulting Agreement, dated May 3, 2021, by and between Nabriva Therapeutics US, Inc. and Jennifer Schranz	10-Q	001-37558	05/06/2021	10.1	
10.52	Open Market Sale Agreement℠, dated May 6, 2021, by and between Nabriva Therapeutics plc and Jefferies LLC	10-Q	001-37558	05/06/2021	10.2	
10.53	Form of Share Option Agreement under the 2020 Share Incentive Plan, as amended	10-Q	001-37558	05/06/2021	10.3	
10.54	Form of Restricted Share Unit Agreement under the 2020 Share Incentive Plan, as amended (Share Withholding)	10-Q	001-37558	05/06/2021	10.4	
10.55	Form of Restricted Share Unit Agreement under the 2020 Share Incentive Plan, as amended (Automatic Sale)	10-Q	0001-37558	05/06/2021	10.5	
10.56	Form of Share Option Agreement under the 2021 Inducement Share Incentive Plan	10-Q	001-37558	05/06/2021	10.6	
10.57#	Form of Contingent RSU Award Agreement under the 2020 Share Incentive Plan, as amended					X
10.58***	Side Agreement to Manufacturing Services Agreement, dated November 19, 2021, by and among Nabriva Therapeutics Ireland DAC and Patheon UK Ltd.					X
21.1	Subsidiaries of Nabriva Therapeutics plc					X
23.1	Consent of KPMG LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X

31.2	Certification of principal financial officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	Inline XBRL Instance Document	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Label Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Presentation Linkbase Document	X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)	X

Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

* Confidential treatment was granted for certain portions that are omitted from this exhibit. The omitted information has been filed separately with the U.S. Securities and Exchange Commission (the "SEC") pursuant to the registrant's application for confidential treatment. In addition, schedules have been omitted from this exhibit pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule will be furnished supplementally to the SEC upon request; provided, however, that the registrant may request confidential treatment for any document so furnished.

** Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

*** Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

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

NABRIVA THERAPEUTICS PLC

Date: March 29, 2022

By: /s/ THEODORE SCHROEDER
Theodore Schroeder
Chief Executive Officer

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

Signature	Title	Date
/s/ THEODORE SCHROEDER Theodore Schroeder	Director, Chief Executive Officer (Principal Executive Officer)	March 29, 2022
/s/ DANIEL DOLAN Daniel Dolan	Chief Financial Officer (Principal Financial and Accounting Officer)	March 29, 2022
/s/ DANIEL BURGESS Daniel Burgess	Chairman of the Board	March 29, 2022
/s/ COLIN BROOM Colin Broom	Director	March 29, 2022
/s/ CARRIE BOURDOW Carrie Bourdow	Director	March 29, 2022
/s/ LISA DALTON Lisa Dalton	Director	March 29, 2022
/s/ CHARLES A. ROWLAND JR. Charles A. Rowland Jr.	Director	March 29, 2022
/s/ STEPHEN WEBSTER Stephen Webster	Director	March 29, 2022
/s/ STEVEN GELONE Steven Gelone	Director, President and Chief Operating Officer	March 29, 2022
/s/ MARK CORRIGAN Mark Corrigan	Director	March 29, 2022

INDEX TO FINANCIAL STATEMENTS

Nabriva Therapeutics plc
Audited Consolidated Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors
Nabriva Therapeutics plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Nabriva Therapeutics plc and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, changes in stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2021, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has incurred recurring losses and negative cash flows from operations that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

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

Evaluation of the net realizable value of XENLETA inventory and potential loss on firm purchase commitments

As discussed in Notes 2 and 15 to the consolidated financial statements, the Company had XENLETA inventory with a carrying value of $10.7 million and had firm purchase commitments of $54.0 million for XENLETA active pharmaceutical ingredient (API) as of December 31, 2021. Inventory is stated at the lower of cost or net realizable value, and valued on a first-in, first-out basis. The Company reviews inventories for realization and records a provision for estimated excess, slow-moving and obsolete inventory, as well as inventory with a carrying value in excess of net realizable value and accrues potential losses on firm purchase commitments.

We identified the evaluation of the net realizable value of excess or obsolete XENLETA inventory and potential loss on firm purchase commitments of XENLETA API as a critical audit matter. A high degree of auditor judgment was required to evaluate XENLETA forecasted sales and the resulting inventory consumption prior to inventory expiration dates and in comparison to firm purchase commitments of XENLETA API.

The following are the primary procedures we performed to address this critical audit matter. To evaluate the XENLENTA forecasted sales, we inquired of operational personnel of the Company and compared them to analyst reports. To evaluate inventory consumption prior to inventory expiration dates and the potential loss on firm purchase commitments of XENLETA API, we compared the forecasted sales quantities to inventory expiration date by manufacturing lot and to firm purchase commitments of XENLETA API. We also performed a sensitivity analysis of XENLENTA forecasted sales used in the Company's analysis.

/s/ KPMG LLP

We have served as the Company's auditor since 2017.

Philadelphia, Pennsylvania
March 29, 2022

NABRIVA THERAPEUTICS plc

Consolidated Balance Sheets

(in thousands, except share data)	As of December 31, 2021	As of December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 47,659	$ 41,359
Restricted cash	175	231
Short-term investments	16	16
Accounts receivable, net and other receivables	12,751	3,909
Inventory	14,509	5,823
Prepaid expenses	5,155	5,880
Total current assets	80,265	57,218
Property, plant and equipment, net	233	768
Intangible assets, net	31	80
Other non-current assets	380	370
Total assets	**$ 80,909**	**$ 58,436**
Liabilities and stockholders´ equity		
Current liabilities:		
Current portion of long-term debt	$ 3,765	$ 2,041
Accounts payable	4,372	2,889
Accrued expense and other current liabilities	13,829	12,844
Deferred revenue	374	750
Total current liabilities	22,340	18,524
Non-current liabilities:		
Long-term debt	4,265	5,686
Other non-current liabilities	954	1,091
Total non-current liabilities	5,219	6,777
Total liabilities	**27,559**	**25,301**
Commitments and contingencies (Note 15)		
Stockholders' equity:		
Ordinary shares, nominal value $0.01, 100,000,000 ordinary shares authorized at December 31, 2021; 56,715,306 and 21,078,781 issued and outstanding at December 31, 2021 and December 31, 2020, respectively	567	211
Preferred shares, nominal value $0.01, 100,000,000 shares authorized at December 31, 2021; None issued and outstanding	—	—
Additional paid in capital	648,432	579,123
Accumulated other comprehensive income	27	27
Accumulated deficit	(595,676)	(546,226)
Total stockholders' equity	**53,350**	**33,135**
Total liabilities and stockholders' equity	**$ 80,909**	**$ 58,436**

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

NABRIVA THERAPEUTICS plc

Consolidated Statements of Operations

(in thousands, except share and per share data)	Year ended December 31, 2021	2020	2019
Revenues:			
Product revenue, net	$ 23,386	$ 108	$ 1,538
Collaboration revenue	3,830	2,756	6,210
Research premium and grant revenue	1,679	2,163	1,733
Total revenue	**28,895**	**5,027**	**9,481**
Operating expenses:			
Cost of revenues	(13,148)	(766)	(70)
Research and development expenses	(12,630)	(15,102)	(26,415)
Selling, general and administrative expenses	(51,645)	(55,285)	(62,485)
Total operating expenses	(77,423)	(71,153)	(88,970)
Loss from operations	**(48,528)**	**(66,126)**	**(79,489)**
Other income (expense):			
Other income (expense), net	469	1,187	215
Interest income (expense), net	(901)	(1,649)	(3,389)
Loss on extinguishment of debt	—	(2,757)	—
Loss before income taxes	**(48,960)**	**(69,345)**	**(82,663)**
Income tax expense	(490)	(139)	(101)
Net loss	**$ (49,450)**	**$ (69,484)**	**$ (82,764)**
Loss per share			
Basic and diluted ($ per share)	**$ (1.14)**	**$ (5.41)**	**$ (11.15)**
Weighted average number of shares:			
Basic and diluted	**43,349,461**	**12,845,089**	**7,419,948**

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

NABRIVA THERAPEUTICS plc

Consolidated Statements of Changes in Stockholders' Equity

(in thousands)	Ordinary shares Number of shares	Ordinary shares Amount	Additional paid in capital	Accumulated other comprehensive income	Accumulated deficit	Total stockholders' equity
January 1, 2019	**6,702**	**$ 67**	**$ 462,514**	**$ 27**	**$ (393,978)**	**$ 68,630**
Issuance of ordinary shares and warrants	2,584	26	48,056	—	—	48,082
Equity transaction costs	—	—	(2,794)	—	—	(2,794)
Stock-based compensation expense	—	—	9,748	—	—	9,748
Shares issued in connection with the vesting of restricted stock units	66	1	(1)	—	—	—
Shares issued in connection with the employee stock purchase plan	21	—	372		—	372
Shares issued in connection with the acquisition of Zavante Therapeutics, Inc.	82	1	(1)		—	—
Net loss	—	—	—	—	(82,764)	(82,764)
December 31, 2019	**9,455**	**95**	**517,894**	**27**	**(476,742)**	**41,274**
Issuance of ordinary shares	11,571	116	60,944	—	—	61,060
Shares issued in connection with the employee stock purchase plan	9	—	43	—	—	43
Shares issued in connection with the vesting of restricted stock units	44	—	—	—	—	—
Equity transaction costs	—	—	(4,977)	—	—	(4,977)
Stock-based compensation expense	—	—	5,219	—	—	5,219
Net loss	—	—	—	—	(69,484)	(69,484)
December 31, 2020	**21,079**	**211**	**579,123**	**27**	**(546,226)**	**33,135**
Issuance of ordinary shares	34,922	348	69,790	—	—	70,138
Shares issued in connection with the vesting of restricted stock units	82	2	—	—	—	2
Equity transaction costs	632	6	(3,772)	—	—	(3,766)
Stock-based compensation expense	—	—	3,291	—	—	3,291
Net loss	—	—	—	—	(49,450)	(49,450)
December 31, 2021	**56,715**	**$ 567**	**$ 648,432**	**$ 27**	**$ (595,676)**	**$ 53,350**

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

NABRIVA THERAPEUTICS plc

Consolidated Statements of Cash Flows

(in thousands)	Year Ended December 31, 2021	2020	2019
Cash flows from operating activities			
Net loss	$ (49,450)	$ (69,484)	$ (82,764)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash other income/expense, net	424	50	(40)
Non-cash interest income	—	—	22
Non-cash interest expense	404	636	519
Loss on extinguishment of debt	—	2,757	—
Depreciation and amortization expense	356	417	396
Decrease in right-of-use assets	281	403	374
Stock-based compensation	3,291	5,219	9,748
Other, net	(6)	62	48
Changes in operating assets and liabilities:			
(Increase)/decrease in other non-current assets	(10)	8	50
(Increase)/decrease in accounts receivable, net and other receivables and prepaid expenses	(8,117)	(5,887)	2,582
Increase in inventory	(8,686)	(5,141)	(682)
Increase/(decrease) in accounts payable	1,581	(1,813)	1,310
Increase/(decrease) in accrued expenses and other liabilities	946	714	(3,209)
Increase/(decrease) in deferred revenue	(376)	750	—
Decrease in other non-current liabilities	(189)	(2)	(172)
Decrease in income tax liabilities	(6)	(20)	(74)
Net cash used in operating activities	(59,557)	(71,331)	(71,892)
Cash flows from investing activities			
Purchases of plant and equipment and intangible assets	(25)	(113)	(61)
Other	(56)	(161)	392
Net cash (used in) provided by investing activities	(81)	(274)	331
Cash flows from financing activities			
Proceeds from exercise of warrants	—	665	—
Proceeds from issuance of ordinary shares and warrants	27,911	53,460	20,138
Proceeds from at-the-market facility	42,280	7,520	27,945
Proceeds from long-term debt, net of issuance costs	—	—	9,980
Proceeds from employee stock purchase plan	—	43	372
Repayments of long-term borrowings	—	(30,000)	—
Equity transaction costs	(3,825)	(4,764)	(2,360)
Net cash provided by financing activities	66,366	26,924	56,075
Effects of exchange rate changes on the balance of cash held in foreign currencies	(484)	(140)	(106)
Net increase/(decrease) in cash, cash equivalents and restricted cash	6,244	(44,821)	(15,592)
Cash, cash equivalents, and restricted cash at beginning of year	41,590	86,411	102,003
Cash, cash equivalents and restricted cash at end of year	$ 47,834	41,590	$ 86,411
Supplemental disclosure of cash flow information:			
Interest paid	497	1,396	2,560
Taxes paid	513	4	11
Equity transaction costs included in accounts payable and accrued expenses	712	765	552

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

NABRIVA THERAPEUTICS plc

Notes to the Consolidated Financial Statements

(in thousands, except per share data)

1. Organization and Business Activities

Nabriva Therapeutics plc, or Nabriva Ireland, together with its wholly owned and consolidated subsidiaries, Nabriva Therapeutics GmbH, or Nabriva Austria, Nabriva Therapeutics US, Inc., Zavante Therapeutics, Inc., or Zavante, and Nabriva Therapeutics Ireland DAC, collectively, Nabriva, or the Company, is a biopharmaceutical company engaged in the commercialization and development of novel anti-infective agents to treat serious infections. The Company's headquarters are located at 25-28 North Wall Quay, Dublin, Ireland.

In September 2021, Sumitomo Pharmaceuticals (Suzhou) and the Company announced the approval received by Sumitomo Pharmaceuticals (Suzhou) to market oral and intravenous formulations of XENLETA for the treatment of community-acquired pneumonia in adults in Taiwan.

In September 2020, the Centers for Medicare & Medicaid Services, or CMS, granted a new technology add-on payment, or NTAP, for XENLETA® (lefamulin) for injection, when administered in the hospital inpatient setting. Both the intravenous, or IV and oral formulations of XENLETA were granted Qualified Infectious Disease Product, or QIDP, and Fast Track designation by the U.S. Food and Drug Administration, or FDA. NTAP was also granted for CONTEPO™ (fosfomycin for injection, previously referred to as ZTI-01 and ZOLYD), making it the first QIDP antibiotic to be granted conditional NTAP approval prior to receiving FDA approval. CONTEPO was granted QIDP and Fast Track Designation by the FDA for the treatment of complicated urinary tract infections, or cUTIs, including acute pyelonephritis.

In July 2020, the Company announced that the European Commission, or EC, issued a legally binding decision for approval of the marketing authorization application for XENLETA™ (lefamulin) for the treatment of community-acquired pneumonia, or CAP, in adults following a review by the European Medicines Agency, or EMA. The EMA approval of XENLETA in CAP patients when it is considered inappropriate to use antibacterial agents that are commonly recommended for initial treatment or when these agents have failed paves the way for the launch of XENLETA across the European Economic Area, or EEA, and United Kingdom, or U.K. The EC approved XENLETA for all countries of the European Economic Area, or EEA, and United Kingdom, or U.K. Nabriva intends to work with a commercial partner to make XENLETA available to patients in the European Economic Area, or EEA, and United Kingdom, or U.K.

In July 2020, the Company announced that Sunovion Pharmaceuticals Canada Inc., or Sunovion, received approval from Health Canada to market oral and IV formulations of XENLETA® (lefamulin) for the treatment of CAP in adults, with the Notice of Compliance from Health Canada dated July 10, 2020. Nabriva entered into a license and commercialization agreement in March 2019 with Sunovion Pharmaceuticals Canada Inc. for XENLETA in Canada.

In July 2020, the Company announced that it entered into a Sales Promotion and Distribution Agreement, or the Distribution Agreement, with MSD International GmbH, or MSD, and Merck Sharp & Dohme Corp., or Supplier, each a subsidiary of Merck & Co. Under the Distribution Agreement, MSD appointed the Company as its sole and exclusive distributor of certain products containing tedizolid phosphate as the active ingredient previously marketed and sold by Supplier and MSD under the trademark SIVEXTRO® for injection, intravenous use and oral use in the United States and its territories. SIVEXTRO is an oxazolidinone-class antibacterial indicated in adults and patients 12 years of age and older for the treatment of acute bacterial skin and skin structure infections caused by certain susceptible Gram-positive microorganisms. Nabriva has also engaged Amplity Health, a leading pharmaceutical contract commercial organization, to provide community-based commercial and sales services for SIVEXTRO and XENLETA® in the United States.

In June 2020 the Company announced that WE Pharma Ltd., or WEP Clinical, a specialist pharmaceutical services company, had signed an exclusive agreement with the Company to supply XENLETA® (lefamulin) on a named

patient or expanded access basis in certain countries outside of the US, China and Canada. The Named Patient Program, or NPP, is designed to ensure that physicians, contingent on meeting the necessary eligibility criteria and receiving approval, can request IV or oral XENLETA on behalf of patients who live in certain countries where it is not yet available and have an unmet medical need.

In September 2019, the Company announced that the oral and IV formulations of XENLETA (lefamulin) are available in the United States for the treatment of community-acquired bacterial pneumonia, or CABP, through major specialty distributors. This followed the approval by the FDA of the Company's New Drug Application, or NDA, for XENLETA on August 19, 2019 for the treatment of adults with CABP. XENLETA is the first oral and IV treatment in the pleuromutilin class of antibiotics available for the systematic administration in humans.

Liquidity

Since its inception, the Company has incurred net losses and generated negative cash flows from its operations which has resulted in a significant accumulated deficit to date. The Company has financed its operations through the sale of equity securities, convertible and term debt financings and research and development support from governmental grants and proceeds from its licensing agreements. As of December 31, 2021, the Company had cash and cash equivalents, restricted cash and short-term investments of $47.9 million.

The Company follows the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 205-40, *Presentation of Financial Statements — Going Concern*, or ASC 205-40, which requires management to assess the Company's ability to continue as a going concern for one year after the date the consolidated financial statements are issued.

The Company expects to continue to invest in critical commercial and medical affairs activities, its commitments per the agreement with Merck & Co., Inc., as well as investing in its supply chain for the commercialization of SIVEXTRO, XENLETA and the potential launch of CONTEPO, if approved. The Company expects to seek additional funding in future periods to support these activities. While the Company has raised capital in the past, the ability to raise capital in future periods is not considered probable, as defined under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises in their assessment of the Company's ability to meet its obligations for the next twelve months.

In April 2020, the Company announced a restructuring of its hospital-based commercial sales force and transition to a community-based sales effort. The restructuring reduced costs to align with the capabilities of the Company's sales effort with its strategic re-focus on making sales of XENLETA to community health care professionals. The termination of the sales force was timed, in part, to coincide with operational changes that were implemented by the Company in response to the outbreak of the novel coronavirus, SARS-CoV-2, causing the disease referred to as "COVID-19". In response to the COVID-19 pandemic, the Company closed its administrative offices and shifted to a remote working business model. The Company implemented a hybrid-remote-working policy for all of its employees, all of which have had, and we believe will continue to have, an impact on our consolidated results of operations, financial position and cash flows. The commercial and medical organizations suspended in-person interactions with physicians and customers and were restricted to conducting educational and promotional activities virtually. The Company has secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace its hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. The Company expanded this effort to 60 sales representatives and may expand it further. The Company also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

The Company's expenses will increase if it suffers any regulatory delays or is required to conduct additional clinical trials to satisfy regulatory requirements. The Company has incurred and expects to continue to incur significant commercialization expenses related to its commitments per the agreement with Merck & Co., Inc., product sales, marketing, distribution and manufacturing for SIVEXTRO, XENLETA and CONTEPO, if approved. It is also uncertain when, if ever, the Company will generate sufficient revenues from product sales to achieve profitability.

As a result, based on the Company's available cash resources, the minimum cash required under the Loan and Security Agreement (the "Loan Agreement") with Hercules Capital, Inc., and in accordance with the requirements of ASC 205-40, management has concluded that substantial doubt exists about the Company's ability to continue as a going concern for one year from the date these consolidated financial statements are issued. A failure to raise the additional funding or to effectively implement cost reductions could harm the Company's business, results of operations and future prospects. If the Company is not able to secure adequate additional funding in future periods, the Company may make additional reductions in certain expenditures. This may include liquidating assets and suspending or curtailing planned programs. The Company may also have to delay, reduce the scope of, suspend or eliminate one or more research and development programs or its commercialization efforts.

In May 2021, the Company entered into an Open Market Sale AgreementSM, or the New Sale Agreement, with Jefferies, as agent, pursuant to which the Company may offer and sell ordinary shares, for aggregate gross sale proceeds of up to $50.0 million, from time to time through Jefferies, by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. As of December 31, 2021, the Company has issued and sold an aggregate of 18,232,689 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $30.5 million and net proceeds of $29.3 million, after deducting commissions to Jefferies and other offering expenses. From January 1, 2022 and through the date of this filing, the Company has issued and sold an aggregate of 1,338,282 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $595,000 and net proceeds of $580,000, after deducting commissions to Jefferies and other offering expenses. As of the date of this filing, the Company may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the New Sale Agreement.

In September 2021, the Company entered into a purchase agreement, or Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which, subject to the terms and conditions, provides that the Company has the right to sell to Lincoln Park and Lincoln Park is obligated to purchase up to $23.0 million of its ordinary shares. In addition, under the Purchase Agreement, the Company agreed to issue a commitment fee of 632,474 ordinary shares, or the Commitment Shares, as consideration for Lincoln Park entering into the Purchase Agreement and for the payment of $0.01 per Commitment Share. Under the Purchase Agreement, the Company may from time to time, at its discretion, direct Lincoln Park to purchase on any single business day, or a Regular Purchase, up to (i) 400,000 ordinary shares if the closing sale price of its ordinary shares is not below $0.25 per share on Nasdaq, (ii) 600,000 ordinary shares if the closing sale price of its ordinary shares is not below $2.00 per share on Nasdaq or (iii) 800,000 ordinary shares if the closing sale price of its ordinary shares is not below $3.00 per share on Nasdaq. In addition to Regular Purchases, the Company may also direct Lincoln Park to purchase other amounts as accelerated purchases or as additional accelerated purchases on the terms and subject to the conditions set forth in the Purchase Agreement. In any case, Lincoln Park's commitment in any single Regular Purchase may not exceed $2.5 million absent a mutual agreement to increase such amount. As of December 31, 2021, the Company has issued and sold an aggregate of 2,400,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $2.4 million. From January 1, 2022 and through the date of this filing, the Company has issued and sold an aggregate of 3,600,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $1.6 million. As of the date of this filing, the Company may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the Purchase Agreement.

Based on its current operating plans, the Company expects that its existing cash, cash equivalents, restricted cash and short-term investments as of the date of this filing will be sufficient to enable the Company to fund its operating expenses, debt service obligations and capital expenditure requirements well into the fourth quarter of 2022. The Company has based this estimate on assumptions that may prove to be wrong, and the Company could use its capital resources sooner than expected. This estimate assumes, among other things, that the Company does not obtain any additional funding through grants and clinical trial support, collaboration agreements or equity or debt financings. This estimate also assumes that the Company remains in compliance with the covenants and no event of default occurs under

the Loan Agreement. The consolidated financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the continuity of operations, the realization of assets and the satisfaction of liabilities and commitments in the normal course of business.

2. Summary of Significant Accounting Policies

Basis of Preparation

The consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America, or US GAAP, and US Securities and Exchange Commission, or SEC, regulations for annual reporting. The consolidated financial statements include the accounts of Nabriva Therapeutics plc and its wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Functional Currency Transactions and Balances

In preparing the consolidated financial statements, transactions in currencies other than the U.S. dollar are recognized at the exchange rates prevailing at the dates of the transactions. Foreign currency exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in the consolidated statements of operations.

Use of Estimates

The preparation of consolidated financial statements in conformity with US GAAP requires management to make estimates and assumptions that affect the amount of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers highly liquid investments with original maturities of three months or less to be cash equivalents.

Short-term Investments

The Company has designated its investments in securities as available-for-sale securities and measures these securities at their respective fair values. Investments that mature in one year or less are classified as short-term available-for-sale securities. Investments that are not considered available for use in current operations are classified as long-term available-for-sale securities. Changes in the fair value of available-for-sale investments are recognized in other comprehensive income (loss).

Inventory

Inventory is stated at the lower of cost or net realizable value. Inventory is valued on a first-in, first-out basis and consists primarily of material costs, third-party manufacturing costs, and related transportation costs along the Company's supply chain. The Company capitalizes inventory upon regulatory approval when, based on management’s judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are recorded as research and development expense. Costs of drug product to be consumed in any current or future clinical trials will continue to be recognized as research and development expense and costs of sample inventory is recorded as selling, general and administrative expense. The Company reviews inventories for realization on a quarterly basis and would record provisions for estimated excess, slow-moving and obsolete inventory, as well as inventory with a carrying value in excess of net realizable value when necessary. As of December 31, 2021, the Company had a $1.0 million non-cash reserve for excess and obsolete inventory due to timing of expiring inventory.

The components of our inventory at December 31, 2021 and 2020 are as follows:

(in thousands)	As of December 31, 2021	As of December 31, 2020
XENLETA raw materials	$ 1,528	$ 952
XENLETA work in process	9,142	4,608
XENLETA finished goods	18	263
Total XENLETA	10,688	5,823
SIVEXTRO finished goods	3,821	—
Total inventory	**$ 14,509**	**$ 5,823**

Property, Plant and Equipment

Property, plant and equipment are stated at cost less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets. The estimated useful lives of property, plant and equipment are as follows: 3-5 years for IT equipment, 5-10 years for laboratory equipment and 3-10 years for other plant and office equipment. The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each reporting date. When assets are sold or otherwise disposed of, the difference between the net proceeds, if any, and the net carrying amount of the asset is recognized as a gain or a loss in other operating income or expenses.

Intangible Assets and Other Long-lived Assets

Intangible assets, such as acquired computer software licenses, are capitalized on the basis of the costs incurred to acquire the software and bring it into use. These costs are amortized on a straight-line basis over their estimated useful lives (3-10 years).

Long-lived assets are assessed for potential impairment when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. An impairment loss would be recognized when undiscounted cash flows expected to be generated by an asset, is less than its carrying amount. The impairment loss would be measured as the amount by which the asset's carrying value exceeds its fair value and recognized in these financial statements.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business as one operating segment, which is the commercialization and development of novel anti-infective agents to treat serious and life-threatening infections.

Revenue Recognition—The Company recognizes revenue from sales of its commercial products in accordance with ASC 606, *Revenue from Contracts with Customers*, or ASC 606.

Net Product Revenue

In September 2019, the Company launched XENLETA and in April 2021 the Company began exclusive distribution of SIVEXTRO in the United States and certain of its territories. The Company sells its products principally to a limited number of specialty distributors and wholesalers. The Company recognizes revenue once it has transferred physical possession of the goods and the customer obtains legal title to the product. Payment terms between Nabriva and its customers are generally approximately 60 days from the invoice date. In addition to distribution agreements with customers, the Company enters into arrangements with health care providers and payers that provide for government mandated and/or privately negotiated rebates, chargebacks and discounts with respect to the purchase of its product.

The transaction price that the Company recognizes as revenue reflects the amount it expects to be entitled to in connection with the sale and transfer of control of product to its customers. At the time that the Company's customers take control of the product, which is when the Company's performance obligation under the sales contracts is complete, the Company records product revenues net of applicable reserves for various types of variable consideration. The types of variable consideration are as follows:

- Fees-for-service
- Product returns
- Chargebacks and rebates
- Government rebates
- Commercial payer and other rebates
- Group Purchasing Organizations, or GPO, administration fees
- Voluntary patient assistance programs

In determining the amounts of certain allowances and accruals, the Company must make significant judgments and estimates. For example, in determining these amounts, the Company estimates prescription demand from retail pharmacies, specialty pharmacies, hospital demand, buying patterns by hospitals, hospital systems and/or group purchasing organizations and the levels of inventory held by distributors and customers. The Company also analyzes third party end usage product consumption patterns to gauge demand for its products. Making these determinations involves analyzing third party industry data to determine whether trends in historical channel distribution patterns will predict future product sales. The Company receives data periodically from its customers on inventory levels and historical channel sales mix, and the Company considers this data when determining the amount of the allowances and accruals for variable consideration.

In assessing the amount of net revenue to record, the Company considers both the likelihood and the magnitude of the revenue reversal. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known. The specific considerations the Company uses in estimating these amounts related to variable consideration associated with the Company's products are as follows:

Fees-for-service – The Company offers discounts and pays certain distributor service fees which are recorded as a reduction of revenue in the period the related product revenue is recognized. The Company does not consider the fees separate from the distributors' purchase of the product. The Company records its fee-for-service accruals based on distributors' purchases and the applicable discount rate.

Product returns – Generally, the Company's customers have the right to return products during the 18-month period beginning six months prior to the labeled expiration date and ending twelve months after the labeled expiration date. Since the Company has a limited history of SIVEXTRO and XENLETA returns, the Company estimated returns based on industry data for comparable products in the market. As the Company distributes its product and establishes historical sales over a longer period of time (i.e., two to three years), the Company will be able to place more reliance on historical purchasing, demand and return patterns of its customers when evaluating its reserves for product returns. The Company's XENLETA product has a forty-eight month shelf life and SIVEXTRO has a thirty-six month shelf life.

The Company's customers also have the right to return excess inventory on new products that do not yield forecasted sales. To the extent the Company's customers determine that the quantities they purchased are in excess of

their customers demand, product returns could increase in excess of what the Company has currently reserved which would result in a reduction to net revenues in future periods.

At the end of each reporting period for any of its products, the Company may decide to constrain revenue for product returns based on information from various sources, including channel inventory levels and dating and sell-through data, the expiration dates of product currently being shipped, price changes of competitive products and introductions of generic products.

Chargebacks and rebates – Chargebacks are discounts that occur when certain contracted customers, which currently consist primarily of group purchasing organizations, public health service institutions, and Federal government entities purchasing via the Federal Supply Schedule, purchase directly from our wholesalers or specialty distributors. Contracted customers generally purchase the product at a discounted price. The Company provides a credit to its wholesaler or specialty distributor customers (i.e., chargeback), representing the difference between the customer's acquisition list price and the discounted price. The calculation of the accrual for chargebacks and rebates is based on estimates of claims and their associated cost that the Company expects to receive associated with product sales that have been recognized as revenue but remain in the distribution channel as inventory at the end of each reporting period.

Government rebates –The Company is subject to discount obligations primarily under state Medicaid and Medicare programs. The Company estimates its Medicaid and Medicare rebates based upon a range of possible outcomes that are probability-weighted for the estimated payer mix. These reserves are recorded in the same period the related product revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability that is included in accrued expenses on the consolidated balance sheet. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The calculation of the accrual for government rebates is based on estimates of claims and their associated cost that the Company expects to receive associated with product sales that have been recognized as revenue but remain in the distribution channel as inventory at the end of each reporting period.

Commercial payer and other rebates – The Company contracts with certain private payer organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of SIVEXTRO and XENLETA and contracted formulary status. The Company estimates these rebates and records reserves for such estimates in the same period the related revenue is recognized. Currently, the reserve for customer payer rebates considers future utilization based on third party studies of payer prescription data; the utilization is applied to product that remains in the distribution and retail pharmacy channel inventories at the end of each reporting period. The calculation of the accrual for commercial payer and other rebates is based on estimates of claims and their associated cost that the Company expects to receive associated with product sales that have been recognized as revenue but remain in the distribution channel as inventory at the end of each reporting period.

GPO administration fees – The Company contracts with GPOs and pays administration fees related to contacting and membership management services provided. In assessing if the consideration paid to the GPO should be recorded as a reduction in the transaction price, the Company determines whether the payment is for a distinct good or service or a combination of both. Since GPO fees are not specifically identifiable, the Company does not consider the fees separate from the purchase of the product. Additionally, the GPO services generally cannot be provided by a third party. Because of these factors, the consideration paid is considered a reduction of revenue.

Patient assistance – The Company offers certain voluntary patient assistance programs for prescriptions, such as co-pay assistance programs, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product sales that have been recognized as revenue but remains in the distribution channel as inventory at the end of each reporting period.

At the end of each reporting period, the Company will adjust its variable consideration estimates for product returns, chargebacks, and rebates when the Company believes actual experience may differ from current estimates.

Cost of Revenues

Cost of revenues for XENLETA primarily represents direct and indirect manufacturing costs, while cost of revenues for SIVEXTRO represent the actual purchase cost for the finished product from Merck. Prior to the FDA approval of XENLETA on August 19, 2019, the inventory costs for XENLETA were expensed as research and development expenses since the approval was outside of our control and therefore not considered probable. As such, the majority of the expenses incurred for our initial inventories of XENLETA has been previously expensed. For the years ended December 31, 2021 and 2020, cost of revenues include a $0.3 million and $0.7 million non-cash reserve adjustment for excess and obsolete inventory due to timing of expiry dating of inventory.

Research Premium and Grant Revenue

Grant revenue comprises (a) the research premium from the Austrian government, (b) grants received from the Austrian Research Promotion Agency (*Österreichische Forschungsförderungsgesellschaft, or FFG*), and (c) the benefit of government loans at below-market interest rates.

The research premium the Company receives from the Austrian government is calculated at a specified percent of specified research and development cost base. The Company recognizes the research premium as long as it has incurred research and development expenses. All grants are non-refundable as long as the conditions of the grant are met. Nabriva is and has been in full compliance with the conditions of the grants and all related regulations.

Research and Development Expenses

All research and development costs are expensed as incurred. Research and development costs included direct personnel and material costs, related overheads, depreciation of equipment used for research or development purposes; costs for clinical research; costs for the utilization of third parties' patents for research and development purposes and other taxes related to research facilities.

Share-based Payments

The Company measures the cost of employee services received in exchange for an award of equity instruments based on the grant-date fair value of the award in accordance with ASC 718, *Compensation—Stock Compensation*. The fair value of stock options is estimated using the Black-Scholes option pricing model. All grants under share-based payment programs are accounted for at fair value and that cost is recognized over the period during which an employee is required to provide service in exchange for the award—the requisite service period (vesting period). The Company accounts for forfeitures as incurred. Compensation expense for options granted to non-employees is determined as the fair value of the consideration received or the fair value of the equity instruments issued, whichever is more reliably measured.

Leases

The Company follows ASC Topic 842, *Leases*, which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors.

The Company determines if an arrangement is a lease at inception. Operating lease right-of-use, or ROU, assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the remaining lease term. ROU assets are included in property, plant and equipment, and operating lease liabilities are included in accrued expenses on the Company's consolidated balance sheet. The Company has elected not to recognize ROU assets or lease liabilities for short-term leases. Since none of the Company's lease agreements provide an implicit rate, the Company estimates an incremental borrowing rate over the lease term in determining the present value of lease payments. Operating lease expense is recognized on a straight-line basis over the lease term, subject to any changes in the lease or expectations regarding the terms. Variable lease costs such as operating costs and property taxes are expensed as incurred.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, the Company determines deferred tax assets and liabilities on the basis of the differences between the financial statement and tax bases of assets and liabilities by using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes deferred tax assets to the extent that it believes that these assets are more likely than not to be realized. In making such a determination, the Company considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If the Company determines that it would be able to realize its deferred tax assets in the future in excess of their net recorded amount, the Company would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

In recognizing the benefit of tax positions, the Company has taken or expects to take, the Company determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and for those tax positions that meet the more-likely-than-not recognition threshold, the Company recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority.

The Company’s policy is to record interest and penalties related to tax matters in income tax expense.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that the Company adopts as of the specified effective date. The Company has not adopted any new accounting pronouncements for the year ended December 31, 2021, nor are there any recently issued accounting pronouncements that are expected to have a material impact on the Company´s consolidated financial statements in future periods.

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3. Fair Value Measurement

US GAAP establishes a valuation hierarchy for disclosure of the inputs to valuation used to measure fair value. This hierarchy prioritizes the inputs into three broad levels as follows:

- Level 1: Quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2: Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly (as prices) or indirectly (as exchange rates).
- Level 3: Valuation techniques that include inputs for the asset or liability that are not based on observable market data (those are unobservable inputs) and significant to the overall fair value measurement.

The following table presents the financial instruments measured at fair value and classified by level according to the fair value measurement hierarchy:

(in thousands)	Level 1	Level 2	Level 3	Total
December 31, 2021				
Assets:				
Cash equivalent:				
Money market fund	$ 8,050	$ —	$ —	$ 8,050
Short-term investments:				
Term deposits	16	—	—	16
Total assets	**$ 8,066**	**$ —**	**$ —**	**$ 8,066**

(in thousands)	Level 1	Level 2	Level 3	Total
December 31, 2020				
Assets:				
Cash equivalent:				
Money market fund	$ 8,050	$ —	$ —	$ 8,050
Short-term investments:				
Term deposits	16	—	—	16
Total assets	**$ 8,066**	**$ —**	**$ —**	**$ 8,066**

There were no transfers between Level 1 and 2 in the years ended December 31, 2021 and 2020. There were no changes in valuation techniques during the years ended December 31, 2021 and 2020.

As of December 31, 2021 and 2020, the Company did not hold any financial instruments as liabilities that were held at fair value. The Company believes that the carrying value of its long-term debt approximates fair value based on current interest rates. Receivables and accounts payable are carried at their historical cost which approximates fair value due to their short-term nature.

4. Accounts Receivable, net and Other Receivables

Accounts receivable, net and other receivables include the following:

	As of December 31	
(in thousands)	2021	2020
Receivables from customers, net	$ 8,778	$ 56
Receivables from collaborative arrangments	2,193	2,426
Research premium	1,237	1,308
Other receivables	543	119
Total accounts receivable, net and other receivables	**$ 12,751**	**$ 3,909**

The following table summarizes balances and activity of product revenue allowances and reserves:

	As of December 31,	
	2021	2020
Receivables from customers, gross	$ 10,149	$ 75
Less: fee for service	(924)	—
Less: chargeback reserve	(249)	(17)
Less: cash discount	(198)	(2)
Receivables from customers, net	**$ 8,778**	**$ 56**

5. Property, Plant and Equipment

Property, plant and equipment was comprised of the following:

(in thousands)	As of December 31 2021	2020
IT equipment	$ 1,083	$ 1,077
Laboratory equipment	3,404	3,392
ROU asset	—	226
Other equipment	101	204
	4,588	**4,899**
Less: Accumulated depreciation	**(4,355)**	**(4,131)**
Property, plant and equipment, net	**$ 233**	**$ 768**

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities include the following:

(in thousands)	As of December 31, 2021	2020
Research and development related costs	$ 789	$ 1,055
Payroll and related costs	5,085	4,049
Accounting, tax and audit services	736	470
Manufacturing and inventory	592	4,779
Product returns	2,282	349
Government rebates	1,751	135
Other accrued gross to net	1,090	178
Other	1,504	1,829
Total other current liabilities	**$ 13,829**	**$ 12,844**

Product return activity during the years ended December 31, 2021 and 2020 was as follows:

	2021	2020
Balance at January 1	$ 349	$ 33
Provision recorded during the period	2,043	431
Credits issued during the period	(110)	(115)
Balance at December 31	**$ 2,282**	**$ 349**

7. Debt

In December 2018, the Company entered into the Loan Agreement by and among the Company, Nabriva Therapeutics Ireland DAC, and certain other subsidiaries of the Company and Hercules Capital, Inc., or Hercules, pursuant to which a term loan of up to an aggregate principal amount of $75.0 million was available to the Company. The Loan Agreement initially provided for an initial term loan advance of $25.0 million, which was funded in December 2018, and, at the Company's option and subject to the occurrence of certain funding conditions, several additional tranches of which $5.0 million became available upon the approval by the FDA of the NDA for XENLETA, which was drawn down. The other tranches are no longer available as their contingencies were not achieved. The Company may request a term loan advance of $5.0 million, or the Tranche Advance, through the Amortization Date discussed below subject to Hercules's sole discretion.

The term loan bears interest at an annual rate equal to the greater of 9.80% or 9.80% plus the prime rate of interest minus 5.50%. The Loan Agreement provided for interest-only payments through July 1, 2021 and repayment of the outstanding principal balance of the term loan thereafter in monthly installments through June 1, 2023, or the Maturity Date. In addition, the Company is required to pay a fee of 6.95% of the aggregate amount of advances under

the Loan Agreement at the Maturity Date, or the End of Term Fee. At the Company's option, the Company may elect to prepay any portion of the outstanding term loan that is greater than or equal to $5.0 million by paying such portion of the principal balance and all accrued and unpaid interest thereon plus a prepayment charge equal to the following percentage of the principal amount being prepaid, or the Prepayment Fee: (i) 3.0% if the term loan is prepaid during the first 12 months following the initial closing, (ii) 2.0% if the term loan is prepaid after 12 months following the initial closing but before 24 months following the initial closing and (iii) 1.0% if the term loan is prepaid any time thereafter but prior to the Maturity Date.

On March 11, 2020, the Company entered into an amendment, or the Third Amendment, to its Loan Agreement with Hercules. Pursuant to the Third Amendment, the Company repaid $30.0 million of the $35.0 million in aggregate principal amount of debt outstanding under the Loan Agreement, or the Prepayment. The Company determined to enter into the Third Amendment following the effectiveness of a performance covenant in February 2020 under which it became obligated to either (1) achieve 80% of its net product revenue sales target over a trailing six-month period, or (2) maintain an amount of cash and cash equivalents in accounts pledged to Hercules plus a specified amount of eligible accounts receivables equal to the greater of the amount outstanding under the Loan Agreement or $40.0 million, or the Liquidity Requirement. Under the Third Amendment, the Company and Hercules agreed to defer the end of term loan charge payment of $2.1 million that would have otherwise become payable on the date of the Prepayment and to reduce the Prepayment Fee with respect to the Prepayment from $600,000 to $300,000 and to defer its payment, in each case, until June 1, 2023 or such earlier date on which all loans under the Loan Agreement are repaid or become due and payable. The Third Amendment also reset the revenue performance covenant to 70% of targeted revenue based on a revised net product revenue forecast and lowered the minimum liquidity requirement to $3.0 million in cash and cash equivalents, in each case, following the Prepayment. The new minimum liquidity requirement will not apply if CONTEPO receives regulatory approval from the U.S. Food and Drug Administration and the Company achieves at least 70% of its revised net product revenue targets under the Loan Agreement.

On June 2, 2021, the Company entered into a further amendment, or the Fourth Amendment, to its Loan and Security Agreement with Hercules. Pursuant to the Fourth Amendment, the date on which the Company must commence repaying principal under the Loan Agreement was extended to April 1, 2022, or the Amortization Date, which date may be extended until July 1, 2022, subject to the receipt by the Company of a specified amount of additional net financing proceeds and the achievement of a specified product revenue milestone. Additionally, the time during which the Tranche Advance may be requested by the Company under the Loan Agreement, was extended until the Amortization Date. In addition, pursuant to the Fourth Amendment, the minimum liquidity requirement of $3.0 million in cash and cash equivalents will be waived at any time the Company has recognized $15.0 million of net product revenue during the applicable trailing three months.

The Company's obligations under the Loan Agreement are guaranteed by all current and future subsidiaries of the Company, and each of the Company and its subsidiaries has granted Hercules a security interest in all of their respective personal property, intellectual property and other assets owned or later acquired. The Loan Agreement also contains certain events of default, representations, warranties and covenants of the Company and its subsidiaries. For example, the Loan Agreement contains representations and covenants that, subject to exceptions, restrict the Company's and its subsidiaries' ability to do the following, among other things: declare dividends or redeem or repurchase equity interests; incur additional indebtedness and liens; make loans and investments; engage in mergers, acquisitions and asset sales; certain transactions with affiliates; undergo a change in control; and add or change business locations or settle in cash potential milestone payment obligations that may become payable by the Company in the future to former security holders of Zavante. The Company was in compliance with all of its Loan Agreement covenants at December 31, 2021.

The Loan Agreement also grants Hercules or its nominee an option to purchase up to an aggregate of $2.0 million of the Company's equity securities, or instruments exercisable for or convertible into equity securities, sold to investors in any private financing upon the same terms and conditions afforded to such other investors for as long as there are amounts outstanding under the Loan Agreement.

The Company incurred $1.3 million of costs in connection with the Loan Agreement which along with the initial fee of $0.7 million paid to Hercules were recorded as debt issuance cost and are being amortized as interest expense using the effective interest method over the term of the loan. In connection with the Third Amendment, the

Company recognized a non-cash $2.7 million loss on the extinguishment of debt during the three months ended March 31, 2020 which represented the excess of the reacquisition price of the $30.0 million debt repaid over the net carrying amount of the extinguished debt. The carrying value of the term loan payable at December 31, 2021 includes the present value of the End of Term Fee and the Prepayment Fee. The End of Term Fee on the remaining $5.0 million principal balance is being accrued as additional interest expense using the effective interest method over the term of the loan.

Long-term debt as December 31, 2021 and 2020 consisted of the following:

	As of December 31,	
(in thousands)	**2021**	**2020**
Term loan payable	$ 5,000	$ 5,000
End of term fee	2,331	2,048
Unamortized debt issuance costs	(145)	(206)
Carrying value of term loan	7,186	6,842
Other long-term debt	844	885
Less: Amounts due within one year	(3,765)	(2,041)
Total long-term debt	**$ 4,265**	**$ 5,686**

As of December 31, 2021, the maturities of our long-term debt were as follows:

(in thousands)	
2022	$ 3,765
2023	$ 4,811

8. Stockholders' Equity

In September 2021, the Company entered into a purchase agreement, or Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which, subject to the terms and conditions, provides that the Company has the right to sell to Lincoln Park and Lincoln Park is obligated to purchase up to $23.0 million of its ordinary shares. In addition, under the Purchase Agreement, the Company agreed to issue a commitment fee of 632,474 ordinary shares, or the Commitment Shares, as consideration for Lincoln Park entering into the Purchase Agreement and for the payment of $0.01 per Commitment Share. Under the Purchase Agreement, the Company may from time to time, at its discretion, direct Lincoln Park to purchase on any single business day, or a Regular Purchase, up to (i) 400,000 ordinary shares if the closing sale price of our ordinary shares is not below $0.25 per share on Nasdaq, (ii) 600,000 ordinary shares if the closing sale price of our ordinary shares is not below $2.00 per share on Nasdaq or (iii) 800,000 ordinary shares if the closing sale price of our ordinary shares is not below $3.00 per share on Nasdaq. In addition to Regular Purchases, the Company may also direct Lincoln Park to purchase other amounts as accelerated purchases or as additional accelerated purchases on the terms and subject to the conditions set forth in the Purchase Agreement. In any case, Lincoln Park's commitment in any single Regular Purchase may not exceed $2.5 million absent a mutual agreement to increase such amount. As of December 31, 2021, the Company has issued and sold an aggregate of 2,400,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $2.4 million. From January 1, 2022 and through the date of this filing, the Company has issued and sold an aggregate of 3,600,000 ordinary shares pursuant to the Purchase Agreement and received net proceeds of $1.6 million. As of the date of this filing, the Company may issue and sell ordinary shares for gross proceeds of up to $19.0 million under the Purchase Agreement.

In May 2021, the Company entered into an Open Market Sale Agreement[SM], or the New Sale Agreement, with Jefferies, as agent, pursuant to which the Company may offer and sell ordinary shares, nominal value $0.01 per share for aggregate gross sale proceeds of up to $50.0 million, from time to time through Jefferies, by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. Upon entry into the New Sale Agreement, the Company´s existing Jefferies ATM Agreement entered into in June 2019 was terminated. The Company did not incur any termination penalties as a result of the replacement of the Jefferies ATM Agreement. As of the effective date of the termination of the Jefferies ATM Agreement, the Company has sold an aggregate of 5,925,699 of our ordinary shares pursuant to the Jefferies ATM Agreement for aggregate gross

proceeds of $33.7 million and net proceeds to the Company of $31.9 million, after deducting commissions and offering expenses payable by the Compamy. The approximately $16.3 million of ordinary shares that had been available for sale pursuant to the Jefferies ATM Agreement remained unsold at the time of its replacement. The replacement of the Jefferies ATM Agreement terminated any future sales of ordinary shares through the Jefferies ATM Agreement. As of December 31, 2021, the Company has issued and sold an aggregate of 18,232,689 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $30.5 million and net proceeds of $29.3 million, after deducting commissions to Jefferies and other offering expenses. From January 1, 2022 and through the date of this filing, the Company has issued and sold an aggregate of 1,338,282 ordinary shares pursuant to the New Sale Agreement and received gross proceeds of $595,000 and net proceeds of $580,000, after deducting commissions to Jefferies and other offering expenses.

In March 2021, the Company entered into a securities purchase agreement with certain institutional investors pursuant to which the Company issued and sold in a registered direct offering (1) an aggregate of 9,761,010 ordinary shares, $0.01 nominal value per share, and accompanying warrants to purchase up to an aggregate of 4,880,505 ordinary shares and (2) pre-funded warrants to purchase up to an aggregate of 600,000 ordinary shares and accompanying ordinary share warrants to purchase up to an aggregate of 300,000 ordinary shares. Each share was issued and sold together with an accompanying ordinary share warrant at a combined price of $2.4525, and each pre-funded warrant was issued and sold together with an accompanying ordinary share warrant at a combined price of $2.4425. The proceeds to the Company from the offering were $25.4 million gross and $23.4 million net after deducting the placement agent's fees and estimated offering expenses. Each pre-funded warrant had an exercise price per ordinary share equal to $0.01 and each pre-funded warrant was exercised in full on the issuance date. Each ordinary share warrant has an exercise price per ordinary share equal to $2.39, is exercisable on the date of issuance and will expire on the five-year anniversary of the date of issuance. As of December 31, 2021, there were 5,180,505 warrants outstanding from the offering at an exercise price of $2.39 per share.

In December 2020, the Company completed a registered public offering in which it sold 6,000,000 ordinary shares at a public offering price of $2.50. The proceeds to the Company from the offering were $15.0 million gross and $13.3 million net, after deducting the placement agent's fees and other offering expenses.

In May 2020, the Company entered into a securities purchase agreement with certain institutional investors, including Fidelity Management & Research Company, LLC pursuant to which the Company issued and sold in a registered direct offering an aggregate of 4,144,537 ordinary shares and accompanying warrants to purchase up to an aggregate of 4,144,537 ordinary shares. Each share the Company issued and sold together with an accompanying warrant at a combined price of $9.1686. The proceeds to the Company from the offering were $38.0 million gross and $35.2 million net, after deducting the placement agent's fees and other offering expenses. Each warrant was immediately exercisable and will expire on the two-year anniversary of the issuance date. As of December 31, 2021, there were 4,059,532 warrants outstanding from the offering at an exercise price of $7.92 per share.

In December 2019, the Company sold to certain institutional investors in a registered direct offering an aggregate of 1,379,310 ordinary shares, and accompanying warrants to purchase up to an aggregate of 1,379,310 ordinary shares. Each share was issued and sold together with an accompanying warrant at a combined price of $14.50 per security. The proceeds to the Company from the offering were $20.0 million gross and $18.3 million net, after deducting the placement agent's fees and other offering expenses. As of December 31, 2021, there were 1,379,310 warrants outstanding from the offering, where each warrant has an exercise price of $19.00 per share and will expire on the date that is three years and six months after the initial issuance date.

9. Revenue

	Year Ended December 31,		
(in thousands)	**2021**	**2020**	**2019**
Product revenue, net	$ 23,386	$ 108	$ 1,538
Collaboration revenues	3,830	2,756	6,210
Research premium and grant revenue	1,679	2,163	1,733
Total revenue	**$ 28,895**	**$ 5,027**	**$ 9,481**

Collaboration revenues for the year ended December 31, 2021 include $2.6 million related to the restructured China Region License Agreement, a portion of which is recognized over the estimated period the manufacturing collaboration and regulatory support will be provided to Sumitomo Pharmaceuticals (Suzhou), as well as $1.2 million of the Company's share of revenues associated with the SIVEXTRO distribution agreement with Merck & Co., Inc. through April 11, 2021 (see Note 14). Collaboration revenues for the year ended December 31, 2020 includes a $0.5 million regulatory milestone payment from Sunovion, $1.8 million for the Company´s share of revenues associated with the SIVEXTRO distribution agreement with Merck & Co., Inc., as well as collaboration revenues associated with the restructuring of the China Region License Agreement. Collaboration revenues for the year ended December 31, 2019 includes a $1.0 million upfront payment under the Sunovion License Agreement received in April 2019, and a $5.0 million milestone payment under the China Region License Agreement.

The Company sells its products to pharmaceutical wholesalers/distributors (i.e., the Company's customers). The Company's wholesalers/distributors in turn sell the Company's products directly to clinics, hospitals, and private practices. Revenue from the Company's product sales is recognized as physical delivery of product occurs (when the Company's customer obtains control of the product), in return for agreed-upon consideration.

SIVEXTRO product revenues, net of gross-to-net accruals and adjustments for returns were $23.8 million since the Company began exclusive distribution of SIVEXTRO under its own National Drug Code, or NDC, on April 12, 2021. For the years ended December 31, 2021, 2020 and 2019 XENLETA product revenues, net of gross-to-net accruals and adjustments for returns, were $(0.4) million, $0.1 million and $1.5 million, respectively, including revenues from the Company´s Named Patient Program of $17,000 for the year ended December 31, 2021. The Company´s gross-to-net, or GTN, estimates are based upon information received from external sources (such as written or oral information obtained from the Company´s customers with respect to their period-end inventory levels and sales to end-users during the period), in combination with management's informed judgments. Due to the inherent uncertainty of these estimates, the actual amount incurred may be materially above or below the amount initially estimated when product revenues are originally recorded, then requiring prospective adjustments to the Company's reported product revenues, net.

For the year ended December 31, 2021, the Company recorded a $1.3 million returns reserve adjustment for shelf life expiration of certain XENLETA products. For the year ended December 31, 2020, the Company recorded a returns reserve adjustment of $0.4 million for slow-moving inventory, representing 50% of XENLETA IV inventory held at its Specialty Distributors, as well as an adjustment for returns from a single mail order specialty pharmacy.

10. Share Based Payments

Stock Plan Activity

On April 2, 2015, the Company's shareholders, management board and supervisory board adopted the Stock Option Plan 2015, or the SOP 2015, as amended. Each vested option grants the beneficiary the right to acquire one share in the Company. The vesting period for the options is four years following the grant date. On the last day of the last calendar month of the first year of the vesting period, 25% of the options attributable to each beneficiary are automatically vested. During the second, third and fourth years of the vesting period, the remaining 75% of the options vest on a monthly pro rata basis (i.e. 2.083% per month). Options granted under the SOP 2015 have a term of no more than ten years from the beneficiary's date of participation. With the approval of the 2017 Share Incentive Plan, there were no further shares available for issuance under the SOP 2015. However, all outstanding awards under SOP 2015 will remain in effect and continue to be governed by the terms of the SOP 2015.

On July 26, 2017, the Company's board of directors adopted the 2017 Share Incentive Plan, or the 2017 Plan, and the shareholders approved the 2017 Plan at the Company's Extraordinary General Meeting of Shareholders on September 15, 2017. The 2017 Plan permitted the award of share options (both incentive and nonstatutory options), share appreciation rights, or SARs, restricted shares, restricted share units, or RSUs, and other share-based awards to the Company's employees, officers, directors, consultants and advisers. The 2017 Plan is administered by the Company's board of directors. Under the 2017 Plan, the Company granted RSUs which vest over a period of four years with 25%

vesting upon the first anniversary of the grant date and on a monthly pro rata basis thereafter over the remaining three years. During 2018, the Company granted RSUs to certain employees where vesting of the RSUs was subject to FDA approval of an NDA for XENLETA. Fifty percent (50%) of each RSU award vested upon FDA approval, and the remaining fifty percent (50%) vested on the one-year anniversary of such approval. In connection with the FDA approval that was received in August 2019, the Company started recognizing compensation expense, as there was no compensation expense recognized on these awards prior to the FDA approval as it was determined that approval was not probable since it was outside of the Company's control. Also during 2018, the Company granted RSUs to certain employees that have vested in three six-month increments beginning in May 2019 and ending in May 2020. Lastly, the Company granted RSUs in 2018 to certain employees where vesting of the RSUs is subject to FDA approval of an NDA for CONTEPO. Fifty percent (50%) of each RSU award will vest upon FDA approval, and the remaining fifty percent (50%) will vest on the one-year anniversary of such approval. With the approval of the 2020 Share Incentive Plan, there were no further shares available for issuance under the 2017 Plan. However, all outstanding awards under 2017 Plan will remain in effect and continue to be governed by the terms of the 2017 Plan.

On March 12, 2019, the Company's board of directors adopted the 2019 Inducement Share Incentive Plan, or the 2019 Inducement Plan and, subject to the adjustment provisions of the 2019 Inducement Plan, reserved 200,000 ordinary shares for issuance pursuant to equity awards granted under the 2019 Inducement Plan. In accordance with Nasdaq Listing Rule 5635(c)(4), awards under the 2019 Inducement Plan may only be made to individuals who were not previously employees or non-employee directors of the Company (or following such individuals' bona fide period of non-employment with the Company), as an inducement material to the individuals' entry into employment with the Company. On April 28, 2020, the board of directors resolved not to make any further awards under the 2019 Inducement Plan.

In July 2018, the Company granted a non-statutory option to purchase 85,000 of its ordinary shares and 15,000 performance-based RSUs to the Company's newly appointed Chief Executive Officer, or the CEO. These equity awards were granted outside of the 2017 Plan and the 2019 Inducement Plan, were approved by the Company's compensation committee and board of directors and were made as an inducement material to the CEO entering into employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4). The exercise price per share for the share option is $35.30 per share, and the option award has a ten-year term and will vest over a four-year period, with 25% of the shares underlying the award vesting on the first anniversary of the grant date and the remaining 75% of the shares underlying the option award to vest monthly over the subsequent 36-month period. The performance-based RSUs are subject to vesting as follows: 50% will vest upon certification by the board of directors of the receipt of approval by the FDA of an NDA for each of lefamulin and CONTEPO for any indication, and 50% will vest on the first anniversary of such certification by the board of directors, provided, in each case, the CEO is performing services to the Company on the applicable vesting dates. If the FDA does not approve an NDA for both lefamulin and CONTEPO by January 31, 2020, the performance-based RSUs will terminate in full. Since CONTEPO was not approved by this date the award was forfeited. The Company also issues non-statutory options to new employees upon the commencement of their employment.

On March 4, 2020, the Company´s board of directors adopted the 2020 Share Incentive Plan, or the 2020 Plan, which was approved by the Company´s shareholders at the 2020 Annual General Meeting of Shareholders in July 2020, or 2020 AGM. As of the date of the 2020 AGM, the total number of ordinary shares reserved for issuance under the 2020 Plan was for the sum of 930,000 ordinary shares, plus the number of the Company´s ordinary shares that remained available for grant under the 2017 Plan as of immediately prior to the AGM and the number of ordinary shares subject to awards granted under the 2017 Plan and the Company´s Amended and Restated Stock Option Plan 2015, that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right. The 2020 Plan provides for the grant of incentive share options, non-statutory share options, share appreciation rights, restricted share awards, restricted share units, other share-based and cash-based awards and performance awards. Under the 2020 Plan the Company granted RSUs to certain employees that vest in three six-month increments beginning in January 2021 and ending in January 2022. The Company also granted RSUs to certain employees, where vesting of the RSUs was subject to individual performance goals. During the year ended December 31, 2021, the Company granted RSUs to certain employees that vest in annual increments beginning January 2022 and ending in January 2025. Additionally, the Company granted 7,000 RSUs to its former Chief Medical Officer

and to its former Chief Financial Officer, which vest as to 50% of the shares underlying the RSUs each year over the term of their respective consulting agreements.

At December 31, 2021, 271,080 ordinary shares were available for future issuance under the 2020 Plan.

On December 9, 2020, the Company´s board of directors adopted without stockholder approval the 2021 Inducement Share Incentive Plan, or the 2021 Inducement Plan and, subject to the adjustment provisions of the 2021 Inducement Plan, reserved 200,000 ordinary shares for issuance pursuant to equity awards granted under the 2021 Inducement Plan. In accordance with Nasdaq Listing Rule 5635(c)(4), awards under the 2021 Inducement Plan may only be made to individuals who were not previously employees or non-employee directors of the Company (or following such individuals' bona fide period of non-employment with the company), as an inducement material to the individuals' entry into employment with the Company. In September 2021, the Company's board of directors adopted an amendment to the 2021 Inducement Plan that increased the amount of shares reserved for issuance under the plan from 200,000 shares to 500,000 shares. Options and SARs granted will be exercisable at such times and subject to such terms and conditions as the board may specify in the applicable option agreement; provided, however, that no option or SAR will be granted with a term in excess of ten years. The board will also determine the terms and conditions of restricted shares and RSUs, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

Stock Options

The following table summarizes information regarding the Company´s stock option awards:

	Options	Weighted average exercise price in $ per share	Weighted Average Remaining Contractual Term (in years)	Aggregate intrinsic value (in thousands)
Outstanding as of January 1, 2019	**609,133**	**65.17**	—	—
Granted	316,645	20.11	—	—
Exercised	—	—	—	—
Cancelled and forfeited	(108,887)	64.33	—	—
Outstanding as of December 31, 2019	**816,891**	**47.82**	—	—
Granted	465,055	11.27	—	—
Exercised	—	—	—	—
Cancelled and forfeited	(229,108)	31.92	—	—
Outstanding as of December 31, 2020	**1,052,838**	**35.08**	—	—
Granted	637,880	1.23	—	—
Exercised	—	—	—	—
Cancelled and forfeited	(342,241)	16.90	—	—
Outstanding as of December 31, 2021	**1,348,477**	**20.46**	**8.0**	**$ —**
Vested and exercisable as of December 31, 2021	**533,564**	**45.05**	**6.7**	**$ —**

The Company has 1,348,477 option grants outstanding at December 31, 2021 with exercise prices ranging from $1.06 per share to $110.00 per share. As of December 31, 2021, there was $1.8 million of total unrecognized compensation expense related to unvested stock options, which will be recognized over the weighted-average remaining vesting period of 0.9 years.

The weighted average fair value of the stock options granted during years ended December 31, 2021, 2020 and 2019 was $0.82, $5.99 and $11.95 per share, respectively, based on a Black Scholes option pricing model using the following assumptions:

Input parameters	2021	2020	2019
Range of expected volatility	75.3% - 77.3%	63.7% - 74.4%	59.8% - 63.1%
Expected term of options (in years)	5.5 - 6.1	5.5 - 6.1	6.0 - 6.1
Range of risk-free interest rate	0.8% - 1.3%	0.8% - 1.5%	1.9% - 3.0%
Dividend yield	—	—	–

The expected price volatility is based on historical trading volatility for the publicly traded peer companies under consideration of the remaining life of the options. The risk-free interest rate is based on the average of five and seven-year market yield on U.S. treasury securities in effect at the time of grant.

Restricted Stock Units ("RSUs")

The following table summarizes information regarding the Company's restricted share unit awards:

	RSUs	Weighted average grant date fair value in $ per share
Outstanding as of January 1, 2019	**137,210**	**33.34**
Granted	47,900	19.00
Vested and issued	(65,758)	31.80
Forfeited	(14,183)	27.87
Outstanding as of December 31, 2019	**105,169**	**28.50**
Granted	244,832	10.99
Vested and issued	(52,640)	31.15
Forfeited	(57,977)	21.74
Outstanding as of December 31, 2020	**239,384**	**11.60**
Granted	769,132	2.02
Vested and issued	(90,330)	12.04
Forfeited	(128,448)	6.93
Outstanding as of December 31, 2021	**789,738**	**2.92**

As of December 31, 2021, there was unrecognized compensation costs of $1.1 million associated with RSUs which are expected to be recognized over the awards average remaining vesting period of 1.7 years. The intrinsic value of RSU's that vested during the years ended December 31, 2021, 2020 and 2019 was $0.2 million, $0.4 million and $1.5 million, respectively.

Stock-based Compensation

The following table presents stock-based compensation expense included in the Company's consolidated statements of operations:

	Year Ended December 31,		
(in thousands)	2021	2020	2019
Research and development expense	$ 565	$ 1,280	$ 2,138
Selling, general and administrative expense	2,726	3,939	7,610
Total stock-based compensation expense	**$ 3,291**	**$ 5,219**	**$ 9,748**

Employee Stock Purchase Plan

The Company's board of directors adopted, and in August 2018 Company's stockholders approved, the 2018 employee stock purchase plan, or the 2018 ESPP. The maximum aggregate number of shares of ordinary shares that may be purchased under the 2018 ESPP is 50,000 shares, or the ESPP Share Pool, subject to adjustment as provided for in the 2018 ESPP. The 2018 ESPP allowed eligible employees to purchase shares at a 15% discount to the lower of the closing share price at the beginning and end of the six-month offering periods commencing November 1 and ending April 30 and commencing May 1 and ending October 31 of each year. The Company suspended the 2018 ESPP in April 2020.

11. Post-employment Benefit Obligations

As required under Austrian labor law, the Company makes contributions to a state plan classified as defined contribution plan (Mitarbeitervorsorgekasse) for its employees in Austria. Monthly contributions to the plan are 1.53% of salary with respect to each employee and are recognized as expense in the period incurred. For the years ended December 31, 2021, 2020 and 2019, contributions costs were $56,000, $57,000 and $68,000, respectively.

For employees of Nabriva Therapeutics US, Inc., the Company makes contributions to a defined contribution plan as defined in subsection 401(k) of the Internal Revenue Code. The Company matches 100% of the first 3% of the employee's voluntary contribution to the plan and 50% of the next 2% contributed by the employee. Contributions are recognized as expense in the period incurred. In the years ended December 31, 2021, 2020 and 2019, contributions were $360,000, $396,000 and $710,000, respectively.

12. Income Tax Expense

Income (loss) before income taxes attributable to domestic and international operations, consists of the following:

	Year ended December 31		
(in thousands)	**2021**	**2020**	**2019**
Domestic	$ (40,540)	$ (71,344)	$ (78,761)
Foreign	(8,420)	1,999	(3,902)
Loss before income taxes	$ (48,960)	$ (69,345)	$ (82,663)

Income tax expense consists of the following:

	Year ended December 31		
(in thousands)	**2021**	**2020**	**2019**
Current tax			
Domestic	$ —	$ —	$ —
Foreign	(490)	(139)	(101)
Deferred tax			
Domestic	—	—	—
Foreign	—	—	—
Total income tax expense	$ (490)	$ (139)	$ (101)

The reconciliation to our effective tax rate from the Irish statutory income tax rate of 12.5% for the years ended December 31, 2021, 2020 and 2019 is as follows:

	Year ended December 31		
(% of pre-tax income)	**2021**	**2020**	**2019**
Statutory income tax rate	12.5 %	12.5 %	12.5 %
Non-deductible expenses	—	—	(0.1)
Income not subject to tax	0.4	0.2	0.3
Tax credits	—	0.6	0.4
Foreign operations	(7.3)	3.0	0.6
Tax audit assessments	—	—	(11.8)
Other	(1.7)	2.3	0.8
Valuation allowance	(4.9)	(18.8)	(2.8)
Effective income tax rate	(1.0)%	(0.2)%	(0.1)%

The following table summarizes the components of deferred income tax balances:

	As of December 31,	
(in thousands)	**2021**	**2020**
Deferred tax assets:		
Net operating loss carryforwards	$ 111,220	$ 108,095
Tax loss on liquidation of subsidiary	2,501	4,029
Equity compensation	4,067	4,449
Non-deductible reserves	905	447
Total deferred tax assets	118,693	117,020
Valuation allowance	(118,583)	(116,200)
Net deferred tax assets	110	820
Deferred tax liabilities:		
Financial liabilities	100	757
Property, plant and equipment	10	63
Total deferred tax liability	110	820
Deferred tax, net	$ —	$ —

The table below summarizes changes in the deferred tax valuation allowance:

	Year ended December 31,		
(in thousands)	**2021**	**2020**	**2019**
Balance at beginning of year	$ (116,200)	$ (103,185)	$ (100,832)
Tax benefit	(2,383)	(13,015)	(2,353)
Balance at end of year	**$ (118,583)**	**$ (116,200)**	**$ (103,185)**

The following table summarizes carryforwards of net operating losses as of December 31, 2021.

(in thousands)	**Amount**	**Expiration**
Ireland	$ 297,453	Indefinite
Austria	$ 239,510	Indefinite
United States	$ 10,403	Indefinite
United States	$ 35,516	2033

Due to uncertainty regarding the ability to realize the benefit of deferred tax assets primarily relating to net operating loss carryforwards and the fact that the Company is in a three year pretax cumulative loss position, a full valuation allowance has been established.

The Company's U.S. subsidiary has net operating loss and tax credit carryforwards that may be subject to annual limitations due to ownership changes as defined by Sections 382 and 383 of the Internal Revenue Code. These limitations could restrict the amount of tax attributes that can be utilized annually to offset future U.S. taxable income or tax liabilities.

On the basis of this evaluation, as of December 31, 2021, 2020 and 2019, the Company has recorded a valuation allowance of $118.6 million, $116.2 million and $103.2 million, respectively, to recognize only the portion of the deferred tax asset that is more likely than not to be realized. The amount of the deferred tax asset considered realizable, however, could be adjusted if estimates of future taxable income during the carryforward period are reduced or increased or if objective negative evidence in the form of cumulative losses is no longer present and additional weight is given to subjective evidence such as our projections for growth.

At December 31, 2021, the Company had no uncertain tax positions and did not expect any material increase or decrease in income tax expense related to examinations or changes in uncertain tax positions. The Company's U.S. subsidiary, Nabriva Therapeutics US, Inc., resolved its examination for tax year 2018 with the Internal Revenue Service with a decrease in a research and development tax credit carryforward of $0.1 million.

The Company files income tax returns in Ireland. In addition, the Company's foreign subsidiaries file separate income tax returns in Austria and the United States and state jurisdictions in which they are located. Tax years 2017 and forward remain open for examination for Ireland tax purposes and 2016 and forward remain open for examination for Austrian tax purposes and years 2018 and forward remain open for examination for United States tax purposes.

The Company's policy is to record interest and penalties related to tax matters in income tax expense.

13. Earnings (Loss) per Share

Basic and Diluted Loss per Share

Basic and diluted loss per share is calculated by dividing the net loss attributable to shareholders by the weighted average number of shares outstanding during the year. Diluted net loss per share is the same as basic net loss per share during the periods presented as the effects of the Company's common stock equivalents are antidilutive and thus not included in the calculation.

	Year ended December 31,		
(in thousands, except per share data)	**2021**	**2020**	**2019**
Net loss for the period	$ (49,450)	$ (69,484)	$ (82,764)
Weighted average number of shares outstanding	43,349,461	12,845,089	7,419,948
Basic and diluted loss per share	**$ (1.14)**	**$ (5.41)**	**$ (11.15)**

The following ordinary share equivalents were excluded from the calculations of diluted loss per share as their effect would be anti-dilutive:

	Year ended December 31		
	2021	**2020**	**2019**
Stock option awards	1,348,477	1,052,838	816,891
Restricted share units	789,738	239,384	105,169
Warrants	10,619,347	5,438,842	1,379,310

14. Significant Arrangements and License Agreements

Sales Promotion and Distribution Agreement with Merck & Co.

On July 15, 2020, the Company entered into a Sales Promotion and Distribution Agreement, or the Distribution Agreement, with MSD International GmbH, or MSD, and Merck Sharp & Dohme Corp., or Supplier, each a subsidiary of Merck & Co., Inc. Under the Distribution Agreement and subject to the satisfaction of certain conditions, MSD appointed the Company as its sole and exclusive distributor of certain products containing tedizolid phosphate as the active ingredient previously marketed and sold by Supplier and MSD under the trademark SIVEXTRO® for injection, intravenous use and oral use, or the Products, in the United States and its territories, or the SIVEXTRO Territory. SIVEXTRO is an oxazolidinone-class antibacterial indicated in adults and pediatric patients 12 years of age and older for the treatment of acute bacterial skin and skin structure infections caused by certain susceptible Gram-positive microorganisms. On April 12, 2021, in accordance with the terms of the Distribution Agreement, the Company began exclusive distribution of SIVEXTRO under its own National Drug Code, or NDC, and the Company recognizes 100% of net product sales of SIVEXTRO in its results of operations.

Under the Distribution Agreement and subject to the fulfillment of certain conditions, including the Company having engaged sufficient sales representatives, restrictions relating to travel and physician office access in the SIVEXTRO Territory due to COVID-19 having continued to decrease in a sufficient portion of the SIVEXTRO Territory so as not to hinder the successful detailing of SIVEXTRO, the Company has been granted the right by MSD initially to promote the Products in the SIVEXTRO Territory and, upon satisfaction of additional conditions, including an increase in sales representatives, the right to exclusively distribute the Products in the SIVEXTRO Territory, including the sole right and responsibility to fill orders with respect to the Products in the SIVEXTRO Territory. The Company successfully satisfied those conditions, including the increase in the number of sales representatives, and began filling orders of SIVEXTRO with its own Nabriva NDC beginning April 12, 2021. Subject to applicable law, the Company is entitled to determine the final selling prices of the Products charged by the Company to its customers at its sole discretion, subject to an overall annual limit on price increases, and will be solely responsible for sales contracting and all market access activities, including bidding, hospital listing and reimbursement. The Company is responsible for all costs related to the promotion, sale and distribution of the Products by the Company, as well as all costs required to meet its staffing obligations under the Distribution Agreement. The Company is obligated to use commercially reasonable efforts to promote and distribute the Products and to maximize the sales of the Products throughout the SIVEXTRO Territory. The Company has agreed to employ a sales force or retain the services of a contract sales organization to fulfill its obligations under the Distribution Agreement. The Company has secured a virtual and in-person sales effort with community-based expertise with Amplity Health, which is a contract sales organization, to replace its hospital-based sale force and began a small and focused sales effort for SIVEXTRO and XENLETA in September 2020. The Company expanded this effort to 60 sales representatives and may expand it further. The Company also piloted a virtual promotion effort with incremental sales representatives in the third quarter of 2021.

Furthermore, a subsidiary of Merck will sell, and the Company has agreed to purchase, SIVEXTRO at specified prices in such quantities as the Company may specify. Although the Company is entitled, subject to appliable law, to determine the final selling prices of SIVEXTRO in its sole discretion, subject to an overall annual limit on price increases, the Company may not be able to sell SIVEXTRO at prices high enough to recoup its investment in a sales force and other commercialization activities.

China Region License Agreement

In March 2018, the Company entered into the China Region License Agreement, with Sinovant Sciences, Ltd., or Sinovant, an affiliate of Roivant Sciences, Ltd., to develop and commercialize lefamulin in the greater China region. As part of the China Region License Agreement, Nabriva Therapeutics Ireland DAC and Nabriva Therapeutics GmbH, the Company’s wholly owned subsidiaries, granted Sinovant an exclusive license to develop and commercialize, and a non-exclusive license to manufacture, certain products containing lefamulin, or the China Region Licensed Products, in the People’s Republic of China, Hong Kong, Macau, and Taiwan, together the Extended China Territory. In May 2021, the Company entered into an assignment, assumption and novation agreement, or the Assignment Agreement, pursuant to which the Company consented to the assignment by Sinovant, an affiliate of Roivant Sciences, Ltd., of the China

Region License Agreement to develop and commercialize lefamulin in the greater China region to Sumitomo Pharmaceuticals (Suzhou), a wholly-owned subsidiary of Sumitomo Dainippon Pharma Co., Ltd. ("Sumitomo"). Pursuant to the Assignment Agreement, the Company agreed to release Sinovant and its affiliates from their obligations under the China Region License Agreement and consented to Sumitomo Pharmaceuticals (Suzhou)'s assumption of such obligations. In addition, Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo, has agreed to guarantee all of the obligations of Sumitomo Pharmaceuticals (Suzhou) under the China Region License Agreement.

Under the China Region License Agreement, Sumitomo Pharmaceuticals (Suzhou) and the Company's subsidiaries have established a joint development committee, or the JDC, to review and oversee development and commercialization plans in the Extended China Territory. The China Region License Agreement includes milestone events consisting of a non-refundable $5.0 million upfront payment, an additional $91.5 million in milestone payments upon the achievement of certain regulatory and commercial milestone events related to lefamulin for CABP, plus an additional $4.0 million in milestone payments if any China Region Licensed Product receives a second or any subsequent regulatory approval in the People's Republic of China. The Company has received the $5.0 million upfront payment, a $1.5 million payment for the submission of a clinical trial application, or CTA, by Sinovant to the Chinese Food and Drug Administration, which was received in the first quarter of 2019 and a $5.0 million milestone payment in the third quarter of 2019 in connection with the FDA approval for lefamulin. The Company will also be eligible to receive low double-digit royalties on sales, if any, of China Region Licensed Products in the Extended China Territory. In December 2020, the Company announced the restructuring of its China Region License Agreement. The restructured agreement provided for additional manufacturing collaboration and regulatory support to be provided to the contract counterparty by the Company that is expected to help expedite the delivery of XENLETA to patients in greater China. The restructured agreement also accelerated $3.0 million of the $5.0 million milestone payment to the Company that was previously payable upon regulatory approval of XENLETA in China, including a non-refundable upfront payment of $1.0 million which was received in the fourth quarter of 2020 and a $1.0 million milestone achieved during the first quarter of 2021. During 2021, management determined that the remaining $1.0 million milestone payment was probable of achievement and therefore the Company is recognizing the $3.0 million of accelerated payments under the restructured agreement as collaboration revenue in the consolidated statements of operations over the estimated period the manufacturing collaboration and regulatory support will be provided to the contract counterparty, which was $2.4 million for the year ended December 31, 2021, based on the proportional performance of the underlying performance obligation. The remaining milestones of $86.0 million are tied to additional regulatory approvals and annual sales targets. The future regulatory and commercial milestone payments under the China Region License Agreement will be recorded during the period the milestones become probable of achievement.

Except for the manufacturing collaboration and regulatory support discussed above, Sumitomo Pharmaceuticals (Suzhou) will be solely responsible for all costs related to developing, obtaining regulatory approval of and commercializing China Region Licensed Products in the Extended China Territory and is obligated to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize China Region Licensed Products in the Extended China Territory. The Company is obligated to use commercially reasonable efforts to supply, pursuant to supply agreements to be negotiated by the parties, to Sumitomo Pharmaceuticals (Suzhou) a sufficient supply of lefamulin for Sumitomo Pharmaceuticals (Suzhou) to manufacture finished drug products for development and commercialization of the China Region Licensed Products in the Extended China Territory.

Unless earlier terminated, the China Region License Agreement will expire upon the expiration of the last royalty term for the last China Region Licensed Product in the Extended China Territory, which the Company expects will occur in 2033. Following the expiration of the last royalty term, the license granted to Sumitomo Pharmaceuticals (Suzhou) will become non-exclusive, fully-paid, royalty-free and irrevocable. The China Region License Agreement may be terminated in its entirety by Sumitomo Pharmaceuticals (Suzhou) upon 180 days' prior written notice at any time. Either party may, subject to specified cure periods, terminate the China Region License Agreement in the event of the other party's uncured material breach. Either party may also terminate the China Region License Agreement under specified circumstances relating to the other party's insolvency. The Company has the right to terminate the China Region License Agreement immediately if Sumitomo Pharmaceuticals (Suzhou) does not reach certain development milestones by certain specified dates (subject to specified cure periods). The China Region License Agreement contemplates that the Company will enter into ancillary agreements with Sumitomo Pharmaceuticals (Suzhou), including clinical and commercial supply agreements and a pharmacovigilance agreement.

Sunovion License Agreement

In March 2019, the Company entered into the Sunovion License Agreement with Sunovion. As part of the Sunovion License Agreement, Nabriva Therapeutics Ireland DAC, the Company's wholly owned subsidiary, granted Sunovion an exclusive license under certain patent rights, trademark rights and know-how to commercialize certain products containing XENLETA in the forms clinically developed by us or any of our affiliates, or the Sunovion Licensed Products, in Canada in all uses in humans in CABP and in any other indication for which the Sunovion Licensed Products have received regulatory approval in Canada. Under the Sunovion License Agreement, Sunovion and DAC established a joint development committee, or the Sunovion JDC, to review and oversee regulatory approval and commercialization plans in Canada. Sunovion will be solely responsible for all costs related to obtaining regulatory approval of and commercializing Sunovion Licensed Products in the Canada and is obligated to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize Licensed Product in the Canada.

On November 7, 2019, the Company, through Sunovion, submitted a New Drug Submission, or NDS. Health Canada determined there was a screening deficiency in December 2019 and a response from the Company/Sunovion was provided on December 18, 2019 and acknowledged by Health Canada on January 13, 2020. The NDS approval occurred on July 10, 2020.

The Company identified two performance obligations at inception: (1) the delivery of the exclusive license to Sunovion, which the Company has determined is a distinct license of functional intellectual property that Sunovion has obtained control of; and, (2) the participation in the Sunovion JDC. The $1.0 million non-refundable upfront payment was allocated entirely to the delivery of the license as the Sunovion JDC deliverable was deemed to be de minimis. With the NDS approval that occurred on July 10, 2020, the Company received a regulatory milestone payment of $0.5 million. Any future regulatory and commercial milestone payments under the Sunovion License Agreement will be recorded during the period the milestones become probable of achievement.

Named Patient Program Agreement with WE Pharma Ltd.

On June 30, 2020 the Company announced that WE Pharma Ltd., or WEP Clinical, a specialist pharmaceutical services company, had signed an exclusive agreement with the Company to supply XENLETA on a named patient or expanded access basis in certain countries outside of the US, China and Canada. The Named Patient Program, or NPP, is designed to ensure that physicians, contingent on meeting the necessary eligibility criteria and receiving approval, can request IV or oral XENLETA on behalf of patients who live in certain countries where it is not yet available and have an unmet medical need.

15. Commitments and Contingencies

Future minimum contractual obligations and commitments at December 31, 2021 are as follows:

		Year ending December 31,					
(in thousands)	**Total**	**2022**	**2023**	**2024**	**2025**	**2026**	**Thereafter**
Operating lease obligations	$ 785	702	83	—	—	—	$ —
XENLETA API purchase	53,985	4,691	4,691	4,691	6,652	6,652	26,608
Other contractual commitments	10,913	5,072	3,983	929	929	—	—
Total contractual commitments and contingencies	**$ 65,683**	**$ 10,465**	**$ 8,757**	**$ 5,620**	**$ 7,581**	**$ 6,652**	**$ 26,608**

The Company has contractual commitments related primarily to contracts entered into with contract manufacturing organizations and contract research organizations in connection with the commercial manufacturing of XENLETA, the purchase of SIVEXTRO finished product and other research and development activities. The estimated payments to the service providers included in the table above are based on the achievement of milestones included within the agreements. Also, some of these contracts are subject to early termination clauses exercisable at the discretion of the Company.

XENLETA API Supply

On August 4, 2021, our wholly-owned subsidiary, Nabriva Therapeutics Ireland DAC, entered into an amendment, or the First Amendment, to its API Supply Agreement, or the Hovione Supply Agreement, with Hovione Limited, or Hovione, which provides for the long-term commercial supply of the active pharmaceutical ingredients, or API, for XENLETA. Under the First Amendment, Hovione agreed to cancel our May 2021 purchase order for XENLETA API, which represented our minimum purchase requirement under the Hovione Supply Agreement. In addition, pursuant to the First Amendment, Hovione agreed to reduce our annual minimum purchase requirements for XENLETA API to no minimum purchase requirement in 2021, by 50% from 2022 to 2024 and by 25% in 2025, in consideration for cash payments from us totaling €3.2 million and the right to a low single-digit royalty on total net sales of XENLETA in the United States for a period commencing on August 4, 2021 and ending on November 22, 2030, or the Royalty Term, which royalty payments shall be no greater than an aggregate of €10.0 million. If the aggregate amount of royalties payments received by Hovione under the First Amendment is less than an aggregate of €4.0 million, we are obligated to pay Hovione the difference in a lump sum payment at the end of the Royalty Term. In addition, pursuant to the First Amendment, Hovione agreed to extend the duration of the Hovione Supply Agreement from November 22, 2025 to November 22, 2030 with annual minimum purchase requirements for 2026 to 2030 at the newly agreed annual minimum purchase amount for 2025. Pursuant to the First Amendment, upon the occurrence of certain events of insolvency for us, any unpaid minimum annual commitment amounts and royalty amounts under the agreement will become immediately due and payable.

Zavante Obligations

In connection with the acquisition of Zavante in July 2018, the Company is obligated to pay up to $97.5 million in contingent consideration to the former Zavante shareholders, of which $25.0 million would become payable upon the first approval of a NDA from the FDA for CONTEPO for any indication, or the Approval Milestone Payment, and an aggregate of up to $72.5 million would become payable upon the achievement of specified sales milestones, or the Net Sales Milestone Payments. The Company's shareholders have approved the issuance of the Company's ordinary shares in settlement of potential milestone payment obligations that may become payable in the future to former Zavante stockholders, including the Approval Milestone Payment which will be settled in Company ordinary shares. The Company also has the right to settle the Net Sales Milestone Payments in Company ordinary shares, except as otherwise provided in the Merger Agreement.

The Company is obligated to pay $3.0 million in cash upon marketing approval by the FDA with respect to any oral, intravenous or other form of fosfomycin, or the Zavante Products, and milestone payments of up to $26.0 million that may be settled in ordinary shares in the aggregate upon the occurrence of various specified levels of net sales with respect to the Zavante Products. In addition, Zavante is obligated to make annual royalty payments of a mid-single-digit percentage of net sales of Zavante Products, subject to adjustment based on net sales thresholds and with such percentage reduced to low single-digits if generic fosfomycin products account for half of the applicable market on a product-by-product and country-by-country basis. Zavante will also pay a mid-single-digit percentage of transaction revenue in connection with the consummation of the grant, sale, license or transfer of market exclusivity rights for a qualified infectious disease product (within the meaning of the 21st Century Cures Act) related to a Zavante Product.

Litigation

The Company has no contingent liabilities in respect of legal claims arising in the ordinary course of business.

16. Subsequent Events

Nasdaq Deficiency Notice

On January 4, 2022, the Company received written notice, or the Notice, from The Nasdaq Stock Market LLC, or Nasdaq, indicating that, based on the closing bid for the last 30 consecutive business days, the Company is not in

compliance with the $1.00 minimum bid price requirement for continued listing on The Nasdaq Global Select Market, as set forth in Listing Rule 5450(a)(1), or the Bid Price Rule. The Notice does not result in the immediate delisting of the Company's ordinary shares from The Nasdaq Global Select Market. In accordance with Listing Rule 5810(c)(3)(A), the Company has a period of 180 calendar days to regain compliance with the Bid Price Rule. As a result, the Company will have until July 5, 2022, or the Compliance Date, to regain compliance with the Bid Price Rule. To regain compliance, the closing bid price of the Company's ordinary shares must be at least $1.00 per share for a minimum of ten consecutive business days on or before the Compliance Date. If the Company does not regain compliance with the Bid Price Rule by the Compliance Date, the Company may be eligible for an additional 180 calendar day compliance period. To qualify, the Company would need to transfer the listing of its ordinary shares to the Nasdaq Capital Market, provided it meets the continued listing requirement for market value of publicly held shares and all other initial listing standards, with the exception of the Bid Price Rule. To effect such a transfer, the Company would also need to pay an application fee to Nasdaq and provide written notice to Nasdaq of its intention to cure the deficiency during the additional compliance period. If the Company does not qualify for the additional compliance period or fails to regain compliance during the additional 180-day period, then Nasdaq will notify the Company of its determination to delist the Company's ordinary shares, at which point the Company would have an opportunity to appeal the delisting determination to a Nasdaq hearing panel. In addition to continuing to monitor the closing bid price of its ordinary shares, the Company expects to consider available options to regain compliance with the Bid Price Rule. However, there can be no assurance that the Company will be able to regain compliance with the Bid Price Rule.

EGM Vote

On March 24, 2022 the Company held an extraordinary general meeting of shareholders, at which time its shareholders voted by a special resolution of over 75% of the votes cast at the meeting to grant the board of directors authority under Irish law to allot and issue ordinary shares (including rights to acquire ordinary shares) for cash without first offering those ordinary shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply through March 23, 2027.

CONTEPO NDA

Given the uncertainties of the timing of onsite inspection at its manufacturing partners in Europe, the Company requested to be able to resubmit the CONTEPO NDA through June 2023, which the FDA granted on March 21, 2022. This extension granted by the FDA provides the Company the flexibility to submit at any time up and through June 2023.

NABRIVA THERAPEUTICS PLC

RESTRICTED SHARE UNIT AGREEMENT
GRANTED UNDER 2020 SHARE INCENTIVE PLAN

This Restricted Share Unit Agreement (this "**Agreement**") is made between Nabriva Therapeutics plc, a public limited company organized under the laws of Ireland (the "**Company**"), and the Participant pursuant to the 2020 Share Incentive Plan (as amended from time to time, the "**Plan**").

NOTICE OF GRANT

I. Participant Information

Participant:	
Participant Address:	

II. Grant Information

Grant Date:	
Number of Restricted Share Units:	

III. Vesting Table

Vesting Date	Number of Restricted Share Units that Vest

This Agreement includes this Notice of Grant and the following Exhibits and Schedules, which are expressly incorporated by reference in their entirety herein:

Exhibit A – General Terms and Conditions
Exhibit B – Nabriva Therapeutics plc 2020 Share Incentive Plan
Schedule 1 – Vesting Schedule
Schedule 2 – Additional Terms and Conditions

IN WITNESS WHEREOF, the parties hereto have executed this Agreement.

NABRIVA THERAPEUTICS PLC

_____
Name:
Title:

PARTICIPANT

_____
Name:

Restricted Share Unit Agreement
2020 Share Incentive Plan

EXHIBIT A

GENERAL TERMS AND CONDITIONS

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Grant of Restricted Share Units. This Agreement evidences the grant by the Company, on the grant date (the "**Grant Date**") set forth in the Notice of Grant that forms part of this Agreement (the "**Notice of Grant**"), to the Participant, subject to the terms and conditions set forth in this Agreement and in the Company's 2020 Share Incentive Plan (as amended from time to time, the "**Plan**"), of an award with respect to the number of restricted share units (the "**RSUs**") set forth in the Notice of Grant. Each RSU granted hereunder represents the right to receive one ordinary share of the Company (an "**Ordinary Share**") upon vesting of the RSU, subject to the terms and conditions set forth herein; provided, however, that if the Company's shareholders do not approve an increase to the number of Ordinary Shares available for issuance under the Plan (the "**Share Pool Increase**") at the Company's 2022 Annual General Meeting of Shareholders (the "**2022 AGM**"), then each RSU represents the right to receive, upon vesting, cash in an amount equal to the fair market value of an Ordinary Share as of the vesting date, subject to the terms and conditions set forth herein. For the avoidance of doubt, in the event that the Share Pool Increase is not approved by Company shareholders at the 2022 AGM, no Ordinary Shares shall be issued upon vesting of this award of RSUs and if the Share Pool Increase is approved by Company shareholders at the 2022 AGM, then only Ordinary Shares and not cash shall be issued upon vesting of this award of RSUs.

1. Vesting.

(a) The RSUs shall vest in accordance with the Vesting Table set forth in the Notice of Grant.

(b) Upon the vesting of the RSUs, the Company will deliver to the Participant, for each RSU that becomes vested, one Ordinary Share, or, if the Company's shareholders do not approve the Share Pool Increase at the 2022 AGM, cash in an amount equal to the fair market value of an Ordinary Share on the date of vesting, subject to the payment of any taxes pursuant to Section 4. Each Ordinary Share, or, if applicable, the cash equivalent thereof, will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

2. Forfeiture of Unvested RSUs Upon Cessation of Service.

In the event that the Participant ceases to perform services to the Company for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs, any Ordinary Shares, or the cash equivalent thereof, as applicable, that may have been issuable with respect thereto. If the Participant provides services to a

subsidiary of the Company, any references in this Agreement to provision of services to the Company shall instead be deemed to refer to service with such subsidiary.

3. Tax Matters.

(a) Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to any or all income tax, social insurance, payroll tax, payment on account or other tax-related items related to participation in the Plan and legally applicable to the Participant ("**Tax-Related Items**") relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's Tax-Related Items that may arise in connection with the grant, vesting and/or settlement of the RSUs and to the extent the RSUs are settled in Ordinary Shares, the subsequent sale of any Ordinary Shares acquired pursuant to the settlement of the RSUs and the receipt of any dividends thereon. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code, as amended, is available with respect to the RSUs and that the Company is under no obligation to structure the terms of the grant or any aspect of the RSUs to reduce or eliminate the Participant's liability for Tax-Related Items or achieve any particular tax result. Further, if the Participant becomes subject to tax in more than one jurisdiction between the Grant Date and the date of any relevant taxable event, as applicable, the Participant acknowledges that the Company may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

(b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other Tax-Related Items of any kind (including Tax-Related Items of jurisdictions outside the United States, as applicable) required by law to be withheld with respect to the RSUs. To the extent the RSUs are to be settled with Ordinary Shares, the Participant may satisfy such Tax-Related Items by instructing the Company to withhold a number of Ordinary Shares having a fair market value (valued in the manner determined by (or in a manner approved by) the Board) on the applicable vesting date equal to the Tax-Related Items, based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income. If the Participant does not instruct the Company to withhold Ordinary Shares to satisfy any applicable Tax-Related Items, or if the RSUs are otherwise settleable in cash, then the Participant agrees that if under applicable law the Participant will owe Tax-Related Items at such time on any portion of the RSUs the Company shall be entitled to satisfy the obligations with regard to all Tax-Related Items by one or a combination of the following:

(1) immediate payment from the Participant of the amount to be withheld by the Company; or
(2) withholding from wages or other cash compensation paid to the Participant by the Company.

To the extent the RSUs shall be settled upon vesting with Ordinary Shares, the Company shall not deliver any Ordinary Shares to the Participant until it is satisfied that all required withholdings have been made and the Participant has complied with the above and applicable obligations in connection with Tax-Related Items.

4. Transfer Restrictions; Clawback.

(a) The Participant shall not sell, assign, transfer, pledge, hypothecate or otherwise dispose of or encumber, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Ordinary Shares or, if applicable, the cash equivalent thereof, to any transferee to whom the such RSUs have been transferred in violation of any of the provisions of this Agreement.

(b) In accepting this award of RSUs, the Participant agrees to be bound by any clawback policy that the Company has adopted or may adopt in the future.

5. Rights as a Shareholder. The Participant shall have no rights as a shareholder of the Company with respect to any Ordinary Shares that may be issuable with respect to the RSUs unless and until Ordinary Shares are issued to the Participant following the vesting of the RSUs.

6. Provisions of the Plan. This Agreement is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is attached hereto as Exhibit B.

7. Miscellaneous.

(a) No Right to Continued Service/Compensation for Loss. The Participant acknowledges and agrees that, notwithstanding the fact that the vesting of the RSUs is contingent upon his or her continued service to the Company, this Agreement does not constitute an express or implied promise of continued service relationship with the Participant or confer upon the Participant any rights with respect to a continued service relationship with the Company. Under no circumstances will the Participant ceasing to be an employee of the Company be entitled to compensation for any loss of any right or benefit or prospective right or benefit under the Plan which the Participant might otherwise have enjoyed whether such compensation is claimed by way of damages for wrongful dismissal or other breach of contract or by way of compensation for loss of office or otherwise howsoever.

(b) Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Internal Revenue Code and the Treasury Regulations issued thereunder ("**Section 409A**"). The delivery of Ordinary Shares or the cash equivalent thereof, as applicable, on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.

(c) Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; and (iv) is fully aware of the legal and binding effect of this Agreement.

(d) Governing Law. This Agreement shall be governed by, except to the extent preempted by other applicable laws (1) with respect to the corporate law requirements applicable to the Company, the validity and authorization of the issuance of Ordinary Shares under the Plan and similar matters, the laws of Ireland (without reference to conflict of law principles thereof) and (2) with respect to all other matters relating to the Plan and Awards, the laws of the State of Delaware, excluding choice-of-law principles of the law of that state.

EXHIBIT B

NABRIVA THERAPEUTICS PLC 2020 SHARE INCENTIVE PLAN

Schedule 1

Vesting Schedule

[N/A for Time-Based Awards]

Schedule 2

Additional terms to Restricted Share Unit Award Agreement

Terms and Conditions

This Schedule (the "**Schedule**") includes additional terms and conditions that govern the RSUs granted to you under the Plan if you reside in one of the countries listed below. Certain capitalized terms used but not defined in this Schedule have the meanings set forth in the Plan and/or the Agreement.

Notifications

This Schedule also includes country-specific information of which you should be aware with respect to your participation in the Plan. The information is based on the securities, exchange control and other laws in effect in the respective countries as of April [__], 2021. Such laws are often complex and change frequently. As a result, the Company strongly recommends that you do not rely on the information noted herein as the only source of information relating to the consequences of your participation in the Plan because the information may be out of date at the time that you vest in the RSUs and, Ordinary Shares, or the cash equivalent thereof, are issued to you or any shares issued upon vesting are sold.

In addition, the information is general in nature and may not apply to your particular situation, and the Company is not in a position to assure you of any particular result. Accordingly, you are advised to seek appropriate professional advice as to how the relevant laws in your country may apply to your particular situation. Finally, please note that if you are a citizen or resident of a country other than the country in which you are currently working, or transfers employment after grant, the information contained in the Schedule may not be applicable.

Ireland

Notifications

Director Notification Obligation. If you are a director, shadow director or secretary of the Company or an Irish subsidiary or affiliate of the Company, and you acquire or dispose of an interest under this Agreement comprising more than 1% of the share capital in the Company, you must notify the entity in which you hold that office (whether the Company itself or an Irish subsidiary or affiliate of the Company) in writing within five business days of receiving or disposing of an interest in the Company, or within five business days of becoming aware of the event giving rise to the notification requirement or within five days of becoming a director or secretary if such an interest exists at the time. This notification requirement also applies with respect to the interests of a spouse or children under the age of 18 (whose interests will be attributed to the director, shadow director or secretary).

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

SIDE AGREEMENT
to the
Manufacturing Services Agreement
effective as of May 08th, 2017

This **Side Agreement** (the "**Side Agreement**") to the above-mentioned Manufacturing Services Agreement, as assigned by Nabriva Therapeutics GmbH (formerly Nabriva Therapeutics AG) to Nabriva Therapeutics Ireland DAC (the "**MSA**"), is entered into by and between **Patheon UK Ltd**, a corporation existing under the laws of United Kingdom, with registered offices at Kingfisher Drive, Covingham, Swindon, SN3 5BZ, UK (**"Patheon"**) and **Nabriva Therapeutics Ireland DAC**, an Irish designated activity company, having its registered office at Alexandra House, Office 225/227, The Sweepstakes, Ballsbridge, Dublin 4, D04 C7H2, Ireland (**"Customer"** or **"Nabriva"**).
Each of Patheon and Customer is hereinafter referred as "Party" or together as "Parties". This Side Agreement is effective as of January 1st, 2021 (the "**Effective Date**").
Capitalized terms shall have the meaning set forth in the MSA unless otherwise defined herein.

WHEREAS, pursuant to Schedule B to the MSA, Customer agreed to order and purchase an annual binding minimum amount of Product following its approval in each relevant Territory so ensuring a certain minimum conversion revenue (i.e: €[**] in Year 1, and €[**] in Year 2 for the amount of € [**]) (the **"Initial Minimum Conversion Revenue"**) for Patheon, and that, if such Minimum Conversion Revenue is not met in a given Year, then Customer will pay such an additional sum at the end of that Year that ensures the Minimum Conversion Revenue is paid to Patheon;

WHEREAS, the Product was approved for the US market in August 2019, and in Europe in July 2020;

WHEREAS, in 2020, Nabriva did not order any volume of Product to Patheon and substantially reduced its demand to [**] batches only in 2021;

WHEREAS, in consideration of the above recitals, Nabriva owes Patheon the amount of (i) €[**] for Year 2020 and, (ii) *provided that* [**] batches of Product are ordered and paid by Nabriva in 2021, the amount of €[**] for Year 2021, equal to the amount of €[**] less the conversion cost of the [**] ordered batched (i.e. €[**]), for an aggregate amount of €[**] (**"Amount Due"**);

WHEREAS, Nabriva asked Patheon to discount the Amount Due of €[**] ("**Discount**"), to defer payment of the Amount Due less the Discount, and to revise its Product volume requirements until 2025;

WHEREAS, Patheon has been available to support Customer with the above matter, at the following terms and conditions;

NOW, THEREFORE, in consideration of the premises contained herein, and other valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. The above recitals form an integral and substantial part of this Side Agreement.

2. The Parties hereby agree to amend Section 8.1 of the MSA to extend the Initial Term of the MSA until 31st December 2025. All other provisions in Section 8.1 shall remain unchanged.

3. Patheon agreed to discount the Amount Due of €[**] ("**Discount**") and Nabriva agrees to reimburse Patheon for the Amount Due less the Discount, for an aggregate amount of €[**], according to the following milestones:

   (a) €[**] by 30th November 2021;
   (b) €[**] by 31st October 2022;
   (c) €[**] by 31st October 2023.

4. The Parties agree to revise the Price for the Manufacturing Services as follows:

(i) each batch of Product manufactured by Patheon in 2021 will be invoiced to Nabriva at the unit price (conversion cost plus components) of €[**];

(ii) each batch of Product manufactured by Patheon starting from the 1st January 2022 will be charged by Patheon to Nabriva at the Price per vial set forth in the Schedule B attached to this agreement as 'Annex 1' that entirely replaces the Schedule B of the MSA.

Section 4.2(a) of the MSA shall apply to the Product Price starting from January 1st, 2022.

5. Starting from Year 2021, the annual binding minimum amount of Product (**"Binding Volume"**) that Nabriva is obliged to order and purchase during the Initial Term of the MSA is the following:

Year	Binding Volume/Vials
2021	[**]
2022	[**]
2023	[**]
2024	[**]
2025	[**]

It is understood and agreed between the Parties that, should Nabriva (i) not pay in full and at the agreed dates the amounts set forth in Section 3 above, or (ii) not order or purchase the above Binding Volume each Year during the Initial Term, in addition to the provisions of Section 4.2.1 of the MSA and save any other remedy that Patheon may have under the MSA, Patheon shall be entitled to and Nabriva shall be obliged to immediately reimburse Patheon for the amounts (if still due by Nabriva) as follows:

(i) €[**] if the Binding Volume is not ordered and paid in full in Year 2021;

(ii) €[**] if the Binding Volume is not ordered and paid in full in Year 2022;

(iii) Any outstanding amount calculated as the difference between the Amount Due, and any other instalment paid by Nabriva in accordance with Section 3 above.

For the sake of clarity, the Parties acknowledge that at the execution date of this Side Agreement, Nabriva has already ordered a paid a batch of Product (#00009) as part of the its 2021 Binding Volume commitment, at the Price applicable in 2020, for a total amount of €[**] instead of the Price agreed in Section 4 above (i.e. €[**]). Therefore, upon execution of this Side Agreement, Patheon will be entitled to charge Nabriva for the batch Price difference equal to €[**].

6. This Side Agreement constitutes a supplement to the MSA, forms an integral and substantial part thereof and, unless otherwise expressly provided herein, shall be subject to the same terms and conditions of the MSA and duly governed thereby. Nothing contained in this Side Agreement shall be deemed to constitute a novation of the terms of the MSA, nor affect any of the rights, powers or remedies of the Parties under the MSA, nor constitute a waiver of any provision thereof, except as specifically set forth in this Side Agreement.

7. This Side Agreement may be executed in one or more counterparts, each of which shall be deemed an original but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the duly authorized representatives of each Party have executed this Side Agreement on the date written above.

Nabriva Therapeutics Ireland DAC	**Patheon UK Ltd.**
Signature: /s/ Dan Dolan	Signature: /s/ Andrew Robinson
Name: Dan Dolan	Name: Andrew Robinson
Title: Director	Title: Director

ANNEX 1

SCHEDULE B

MINIMUM ORDER QUANTITY, ANNUAL VOLUME, AND PRICE

Long Term Forecast (binding minimum batches) (*)

Product	Annual Volume Forecast				
	2021	2022	2023	2024	2025
Lefamulin Vials	[**]	[**]	[**]	[**]	[**]

Manufacturing Prices
Bulk Prices:

Product	Minimum Order Quantity: Batch Size (Vials) x Campaign Length (Batches)	Price Per Bulk Unlabelled Vial		
		Component Price	Conversion Price	Bulk Price
Lefamulin Vials	[**]	**[**]**	**[**]**	[**]
Lefamulin Vials	[**]	**[**]**	**[**]**	[**]

[**]

Exhibit 21.1

SUBSIDIARIES OF NABRIVA THERAPEUTICS plc

Nabriva Therapeutics GmbH	**Austria**
Nabriva Therapeutics Ireland Designated Activity Company	**Ireland**
Zavante Therapeutics, Inc.	**Delaware**
Nabriva Therapeutics US, Inc.	**Delaware**

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (Nos. 333-208097, 333-222003, 333-226330, 333-228094, 333-230216, 333-240178, 333-254157 and 333-260927) on Form S-8, (Nos. 333-219567, 333-223739 and 333-248530) on Form S-3 and (No. 333-260146) on Form S-1 of our report dated March 29, 2022, with respect to the consolidated financial statements of Nabriva Therapeutics plc.

/s/ KPMG LLP

Philadelphia, Pennsylvania
March 29, 2022

EXHIBIT 31.1

CERTIFICATIONS

I, Theodore Schroeder, certify that:

1. I have reviewed this Annual Report on Form 10-K of Nabriva Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ Theodore Schroeder

Theodore Schroeder
Chief Executive Officer
(Principal Executive Officer)

Dated: March 29, 2022

EXHIBIT 31.2

CERTIFICATIONS

I, Daniel Dolan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Nabriva Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ Daniel Dolan

Daniel Dolan
Chief Financial Officer
(Principal Financial Officer)

Dated: March 29, 2022

EXHIBIT 32.1

CERTIFICATION
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Nabriva Therapeutics plc (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Theodore Schroeder, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Theodore Schroeder

Theodore Schroeder
Chief Executive Officer
(Principal Executive Officer)

Dated: March 29, 2022

EXHIBIT 32.2

CERTIFICATION
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Nabriva Therapeutics plc (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Daniel Dolan, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Daniel Dolan

Daniel Dolan
Chief Financial Officer
(Principal Financial Officer)

Dated: March 29, 2022